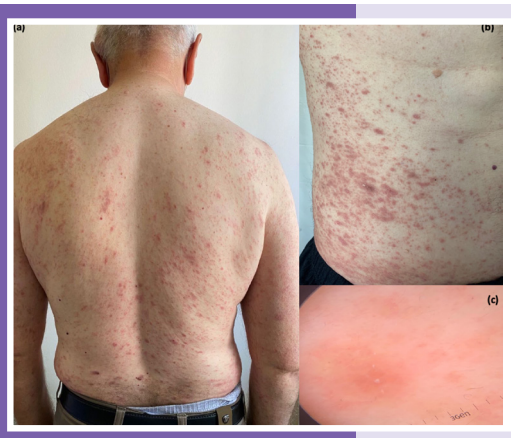
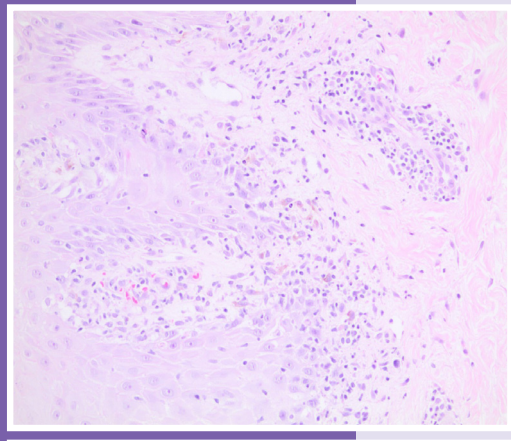
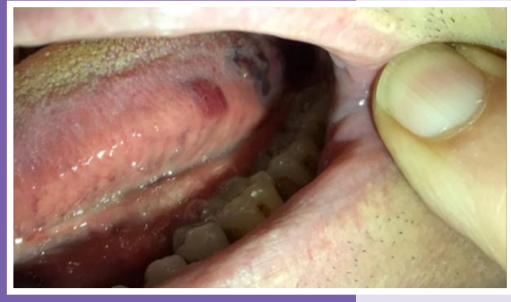
E-ISSN: 1307-394X

Journal of the Turkish Academy of Dermatology

Volume: 17 Issue: 4 December 2023







REVIEW

Current Approaches in Fungal Infections
Bilal Doğan, Nebahat Demet Akpolat, Zekayi Kutlubay; Istanbul, Turkey

ORIGINAL ARTICLES

Phototherapy Treatment and Dermatology Life Quality Index
Nasim Behkami, Zeynep Altan Ferhatoğlu; Istanbul, Turkey

Evaluation of Geriatric Patients with Psoriasis
Tuğba Kevser Uzunçakmak, Selim Gümüş, Ayşenur Özdil Eser, Burhan Engin; Istanbul, Turkey

QuantiFERONs of Patients Receiving Biological Therapy
Burhan Engin, Turana Mammadova, Şermin Börekçi, Beril Kara Esen; Istanbul, Turkey

CASE REPORT

Angina Bullosa Hemorrhagica: A Case Report
Osmanege Atliya, Mahmut Esat Tanrıbilir, İrem Ayşe Karaköse, Esra Adışen; Ankara, Turkey

LETTER TO THE EDITOR

COVID-19 Vaccine Induced Lichenoid Reaction
Tuğcan Yüksek, Selda Pelin Kartal, Evrim Önder; Ankara, Turkey

www.jtad.org

galenos yayınevi

Journal of the Turkish Academy of Dermatology

EDITORIAL BOARD

galenos yayınevi

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1
34093 İstanbul, Turkey
Phone: +90 (530) 177 30 97
E-mail: info@galenos.com.tr/yayin@galenos.com.tr

Web: www.galenos.com.tr
Publisher Certificate Number: 14521
Online Publishing Date: December 2023
E-ISSN: 1307-394X
International scientific journal published quarterly.

Journal of the Turkish Academy of Dermatology

AIM AND SCOPE

Journal of the Turkish Academy of Dermatology is a refereed publication designed to provide reference and up-to-date information needs of the international dermatologic community. This journal was created in an effort to explore the educational potential of distributed hypermedia served via the World Wide Web. The official organ of the Society of Academy of Cosmetology and Dermatology in Turkey, "Journal of the Turkish Academy of Dermatology" is attempting to improve the way in which information is transferred and accessed. In addition, access to PubMed reference numbers is enabled. The journal is published quarterly in March, June, September and December.

The journal is indexed in **Turkey Citation Index, EBSCO, Gale** and **J-Gate.**

Authors who have a new concept for on-line presentation are invited to contact the Editors to initiate a dialog.

Processing and publication are free of charge with Journal of the Turkish Academy of Dermatology. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system which is available through the journal's web page.

Subscription / Permissions / Advertisement

Free full-text manuscripts are available online at jtad.org. Applications for copyright permissions and announcements should be made to Editorial office.

Copyright Statement

Material Disclaimer

The author(s) is (are) responsible for the articles published in the Journal of the Turkish Academy of Dermatology. The editor, editorial board and publisher do not accept any responsibility for the articles.

Open Access Policy

This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge.

Open Access Policy is based on the rules of the Budapest Open Access Initiative (BOAI) http://www.budapestopenaccessinitiative.org/. By "open access" to peer-reviewed research literature, we mean its free availability on the public internet, permitting any users to read, download, copy, distribute, print, search, or link to the full texts of these articles, crawl them for indexing, pass them as data to software, or use them for any other lawful purpose, without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. The only constraint on reproduction and distribution, and the only role for copyright in this domain, should be to give authors control over the integrity of their work and the right to be appropriately acknowledged and cited.

Publisher Corresponding Address

Galenos Yayınevi Tic. Ltd. Şti.

Address: Molla Gürani Mah. Kaçamak Sk. No: 21, 34093

Fındıkzade-İstanbul-Turkey

Phone: +90 (530) 177 30 97

E-mail: info@galenos.com.tr

OPEN ACCESS

Journal of the Turkish Academy of Dermatology

INSTRUCTIONS TO THE AUTHORS

Coverage of Journal of the Turkish Academy of Dermatology

The journal is created with a general concept to accommodate the coverage of topics of current concern where accepted articles regularly cover:

Continuing Medical Education: Substantial educational articles presenting core information for the continuing medical education of the practicing dermatologist.

Original Articles: Original in-depth epidemiological studies or clinical and investigative laboratory research articles.

Case Reports: Brief individual case reports of unusual interest.

Correspondence: Brief letters to the editor that comment on previous articles or that involve brief case presentations.

Editorial Policies

Journal of the Turkish Academy of Dermatology is a refereed journal. Original manuscripts will be considered for publication. Information that has been published or is being considered for publication elsewhere will not be accepted. Manuscripts that appear to meet the goals of the Journal will be reviewed by two independent reviewers before a decision is made on publication.

All submissions must be accompanied by a signed statement of scientific contributions and responsibilities of all authors and a statement declaring the absence of conflict of interests. Any institution, organization, pharmaceutical or medical company providing any financial or material support, in whole or in part, must be disclosed in a footnote (ICMJE Disclosure Form for Potential Conflict of Interest(s)).

Manuscript format must comply with the ICMJE-Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals (updated in December 2018- http://www.icmje.org/icmje-recommendations).

The presentation of Original Researches and Reviews must be designed in accordance with trial reporting guidelines: randomized study-CONSORT, observational study-STROBE, study on diagnostic accuracy-STARD, systematic reviews and meta-analysis PRISMA, animal experimental studies-ARRIVE, nonrandomized behavioural and public health intervention studies-TREND.

Experimental, clinical and drug studies requiring approval by an ethics committee must be submitted to the Journal of the Turkish Academy of Dermatology with an ethics committee approval report confirming that the study was conducted in accordance with international agreements and the Declaration of Helsinki (revised 2013) (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). The approval of the ethics committee and the presence of informed consent given by the patients should be indicated in the Materials and Methods section. In experimental animal studies, the authors should indicate that the procedures followed are in accordance with animal rights as per the Guide for the Care and Use of Laboratory Animals (http://oacu.od.nih.gov/regs/guide/guide.pdf) and they should obtain animal ethics committee approval.

Authors must provide disclosure/acknowledgment of financial or material support, if any was received, for the current study.

If the article includes any direct or indirect commercial links or if any institution has provided material support to the study, authors must state in the cover letter that they have no relationship with the commercial product, drug, pharmaceutical company, etc. concerned; or specify the type of relationship (consultant, other agreements), if any.

Style

Manuscripts should conform to acceptable language usage. Abbreviations must be limited primarily to those in general usage. Generic names must be used. If a trade name is included, it should follow the generic name in parentheses the first time mentioned. Thereafter, generic names only should be used. Weights and measurements should be expressed in metric units, and temperatures in degrees centigrade.

Items may link back to the primary manuscript path or link to additional supplemental content.

All manuscripts submitted to the journal are screened for plagiarism using the 'iThenticate' software.

Preparation of Manuscripts

By submitting your article for publication, you grant Journal of the Turkish Academy of Dermatology the copyright to reproduce that work and associated images in electronic format (on the Internet or as a CD-ROM version of the Internet site) or in paper format derived from the on-line work. Otherwise the author still retains copyright to the written material and any associated images.

Original articles may be submitted in English. Send your manuscript in digital format in simple text, Microsoft Word, or RTF to the Editors. The Journal uses the accepted standard scientific format:

GENERIC FORMAT

the title page

Title:

Authors:

Affiliations:

Keywords:

CONTACT

the body of the manuscript

Abstract:

I:Introduction

II:Methods

III:Results

IV:Conclusions

References

the appendices

FIGURE LEGENDS

TABLES

Journal of the Turkish Academy of Dermatology

INSTRUCTIONS TO THE AUTHORS

References: Reference citations within the article should be noted with square brackets following punctuation like this [2, 3, 4]. If necessary one may also place a citation in the middle of a sentence (The sentence may need to pinpoint the citation to a specific comment [5] and not link it to the subsequent remarks.) In the reference section, list the references by a simple number at the start of a line, followed by a period and space. Use the citation format of PubMed, including the PMID number:

References:

Mareledwane NG. A randomized, open-label, comparative study of oral doxycycline 100 mg vs. 5% topical benzoyl peroxide in the treatment of mild to moderate acne vulgaris. Int J Dermatol 2006; 45: 1438-1439. PMID: 17184250

Doger FK, Dikicioglu E, Ergin F, Unal E, Sendur N, Uslu M. Nature of cell kinetics in psoriatic epidermis. J Cutan Pathol 2007; 34: 257-263. PMID: 17302610

Book: - Monsel G, Delaunay P, Chosidow O. Arthropods. In: Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's Textbook of Dermatology, 9th ed. Singapore: Blackwell Science; 2016. p. 32-34.

Tables and figures may be included in the document, and like images will need to be transferred as separate files, one file per table or figure. Unless the tables are less than 420 px wide, they will be linked from the text rather than put in-line.

Images

The extensive use of images is encouraged. The standard size for images is 768*512 pixels. The journal may edits the images to make in-line representations that will be linked to the larger versions. Unless you have written permission from the patient, photographs should not be identifying. If facial images are to be used, please mask the eyes or in some way de-identify the image. Clinical photographs should be saved in medium JPEG compression format. Line drawings or tables should be in Compuserve GIF format. Please limit the width of any in-line material to 434 pixels. Please avoid spaces when numbering your images and use the extension to indicate the compression algorithm (e.g., figure1.jpg, figure2.gif, etc.). It would be helpful for you to indicate the appropriate location of your figures within your text. You may use square braces for these remarks. Please place these remarks on the line preceding the appropriate paragraph. Two figures will appear side-by-side above the indicated paragraph.

HOW TO TRANSMIT YOUR WORK TO THE JOURNAL

The core text material should be submitted via the online article system from the link below:

https://www.journalagent.com/jtad/

Journal of the Turkish Academy of Dermatology

CONTENTS

REVIEW

83 Current Approaches in the Treatment of Superficial Fungal Infections
Bilal Doğan, Nebahat Demet Akpolat, Zekayi Kutlubay; Istanbul, Turkey

ORIGINAL ARTICLES

87 Evaluation of the effect of phototherapy treatment on dermatology quality of life index (DLQI)
Nasim Behkami, Zeynep Altan Ferhatoğlu; Istanbul, Turkey

92 Demographic and Clinical Characteristics of Geriatric Patients with Psoriasis: A Single-center, Cross-sectional, Retrospective Study in Turkish Population
Tuğba Kevser Uzunçakmak, Selim Gümüş, Ayşenur Özdil Eser, Burhan Engin; Istanbul, Turkey

97 QuantiFERON-TB Gold Test Results in Patients with Psoriasis Receiving Biologic Therapy
Burhan Engin, Turana Mammadova, Şermin Börekçi, Beril Kara Esen; Istanbul, Turkey

CASE REPORT

103 Angina Bullosa Hemorrhagica: A Case Report
Osmanege Atliya, Mahmut Esat Tanrıbilir, İrem Ayşe Karaköse, Esra Adışen; Ankara, Turkey

LETTER TO THE EDITOR

106 Lichenoid Drug Eruption Induced By COVID-19 mRNA Vaccine
Tuğcan Yüksek, Selda Pelin Kartal, Evrim Önder; Ankara, Turkey

INDEX

2023 Referee Index
2023 Author Index
2023 Subject Index

REVIEW

DOI: 10.4274/jtad.galenos.2023.78942
J Turk Acad Dermatol 2023;17(4):83-86

Current Approaches in the Treatment of Superficial Fungal Infections

Bilal Doğan[1], Nebahat Demet Akpolat[2], Zekayi Kutlubay[3]

[1]Maltepe University Faculty of Medicine Hospital, Department of Dermatology and Venereology, Istanbul, Turkey
[2]Dr Demet Akpolat Clinic, Istanbul, Turkey
[3]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey

ABSTRACT

Fungal infections are divided into two groups according to location: superficial and deep fungal infections. Superficial fungal infections (SFI) of the skin are mainly caused by dermatophytes from the genera "Microsporum, Trichophyton and Epidermophyton". Dermatophytoses are common skin diseases and affect 25% of the global population. The type of treatment firstly depends on the severity of the infection. The location of the disease also influences the type of treatment. Topical treatment is mostly enough for tinea corporis, pedis and inguinalis. Especially in immunocompromised patients and in the presence of tinea capitis, tinea unguium, oral treatment should be started. Besides, if the infestation is extensive and/or topical treatment is unsuccessful, oral treatment should again be considered. Oral terbinafine seems as the first step in the treatment of SFI because it has lower potential drug interactions, provides more mycological cure, and has fewer side effects compared to itraconazole treatment.

Keywords: Superficial fungal infections, Treatment, Antifungal

Introduction

Fungal infections are divided into two groups according to location: superficial and deep fungal infections. Superficial fungal infections (SFI) of the skin are mainly caused by dermatophytes [1]. Dermatophytes have evolved over time to live on the keratin protein, which is resistant to many other microorganisms. For this reason, they cause diseases in structures such as skin, hair and nails, where keratin is the major protein. Dermatophytoses are common skin diseases and affect 25% of the global population [2]. It is also a fact that increased mobility of people around the world has been changing the epidemiological trends [3]. Therefore, recognizing diseases in this group is especially important for preventive medicine.

Clinical Features

The naming is done by adding the word "tinea" placed at the beginning and the Latin word indicating "anatomical infection site". The main superficial dermatophyte infections of the skin are examined in detail below:

Tinea Capitis

This is an infection of scalp and hair invaded by dematophytes and especially seen in children [4]. The most common agents are Microsporum and Trichophyton species. Clinical appearance in tinea capitis varies depending on the agent, hair involvement type, and the degree of the host's inflammatory response according to his/her immune status. Clinically, scaly alopecic patches, alopecic patches where the hair broken off from the skin level (are observed

Address for Correspondence: Nebahat Demet Akpolat, Assoc. Prof., Dr Demet Akpolat Clinic, Istanbul, Turkey
Phone: +90 532 159 03 97 E-mail: drdemetakpolat@gmail.com ORCID ID: orcid.org/0000-0001-5080-0733
Received: 07.11.2023 Accepted: 09.11.2023

as black dots in the follicular opening), or seborrheic dermatitis-like lesions accompanied by dandruff on the scalp are observed. The severe form of tinea capitis, characterized by pustules and nodules, is called "kerion" [5]. If it is not treated early, it may cause cicatricial alopecia.

Tinea Barba

It is a dermatophyte infection observed in the beard and mustache area in men. Generally, zoophilic dermatophytes are the causative agent. It can be transmitted from animals through direct contact with the diseased area or indirect contact with materials that have come into contact with the diseased area [6]. The use of contaminated shaving materials may cause human-to-human transmission. It can have three different clinical presentations; tinea corporis-like lesions, folliculitis-like form and kerion-like form.

Tinea Corporis

Tinea corporis is the dermatophyte infection of integument other than feet, groin, hands and face. Tinea corporis observed in the hairless areas of the face is called "tinea facialis". It is transmitted directly by contact with the diseased lesion or indirectly through clothing that comes into contact with the diseased area. The lesion begins as an erythematous papule, and over time, its center fades and turns into a ring-shaped plaque. Squams, pustules or vesicles may be present on active edges [7].

Tinea Inguinalis (Tinea Cruris)

It is a dermatophyte infection of the inguinal region and also known as "jock itch" and is more common in adult men. Typical lesion is in the form of an erythematous ring in the inguinal region, with a skin-colored center and edge activation. It can spread to the pubic area, perineal and perianal areas. Itching is a common symptom [7]. Infection to this area often occurs from the foot area, so patients should also be evaluated for the infection of feet.

Tinea Pedis

Tinea pedis is a very common infection in society. The prevalence is higher in older population [8]. Wearing closed shoes for a long time, hyperhidrosis, working in a wet environment and common areas are predisposing factors for tinea pedis [9]. It has four clinical forms. The intertriginous subtype manifests itself with maceration, cracking and some scaling between the toes [10]. Hyperkeratotic tinea pedis is a chronic type and manifests itself with dense plantar scaling and erythema. It also involves the lateral surfaces of feet. There is usually no involvement on the dorsal surfaces. It is usually bilateral and can infect the hands [11]. The prevalence of vesiculobullous form of tinea pedis is relatively low and the similarity to dyshidrotic eczema makes them difficult to differentiate clinically. Acute ulcerative type is the rarest form of tinea pedis. The cause of the recurrences of tinea pedis may be the nail fungal infections which did not treated sufficiently. Therefore one should be careful to examine the nails also if the patient has tinea pedis.

Tinea Unguium

Tinea unguium is also known as onychomycosis and it is the name given to dermatophytic fungal infection of the nails. Its prevalence is close to 50% in people over the age of 70 [12]. Approximately 80% of patients with tinea unguium also have dermatophyte infection in other body parts (often tinea pedis) [10]. The risk of developing tinea unguium increases in people with any underlying nail disease. Distal lateral subungual onychomycosis is the most seen fungal infection of the nails and in the clinical appearance there are yellowish or brownish discolorations, subungual hyperkeratosis and onycholysis [13]. In white superficial onychomycosis subtype, there are some white spots appearances on the surface of the nails. The least common form is proximal subungual onychomycosis [13]. It is frequently seen in immunocompromised cases. It is observed as whitish or white-brown areas on the proximal part of the nail. Onychomycosis has many imitations, so it is required that one should reach a mycological diagnosis before starting antifungal treatment to avoid unnecessary treatments.

Tinea Incognito

Tinea incognito is named for a tinea infection that has been treated with a topical corticosteroid or some other immunosuppressive agents mistakenly [1]. The typical clinical appearance of superficial fungal infection disappear and diagnosis becomes difficult. Dermatophytic invasion of the dermis or subcutaneous tissue may cause deep-seated folliculitis (Majocchi granuloma) [7].

Treatment Modalities

The severity and location of the infection determine the type of the treatment [1]. Topical treatment is mostly enough for tinea corporis, pedis and inguinalis. Especially in immunocompromised patients and in the presence of tinea capitis, tinea unguium, oral treatment should be started. Besides, if the infestation is extensive and/or topical treatment is unsuccessful, oral treatment should again be considered.

Topical Treatment

The most effective and widely used topical antifungals are mainly allylamines, azoles and tolnaftate. Terbinafine 1% cream is recommended in the first step, because it is more effective. In resistant or unusable cases, other groups can be tried. It is recommended to use it one time a day for 2 weeks. But sometimes it should be used 2 times a day for until 4 weeks. Duration varies depending on the area of involvement. While up to 4 weeks may be required in areas with thick skin, such as hand or foot involvement,

2 weeks may be sufficient in other parts of the body with thinner skin [14,15].

Combined Topical Treatments

SFIs affect 20-25% of the population and can present in many different ways. Therefore, treatment approaches should be planned specifically for each patient. Especially in cases with an inflammatory component, the patient's complaints are more pronounced and may need to be taken under control more quickly.

Keratin degradation during SFI creates the initial immune response, causing the release of proinflammatory cytokines. This causes typical inflammation symptoms such as itching, erythema, swelling, and burning at the infection site. These symptoms are not only cause discomfort to the patient and impair compliance with treatment, but may also disrupt the integrity of the skin, causing the infection to spread and making the environment suitable for bacterial contamination.

Topical steroids, which are used in many skin diseases due to their anti-inflammatory, immunosuppressive, antimitotic and vasoconstrictive effects, constitute a good treatment option when used in combination with antifungals in SFIs with an inflammatory component. The combined use of corticosteroids (hydrocortisone, diflucortolone valerate, mometasone furoate) and antifungals (terbinafine, isoconazole nitrate) is increasingly recommended in international guidelines. In this way, rapid relief can be achieved in inflamed lesions.

Combination treatments are usually used in the first 1-2 weeks of treatment and then treatment is continued with a topical antifungal. In follow-up treatment, it is recommended to choose the antifungal in combination to prevent the development of resistance.

In summary, the addition of a topical steroid to a topical antifungal agent reduces inflammatory symptoms and the risk of bacterial superinfection, increases patient compliance with treatment, and increases the effect of the antifungal agent [16,17,18,19].

Oral Treatment

The first-line treatment agent for adults is terbinafine, and the treatment dose is 250 mg terbinafine once daily. Terbinafine works by inhibiting fungal ergosterol synthesis via squalene epoxidase [20]. Food and Drug Administration (FDA) approved terbinafine as the alternative to griseofulvin, which is not available in Turkey, for tinea capitis infection, which is very common in children [6]. 62.5 mg/day is used for children under 20 kg, and 125 mg/day is used for children between 20-40 kg [6]. Terbinafine is generally a safe drug and there is usually no need any blood monitoring [21]. The FDA removed its recommendation for monitoring liver function tests (LFT) from terbinafine, following long-term safety data [22]. Pregnancy category is B1. The location of the dermatophyte infection determines the duration of oral treatment: four weeks for the scalp, six weeks for fingernails and 12 weeks for toenails (especially in the elderly, longer treatment is required due to reduced blood flow in the area). A Cochrane review by Kreijkamp-Kaspers et al. [23] in 2017 determined that in the clinical and mycological treatment of tinea unguium, terbinafine was superior to both itraconazole and fluconazole. Terbinafine is metabolized by cytochrome P450 enzymes. By inhibiting CYP2D6, the cytochrome P450 enzyme responsible for the metabolism of tricyclic antidepressants, beta-blockers and SSRIs, it may increase blood levels of these drugs [24]. Adverse effects reported with oral terbinafine include the central nervous system (e.g., headache, difficulty concentrating), the gastrointestinal tract (e.g., diarrhea, dyspepsia, nausea) and effects on the cutaneous system (e.g., erythema, pruritus) [20].

In adults, itraconazole and fluconazole are recommended as second-line treatments. Itraconazole inhibits C-14a-demethylation of lanosterol and prevents fungal ergosterol synthesis by disrupting fungal cell membranes [20]. Both intermittent and continuous treatments with itraconazole have similar efficacy. Intermittent itraconazole treatment means 200 mg twice a day for one week a month. This type of treatment should be used for two months for the fingernails and three months for the toenails. Continuous itraconazole treatment requires continuous use of 200 mg daily. The duration of this type of treatment is six weeks for fingernails and 12 weeks for toenails [6,21,22,23,24,25]. Regular LFT monitoring every four to six weeks (depends on the patient's background) are recommended when initiating oral itraconazole therapy. Pregnancy category is C. Itraconazole undergoes hepatic metabolism mainly by CYP3A4, forming more than 30 metabolites, including hydroxy-itraconazole with antifungal activity. All resulting metabolites are CYP3A4 inhibitors with a higher affinity for CYP3A4 than the parent drug. Increased itraconazole exposure may cause cardiac toxicity through decreased CYP3A4 activity [26]. Contraindicated in patients with congestive heart failure due to increased risk of negative inotropic effects [27]. Coadministration of cisapride, pimozide, and quinidine is contraindicated due to the risk of prolonging the QT interval and increasing the risk of arrhythmia [24]. Also there are some side effects on central nervous system (e.g., headache, dizziness), gastrointestinal system (e.g., diarrhea, dyspepsia, abdominal pain) and skin system [20].

Fluconazole acts by inhibiting C-14a-demethylation of lanosterol and has the potential to inhibit human host cytochromes (e.g., CYP2C9 and CYP2C19) [20]. Fluconazole, in 150-300 mg per week, must be used for longer durations compared to terbinafin and itraconazole for the treatment of onycomycosis. It is for 12-24 weeks for fingernails and for 24-52 weeks for toenails [6,21,22,23,24,25]. LFT and full blood tests are required before starting fluconazole treatment. Fluconazole inhibits both CYP3A4 and CYP2C9 and

requires close monitoring when prescribed with drugs metabolized by these enzymes. Concomitant use of fluconazole with terfenadine or cisapridine is contraindicated [28,29]. Pregnancy category is D. Fluconazole may have similar side effects to terbinafine and itraconazole, including headache, nausea, and skin rash [20].

Conclusion

Oral terbinafine is the first step in the treatment of SFI because it has lower potential drug interactions, provides more mycological cure, and has fewer side effects compared to itraconazole treatment. In cases where it cannot be used, other agents may be preferred.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: B.D., N.D.A., Z.K., Data Collection or Processing: B.D., N.D.A., Z.K., Analysis or Interpretation: B.D., N.D.A., Literature Search: B.D., N.D.A., Z.K., Writing: B.D., N.D.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Kovitwanichkanont T, Chong AH. Superficial fungal infections. Aust J Gen Pract 2019;48:706-711.
2. Shen JJ, Jemec GBE, Arendrup MC, Saunte DML. Photodynamic therapy treatment of superficial fungal infections: A systematic review. Photodiagnosis Photodyn Ther 2020;31:101774.
3. Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses 2008;51(Suppl 4):2-15.
4. Moriarty B, Hay R, Morris-Jones R. The diagnosis and management of tinea. BMJ 2012;345:e4380.
5. John AM, Schwartz RA, Janniger CK. The kerion: an angry tinea capitis. Int J Dermatol 2018;57:3-9.
6. Expert Group for Dermatology. Tinea. In: eTG complete. Melbourne: Therapeutic Guidelines Limited; 2015.
7. Ilkit M, Durdu M, Karakaş M. Majocchi's granuloma: a symptom complex caused by fungal pathogens. Med Mycol 2012;50:449-457.
8. Drakensjö IT, Chryssanthou E. Epidemiology of dermatophyte infections in Stockholm, Sweden: a retrospective study from 2005-2009. Med Mycol 2011;49:484-488.
9. Field LA, Adams BB. Tinea pedis in athletes. Int J Dermatol 2008;47:485-492.
10. Szepietowski JC, Reich A, Garlowska E, Kulig M, Baran E; Onychomycosis Epidemiology Study Group. Factors influencing coexistence of toenail onychomycosis with tinea pedis and other dermatomycoses: a survey of 2761 patients. Arch Dermatol 2006;142:1279-1284.
11. Morris RE. An adolescent boy with blistered feet. West J Med 2001;175:375-376.
12. Thomas J, Jacobson GA, Narkowicz CK, Peterson GM, Burnet H, Sharpe C. Toenail onychomycosis: an important global disease burden. J Clin Pharm Ther 2010;35:497-519.
13. Fletcher CL, Hay RJ, Smeeton NC. Onychomycosis: the development of a clinical diagnostic aid for toenail disease. Part I. Establishing discriminating historical and clinical features. Br J Dermatol 2004;150:701-705.
14. Kovitwanichkanont T, Chong AH. Superficial fungal infections. Aust J Gen Pract 2019;48:706-711.
15. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. Cochrane Database Syst Rev 2007;2007:CD001434.
16. Schaller M, Friedrich M, Papini M, Pujol RM, Veraldi S. Topical antifungal-corticosteroid combination therapy for the treatment of superficial mycoses: conclusions of an expert panel meeting. Mycoses 2016;59:365-373.
17. Rotta I, Sanchez A, Gonçalves PR, Otuki MF, Correr CJ. Efficacy and safety of topical antifungals in the treatment of dermatomycosis: a systematic review. Br J Dermatol 2012;166:927-933.
18. Czaika VA, Zuberbier T. Lokale Kombinationstherapie bei entzündlichen Dermatomykosen : Review zu den Therapieempfehlungen in nationalen und internationalen Leitlinien [Local combination therapy of inflammatory dermatomycosis: A review of recommendations in national and international guidelines]. Hautarzt 2015;66:360-369.
19. Pereiro Ferreirós M Jr, García-Martínez FJ, Alonso-González J. Update on the treatment of superficial mycoses. Actas Dermosifiliogr 2012;103:778-783.
20. Gupta AK, Cooper EA. Update in antifungal therapy of dermatophytosis. Mycopathologia 2008;166:353-367.
21. Stolmeier DA, Stratman HB, McIntee TJ, Stratman EJ. Utility of Laboratory Test Result Monitoring in Patients Taking Oral Terbinafine or Griseofulvin for Dermatophyte Infections. JAMA Dermatol 2018;154:1409-1416.
22. Elewski B, Tavakkol A. Safety and tolerability of oral antifungal agents in the treatment of fungal nail disease: a proven reality. Ther Clin Risk Manag 2005;1:299-306.
23. Kreijkamp-Kaspers S, Hawke K, Guo L, Kerin G, Bell-Syer SE, Magin P, Bell-Syer SV, van Driel ML. Oral antifungal medication for toenail onychomycosis. Cochrane Database Syst Rev 2017;7:CD010031.
24. Singal A, Khanna D. Onychomycosis: Diagnosis and management. Indian J Dermatol Venereol Leprol 2011;77:659-672.
25. Ely JW, Rosenfeld S, Seabury Stone M. Diagnosis and management of tinea infections. Am Fam Physician 2014;90:702-710.
26. Teaford HR, Abu Saleh OM, Villarraga HR, Enzler MJ, Rivera CG. The Many Faces of Itraconazole Cardiac Toxicity. Mayo Clin Proc Innov Qual Outcomes 2020;4:588-594.
27. Cathcart S, Cantrell W, Elewski Be. Onychomycosis and diabetes. J Eur Acad Dermatol Venereol 2009;23:1119-1122.
28. Arrese JE, Piérard GE. Treatment failures and relapses in onychomycosis: a stubborn clinical problem. Dermatology 2003;207:255-260.
29. Schmitt JV, Bombonatto G, Trierweiler SM, Fabri AB. General aspects of drug interactions with systemic antifungals in a retrospective study sample. An Bras Dermatol 2013;88:476-479.

ORIGINAL ARTICLE

DOI: 10.4274/jtad.galenos.2023.92408
J Turk Acad Dermatol 2023;17(4):87-91

Evaluation of the Effect of Phototherapy Treatment on Dermatology Quality of Life Index

Nasim Behkami[1], Zeynep Altan Ferhatoğlu[1]

Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey

ABSTRACT

Background: Dermatology Quality of Life Index (DLQI) was first introduced for routine use in 1994 by Finlay and Khan in order to evaluate the quality of life index of various skin diseases. The aim of this study is to evaluate the effect of phototherapy treatment [narrowband ultraviolet-B (NB-UVB)] on the DLQI of patients who are followed in our clinic and receive phototherapy treatment for various dermatological reasons.

Materials and Methods: A total of 40 patients were included in the study. Patients were asked to fill out DLQI questionnaires before phototherapy treatment (NB-UVB) and at the 6th month of treatment. Statistical analysis was done with SPSS-21.

Results: The mean age of the patients was 37.9±10.07 years (18-63 years). Patients receiving phototherapy were evaluated in 4 groups. The first group was vitiligo (n=14, 35.0%), the second group was psoriasis vulgaris (n=10, 25%), the third group was mycosis fungoides (MF) (n=7, 17.5%) and the fourth group was lichen planus (n=9, 22.5%). was. In the 6th month of treatment, the DLQI score before and after phototherapy in vitiligo patients decreased from 14.79±8.239 to 5.86±6.075, in psoriasis vulgaris patients from 9.00±7.165 to 2.20±3.795, and in MF patients from 9.00±7.188 to 2.29±3.147, and it was found to be significantly lower in lichen planus patients, from 9.55±6.023 to 3.33±3.873.

Conclusion: In the cross-sectional study we conducted with DLQI, a current scale, in our patients receiving phototherapy treatment at our center, significant improvement was observed after treatment, proving that phototherapy has a significant benefit on quality of life.

Keywords: Dermatology Quality of Life Index, DLQI, Phototherapy

Introduction

Dermatology Quality of Life Index (DLQI) in dermatology is of great importance for many reasons. Measuring dermatological patients' pre-treatment or treatment-related quality of life indexes gives us information about the effectiveness of the treatment, the course of the disease, and the clinical course [1,2,3]. The most important feature of quality of life measurements is that they are only an indicator of the quality of life at the point in time when the measurement is made [4,5]. DLQI is an evaluation in the form of a survey consisting of simple, understandable and short questions that are not specific to any dermatological disease. DLQI consists of a total of 10 questions. Questions 1 and 2 are based on mood, 3 and 4 are based on day-long activities, 5 and 6 are based on leisure activities, 7 are occupational, 8 and 9 are social activities and 10 are treatment (Annex-1). Oztürkcan et al. [6] tested the functionality of DLQI in Turkish and ensured its safety. Phototherapy is used in the treatment of various dermatological diseases for therapeutic purposes using natural sunlight or artificial light sources [7,8].

Address for Correspondence: Nasim Behkami MD, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey
Phone: +90 552 437 70 66 E-mail: nasimbehkami@gmail.com ORCID ID: orcid.org/0009-0009-9225-1723
Received: 01.11.2023 Accepted: 09.11.2023

Materials and Methods

The study included 40 patients who received NB-UVB treatment for various dermatological diseases at Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, and the patients who received phototherapy treatment were divided into 4 groups (first group: vitiligo, second group: psoriasis vulgaris, third group: mycosis fungoides (MF), fourth group: lichen planus). Patients were asked to fill out DLQI questionnaires, each consisting of 10 questions, before treatment and at the sixth month of treatment. We used the Turkish version of these questionnaires [6]. These questionnaires consist of 20 items, each scored from 0 to 3 (very much, a lot, sometimes and never), with a final maximum score of 30. A score above 10 represents poor quality of life.

The approval of Istanbul Univeristy-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethics Committee was taken before initiating the study (number: E-83045809-60401.01-712168, date: 13.06.2023).

Statistical Analysis

The statistical analysis was performed with SPSS-21. The descriptive statistic method and frequency analysis were used for the data distribution. In continuous data, those with normal distribution were shown as median ± standard deviation, and those that did not fit into the normal distribution were shown as median (minimum-maximum). Categorical data were presented with frequency and percentage. For comparison of continuous data, Mann-Whitney U test was used for two groups, one-way ANOVA or Kruskal-Wallis test was used for comparison of three groups. Chi-square test and Fisher's test in categorical data exact test was used. All tests were bilateral and statistical significance was accepted as $p<0.05$.

Results

Of the 40 patients included in the study, 17 (42.5%) were male and 23 (57.5%) were female. The ages of the patients ranged between 18 and 63, and the average age was 37.9±10.07. Information was obtained about the educational status of the patients participating in the study; 6 (15%) were primary school graduates, 20 (50.0%) were high school graduates, and 7 (17%) were university graduates, respectively. Patients receiving NB-UVB were evaluated in 4 groups. The first group was vitiligo (n=14, 35.0%), the second group was psoriasis vulgaris (n=10, 25%), the third group was MF (n=7, 17.5%) and the fourth group was lichen planus (n=9, 22.5%) it consisted of patients. Information was obtained from the patients about their previous treatments; 5 people (12.5%) had never received treatment before or could not remember whether they had received treatment. 31 people (77.5%) stated that they received topical treatments, one person (2.5%) stated that they received systemic corticosteroids, and 3 people (7.5%) stated that they received other immunosuppressive treatments. The mean score calculated for DLQI before phototherapy treatment (NB-UVB) was 11.15±7,564, and the mean score after phototherapy treatment (NB-UVB) was 3.75±4,781. The maximum score in dermatology quality of life measure is scored out of 30. On the scoring scale, 0-1= no impact on the patient's quality of life, 2-5= minimal impact, 6-10= moderate impact, 11-20= very major impact, 21-30= extremely major impact. A score above 10 it is considered a high score and indicates a poorer quality of life [9-10]. When the quality of life indexes of vitiligo, psoriasis vulgaris, MF and lichen planus patients were compared with the Wilcoxon signed ranks test before and after phototherapy treatment, the quality of life index score of vitiligo patients before phototherapy treatment (NB-UVB) ($\bar{X}$= 14.79, S= 8,239) was compared to the quality of life index score after phototherapy treatment (NB-UVB) respectively. It is seen that it is higher in statistical significance than ($\bar{X}$= 5.86, S= 6,075) ($p<0.001$). It is seen that the quality of life index score of psoriasis vulgaris patients before phototherapy treatment (NB-UVB) ($\bar{X}$= 9.00, S= 7,165) is statistically significantly higher than the quality of life index score after phototherapy treatment (NB-UVB) ($\bar{X}$= 2.20, S= 3,795) ($p<0.008$). It is seen that the quality of life index score of MF patients before phototherapy treatment (NB-UVB) ($\bar{X}$= 9.00, S= 7,188) is statistically significantly higher than the quality of life index score after phototherapy treatment (DB-UVB) ($\bar{X}$= 2.29, S= 3,147) ($p<0.017$). It is seen that the quality of life index score of lichen planus patients before phototherapy treatment (NB-UVB) ($\bar{X}$= 9.55, S= 6,023) is statistically significantly higher than the quality of life index score after phototherapy treatment (NB-UVB) ($\bar{X}$= 3.33, S= 3.873) ($p<0.008$).

Discussion

DLQI was first introduced for routine use in 1994 by Finlay and Khan [1] in order to evaluate the quality of life index of various skin diseases. It is designed to evaluate the effects on the quality of life of symptoms and emotions, daily activities, leisure, school and work life, personal relationships, and treatment of various dermatological diseases [9,10,11]. Quality of life indexes of a total of 40 patients (vitiligo, psoriasis vulgaris, MF and lichen planus) who applied to the phototherapy unit in our center for treatment were calculated and evaluated for each group at the time of admission and in the sixth month of treatment.

Vitiligo is a dermatosis that results in the destruction of epideramal melanocytes and consists of depigmented patches. The global prevalence of vitiligo is between 0.1-8% [12]. Although Psoralen ultraviolet A (PUVA) constitutes the first-line treatment for vitiligo, various studies have shown that NB-UVB therapy is more effective, superior and safe compared to PUVA therapy. In our study, the

quality of life index score of a total of 14 vitiligo patients who responded to phototherapy treatment (NB-UVB) was 14.79±8.239 before treatment and 5.86±6.075 after treatment, and it was observed to decrease significantly after treatment ($p<0.01$). Similar results are observed in various studies in the literature. In the study conducted by Chahar et al. [13] in 2018 with 54 cases diagnosed with vitiligo, DLQI decreased from 8.64±4.32 to 5.86±2.15 after NB-UVB treatment. Similarly, in a study conducted by Mou et al. [14] in China they reported that DLQI before and after NB-UVB treatment were 6.3±4.8 and 3.1±2.4 respectively, and the difference was significant. In light of these studies, it has been shown that phototherapy treatment has a positive therapeutic result in vitiligo.

The relationship between psoriasis and quality of life was first prepared in 1987 by Finaly and Kell as the Psoriasis Dysfunction Index [15]. Afterwards, DLQI was designed as a simple and practical scale that can be applied routinely to measure the impact of psoriasis and different skin diseases on the quality of life [1]. There are many studies in the literature investigating the effects of treatment agents on disease severity and quality of life. In the study conducted by Couto et al. [16] with twenty male and female patients, a positive and moderate correlation was found between DLQI and Psoriasis Area Severity Index (PASI) of psoriasis patients before and after 32 phototherapy sessions ($r=0.48$, $p=0.03$). In the study conducted by Robaee et al. [17] with a total of 72 patients, it was found that DLQI improved significantly after phototherapy and was positively correlated with PASI. In our study, we found that the DLQI of psoriasis patients before and after phototherapy treatment were 9±7.165 and 2.2±3.795, respectively, and the difference was significant.

MF is a lymphoproliferative disease characterized by atypical lymphocytes accumulating in the skin. Phototherapy is one of the most commonly used therapeutic approaches in early-stage MF [18]. There are a few studies investigating the effect of treatment on quality of life in MF, but none of these studies address psychological health [19,20,21,22]. In a study conducted by Graier et al. [23] with 24 MF patients, they found that PUVA treatment significantly increased the overall quality of life by reducing DLQI scores by an average of 58.6%. With or without maintenance treatment, improvements in quality of life and psychological well-being continued [23]. In our study, the quality of life index score of a total of 7 MF patients who responded to phototherapy was 9±7.188 before treatment and 2.29±3.147 after treatment, and it was observed to decrease significantly after treatment ($p<0.017$).

Lichen planus is a dermatosis that affects the skin and mucosa and is accompanied by itching and ulcerations [24,25]. Although this disease can widely affect many aspects of life, such as sexual activity and body image perception, its effect on quality of life and psychopathological relationships have not been adequately investigated [25,26,27]. Flocco et al.'s [26,27,28] study of 100 cases diagnosed with lichen planus, quality of life was affected in 78% of the cases. Additionally, different mean scores were determined for different affected localizations [29,30]. The DLQI of patients with genital lichen planus (8.68±6.96) was significantly higher than that of patients whose genital area was not affected (5.01±5.49; $p=0.009$). In our study, the average DLQI score of lichen planus patients before receiving phototherapy was 9.55±6.023. After the treatment, a significant improvement was observed in the patients' quality of life indexes ($p<0.008$). In our study, it was determined that quality of life indexes, which were worse before phototherapy, improved significantly as a result of treatment or during treatment follow-up (Table 1).

Study Limitation

The main limitation of our study is being a retrospective study that was conducted from a single center with a limited number of patients.

Conclusion

As a result, in the cross-sectional study we conducted with DLQI, a current scale, in our patients receiving phototherapy treatment at our center, significant improvement was observed after treatment, proving that phototherapy has a significant benefit on quality of life.

Table 1. Demographic characteristics of the patients and quality of life index scores

Category	Total
Age	
Mean ± SD	37.9±10.07
Median (min-max)	37.5 (18-63)
Gender n (%)	40 (100%)
Woman	23 (57.5%)
Male	17 (42.5%)
Illness n (%)	
Vitiligo	14 (35%)
Psoriasis vulgaris	10 (25%)
Mycosis fungoides	7 (17.5%)
Lichen planus	9 (22.5%)
DLQI score (before phototherapy)	
Mean ± SD	11.15±7,564
Median (min-max)	11 (0-30)
DLQI skoru (after phototherapy)	
Mean ± SD	3.75±4,781

SD: Standard deviation, DLQI: Dermatology Life Quality Index

Ethics

Ethics Committee Approval: The approval of Istanbul Univeristy-Cerrahpasa, Cerrahpasa Faculty of Medicine Ethics Committee was taken before initiating the study (number: E-83045809-60401.01-712168, date: 13.06.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.B., Design: Z.A.F., Data Collection or Processing: N.B., Analysis or Interpretation: N.B., Literature Search: Z.A.F., Writing: N.B., Z.A.F.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-216.
2. Hughes JE, Barraclough BM, Hamblin LG, White JE. Psychiatric symptoms in dermatology patients. Br J Psychiatry 1983;143:51-54.
3. Montgomery K, Norman P, Messenger AG, Thompson AR. The importance of mindfulness in psychosocial distress and quality of life in dermatology patients. Br J Dermatol 2016;175:930-936.
4. Goldberg DP. The Detection of Psychiatric Illness by Questionnaire. Maudsley Monograph 21. Oxford University Press, Oxford, 1972.
5. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. Br J Dermatol 2008;159:997-1035.
6. Oztürkcan S, Ermertcan AT, Eser E, Sahin MT. Cross validation of the Turkish version of dermatology life quality index. Int J Dermatol 2006;45:1300-1307.
7. Wulf HC Method and an apparatus for determining an individual's ability to stand exposure to ultraviolet radiation. US Patent. 1989;4:882-598. 1-38.
8. Gordon PM, Diffey BL, Matthews JN, Farr PM. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999;41:728-732.
9. Zachariae R, Zachariae C, Ibsen H, Mortensen JT, Wulf HC. Dermatology life quality index: data from Danish inpatients and outpatients. Acta Derm Venereol 2000;80:272-276.
10. Shikiar R, Willian MK, Okun MM, Thompson CS, Revicki DA. The validity and responsiveness of three quality of life measures in the assessment of psoriasis patients: results of a phase II study. Health Qual Life Outcomes 2006;4:71.
11. Kıvanç Altunay İ. Quality of Life in Psoriasis. Turkiye Klinikleri J Dermatol-Special Topics 2012;5:77-82.
12. Krüger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. Int J Dermatol 2012;51:1206-1212.
13. Chahar YS, Singh PK, Sonkar VK, Rajani I, Adil M. Impact on Quality of Life in Vitiligo Patients Treated with Narrowband Ultraviolet B Phototherapy. Indian J Dermatol 2018;63:399-402.
14. Mou KH, Han D, Liu WL, Li P. Combination therapy of orally administered glycyrrhizin and UVB improved active-stage generalized vitiligo. Braz J Med Biol Res 2016;49:e5354.
15. Finlay AY, Kelly SE. Psoriasis--an index of disability. Clin Exp Dermatol. 1987;12:8-11.
16. Couto MI, Carneiro S, Niemeyer-Corbellini JP, Yoshio JH, Ramos-E-Silva M. Correlation Between Severity Index and Quality of Life Index in Patients With Psoriasis Assessed Before and After Phototherapy. Skinmed 2016;14:93-97.
17. Al Robaee AA, Alzolibani AA. Narrowband ultraviolet B phototherapy improves the quality of life in patients with psoriasis. Saudi Med J 2011;32:603-606.
18. Guitart J. Psoralen Plus UV-A Therapy in the 21st Century: Use It or Lose It. JAMA Dermatol 2019;155:529-531.
19. Prince HM, Kim YH, Horwitz SM, Dummer R, Scarisbrick J, Quaglino P, Zinzani PL, Wolter P, Sanches JA, Ortiz-Romero PL, Akilov OE, Geskin L, Trotman J, Taylor K, Dalle S, Weichenthal M, Walewski J, Fisher D, Dréno B, Stadler R, Feldman T, Kuzel TM, Wang Y, Palanca-Wessels MC, Zagadailov E, Trepicchio WL, Zhang W, Lin HM, Liu Y, Huebner D, Little M, Whittaker S, Duvic M; ALCANZA study group. Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial. Lancet 2017;390:555-566.
20. Illidge T, Chan C, Counsell N, Morris S, Scarisbrick J, Gilson D, Popova B, Patrick P, Smith P, Whittaker S, Cowan R. Phase II study of gemcitabine and bexarotene (GEMBEX) in the treatment of cutaneous T-cell lymphoma. Br J Cancer 2013;109:2566-2573.
21. Duvic M, Hymes K, Heald P, Breneman D, Martin AG, Myskowski P, Crowley C, Yocum RC; Bexarotene Worldwide Study Group. Bexarotene is effective and safe for treatment of refractory advanced-stage cutaneous T-cell lymphoma: multinational phase II-III trial results. J Clin Oncol 2001;19:2456-2471.
22. Heald P, Mehlmauer M, Martin AG, Crowley CA, Yocum RC, Reich SD; Worldwide Bexarotene Study Group. Topical bexarotene therapy for patients with refractory or persistent early-stage cutaneous T-cell lymphoma: results of the phase III clinical trial. J Am Acad Dermatol 2003;49:801-815.
23. Graier T, Fink-Puches R, Porkert S, Lang R, Pöchlauer S, Ratzinger G, Tanew A, Selhofer S, Sator PG, Hofer A, Gruber-Wackernagel A, Legat FJ, Vieyra-Garcia PA, Quehenberger F, Wolf P. Quality of Life, Anxiety, and Depression in Patients With Early-Stage Mycosis Fungoides and the Effect of Oral Psoralen Plus UV-A (PUVA) Photochemotherapy on it. Front Med (Lausanne) 2020;7:330.
24. Cheng H, Oakley A, Conaglen JV, Conaglen HM. Quality of Life and Sexual Distress in Women With Erosive Vulvovaginal Lichen Planus. J Low Genit Tract Dis 2017;21:145-149.
25. Radwan-Oczko M, Zwyrtek E, Owczarek JE, Szcześniak D. Psychopathological profile and quality of life of patients with oral lichen planus. J Appl Oral Sci 2018;26:e20170146.
26. Fiocco Z, Kupf S, Patzak L, Kämmerer T, Pumnea T, French LE, Reinholz M. Quality of Life and Psychopathology in Lichen Planus: A Neglected Disease Burden. Acta Derm Venereol. 2021;101:adv00619.
27. Mansur AT, Kilic Z, Atalay F. Psychological evaluation of patients with cutaneous lichen planus. Dermatology and Psychosomatics / Dermatologie und Psychosomatik 2004;3:132-136.
28. Manolache L, Seceleanu-Petrescu D, Benea V. Lichen planus patients and stressful events. J Eur Acad Dermatol Venereol 2008;22:437-441.
29. Allen CM, Beck FM, Rossie KM, Kaul TJ. Relation of stress and anxiety to oral lichen planus. Oral Surg Oral Med Oral Pathol 1986;61:44-46.
30. Rojo-Moreno JL, Bagán JV, Rojo-Moreno J, Donat JS, Milián MA, Jiménez Y. Psychologic factors and oral lichen planus. A psychometric evaluation of 100 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;86:687-691.

Questionnaire

The purpose of this questionnaire is to measure how much your skin disease affects your life in the last 7 days. Please tick only one option that you think is most appropriate for each question [6].

During the last week, how itchy, painful or stinging was your skin condition				
Very much	A lot	A little	Not at all	Not relevant
During the past week, how embarrassed have you been about the condition of your skin or have you found yourself uncomfortable with the appearance of your skin?				
Very much	A lot	A little	Not at all	Not relevant
During the last week, how much did your skin condition prevent you from going shopping or tending to your garden?				
Very much	A lot	A little	Not at all	Not relevant
During the past week, how much did your skin condition affect the clothes you wore??				
Very much	A lot	A little	Not at all	Not relevant
Over the past week, how much has the condition of your skin affected your social or leisure activities?				
Very much	A lot	A little	Not at all	Not relevant
Over the past week, how difficult has your skin condition made it for you to do any sports?				
Very much	A lot	A little	Not at all	Not relevant
During the past week, has your skin condition prevented you from working or studying? yes no not suitable, if your answer is "no", how much of a problem has your skin condition caused you to work or work during the past week?				
Very much	A lot	A little	Not at all	Not relevant
How much of a problem has your skin condition caused your partner, friend, or relative during the past week?				
Very much	A lot	A little	Not at all	Not relevant
To what extent has your skin condition caused sexual distress during the past week?				
Very much	A lot	A little	Not at all	Not relevant
How much of a problem has the treatment for your skin been over the past week? (for example, by causing disorganization and clutter in your home or by taking up your time.)				
Very much	A lot	A little	Not at all	Not relevant

Thank you for participating in the survey.

ORIGINAL ARTICLE

DOI: 10.4274/jtad.galenos.2023.63325
J Turk Acad Dermatol 2023;17(4):92-96

Demographic and Clinical Characteristics of Geriatric Patients with Psoriasis: A Single-center, Cross-sectional, Retrospective Study in Turkish Population

Tuğba Kevser Uzunçakmak[1], Selim Gümüş[2], Ayşenur Özdil Eser[3], Burhan Engin[1]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology, Istanbul, Turkey
[2]University of Health Sciences Turkey, Gaziosmanpasa Training and Research Hospital, Clinic of Dermatology, Istanbul, Turkey
[3]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Public Health, Istanbul, Turkey

ABSTRACT

Background: Psoriasis is a common, chronic, inflammatory skin disorder affecting almost 2-3% of the population. Studies on the epidemiological data and the course of the disease have generally been published in pediatric and middle-aged patients, where the disease is more common. This study aimed to provide more insight into the disease and treatment characteristics of psoriasis patients over 65.

Materials and Methods: In this retrospective, cross-sectional, single-center, hospital-based study, patients over 65 who visited our department between 01.06.2017 and 01.06.2020 were included.

Results: Ninety six patients with psoriasis were admitted to our outpatient clinic during the study period. The mean age of the patients was 69.92±4.73 years. Women and men were equally affected. Almost 9.4% of the patients had psoriatic arthritis. The patients' mean Psoriasis Area Severity Index score was 8.39±7.11, and the disease duration was 13.76±12.71 years. Nail involvement was detected in 43.8% of the patients. Family history was positive in 19.8% of the patients. Smoking was positive in 28.1% of the patients, and regular alcohol use was positive in 6.3%.

Conclusion: The clinical course of psoriasis is usually milder in elderly onset patients. Further studies are warranted to determine the best management of psoriasis in elderly patients. Drug interactions and metabolism should be carefully managed in these patients.

Keywords: Alcohol consumption, Biologic agents, Conventional treatments, Comorbidity, Dermatology, Geriatric, Inflammation, Nail psoriasis, Psoriasis, Psoriatic arthritis, Smoking

Introduction

Psoriasis is one of the most common inflammatory skin disorders, which affects approximately 2-8% of the population without any race or sex predilection [1,2]. In epidemiologic studies, it is reported to be more common in the middle age, followed by the pediatric age group. In many epidemiologic studies, it has been shown that the disease's onset has a bimodal distribution. In the early 30s, the first peak occurs and the second peak usually occurs in the early 60s [3]. Today, people over 65 are considered the geriatric population, and some differences distinguish this age group from other age groups [4]. Polypharmacy and many comorbidities in this age group challenge clinicians in managing psoriasis [5].

This study evaluated our department's demographic, clinical, and treatment characteristics of older adults with psoriasis.

Address for Correspondence: Tuğba Kevser Uzunçakmak, Assoc. Prof., Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology, Istanbul, Turkey
Phone: +90 530 664 02 26 E-mail: drtugbakevser@gmail.com ORCID ID: orcid.org/0000-0002-0328-4171
Received: 21.11.2023 Accepted: 28.11.2023

Materials and Method

Patient Group

This study was conducted in the dermatology clinic of a public university hospital and the study protocol was approved by the Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine Clinical Research Ethics Committee (number: 43710, date: 02.03.2021). Informed voluntary consent forms were obtained from the patients included in the study to use their information. The outpatient dermatology service database was reviewed retrospectively. Patient characteristics, including sex, body mass index (BMI), family history, psoriasis area and severity index (PASI) scores, disease duration, nail or joint involvement and all medications used for psoriasis including topical and systemic treatments were included in the analysis. Comorbidities associated with psoriasis, such as metabolic syndrome, coronary artery disease (CAD), diabetes mellitus (DM), hypertension (HT) and dyslipidemia, smoking and alcohol intake were also evaluated.

Statistical Analysis

Descriptive statistics in the study are given as mean, percentage, frequency and standard deviation. Kruskal-Wallis and Mann-Whitney U tests were used to examine the difference in PASI scores according to patient groups. The all-pairwise method was used to identify different groups. The Mann-Whitney U test was used to investigate the patients' age differences according to gender. Spearman correlation analysis was performed to investigate the relationship between smoking years and duration of illness with PASI scores. In the study, a chi-square analysis was used to examine the difference in nail involvement rates according to comorbidity and treatment levels. The critical decision value in the research was taken as 0.05. The analyses were concluded with the SPSS 25.00 package program.

Results

Ninety-six patients with psoriasis were applied to our outpatient clinic between 01.06.2017 and 01.06.2020. Among these patients, 50% were women and 50% were men. Psoriatic arthritis was present in 9.4% of the patients. Nail involvement was detected in 43.75% (n=42) of the patients. The mean age of the patients was 69.92±4.73. Of 96 patients, 86 (89.6%) had plaque-type psoriasis, three (3.1%) had palmoplantar psoriasis, and 7 had (7.3%) pustular psoriasis. The overall mean age of the patients was 69.92±4.73. The mean ages of the female patients were 69.69±4.68, and the male patients were 70.15±4.81. BMI levels were found to be 30.27±4.99. The mean PASI score of the patients was 9.04±6.9, and the mean duration of the disease was 13.76±12.71 (1-50) years. The mean period of smoking was 10.04±18.84 years. Almost 67.7% of the patients were using an additional medication, and 72.9% of the patients had comorbidities. The most common comorbidities were HT (n=48, 50%), CAD (n=20, 20.8%), and DM (n=17, 17.7%) (Table 1).

It was found that the PASI scores were not statistically different according to the patient's comorbidities, and the PASI score measurements of the patients with or without comorbidity were similar (p=0.76). Family history was positive in 19.8% of the patients. PASI scores were not at different levels according to the patient's

Table 1. Clinical, demographic data and comorbidities of the patients

Characteristics	**n=96**
Sex - no. (%)	
Female	48 (50%)
Male	48 (50%)
Age - (years) 69.9±4.7	
Female	69.7±4.5
Male	70.2±4.8
Clinical subtype - no. (%)	
Plaque type psoriasis	86 (89.6%)
Palmoplantar	3 (3.1%)
Pustular psoriasis	7 (7.3%)
Weight, height, and BMI	
Weight (kg)	81.1±14.2
Height	163.7±9.7
BMI	30.3±5
PASI score	9.04±6.9 (minimum 0 - maximum 32)
Comorbidities (n%)	
Epilepsy	1 (1.1%)
Vasculitis	1 (1.1%)
Osteoporosis	1 (1.1%)
Inflammatory bowel disease	1 (1.1%)
Chronic renal failure	1 (1.1%)
Rheumatoid arthritis	1 (1.1%)
Hypothyroidism	1 (1.1%)
Hepatitis	2 (2.1%)
Migraine	1 (1.1%)
Psychiatric disorders	2 (2.1%)
Diabetes mellitus	17 (17.1%)
Osteoarthritis	4 (4.2%)
Benign prostatic hyperplasia	2 (2.1%)
Coronary artery disease	20 (20.8%)
Hypercholesterolemia	11 (11.5%)
Asthma	3 (3.1%)
Hypertension	48 (50%)

no: Number, BMI: Body mass index, kg: Kilogram, min: Minimum, max: Maximum

family history. The PASI score measurements of the patients with or without a family history were similar (p=0.341). Smoking history was positive in 28.1% of the patients, and regular alcohol consumption was positive in 6.3%. No significant correlation was found between the smoking durations of the patients and the PASI scores. There was no significant correlation between the duration of smoking and the PASI scores (p=0.462, p>0.05). Also, no significant difference was found between PASI scores and the alcohol consumption of the patients, and the PASI score measurements of the patients who used or did not use alcohol were similar (p=0.383).

Almost 63.5% (n=61) of the patients were using topical treatments. 29.2% (n=28) of the patients were using conventional treatments; 6.3% (n=6) were using acitretin, 4.2% (n=4) were using methotrexate, and 18.7% (n=18) were receiving phototherapy. Seven geriatric patients (7.3%) were using biological therapies; in this group, 2 (2.1%) patients were using adalimumab, 1 (1%) patient was using secukinumab, 2 (2.1%) patients were using ustekinumab, 1 (1%) patient was using infliximab and similar 1 (1%) patient was using ixekizumab therapy (Table 2).

There were no statistically significant correlation between the disease duration and PASI scores (r=0.13, p=0.19, p>0.05). The prevalence of nail involvement was higher in patients who have comorbid diseases (p=0.01)

Discussion

Almost 30% of all cases of psoriasis have a late-onset disease that occurs after the age of 40 years. The clinical studies focusing on the late-onset group set a cut-off of these groups as 60. These patients usually had a milder clinical course when compared with early and middle-aged-onset groups [1,6]. Similarly, in our study, lower PASI scores, less psoriatic arthritis, and lower systemic treatment usage were detected. The differences in the pathogenesis and clinical characteristics between early-onset and late-onset psoriasis are still unknown. Still, the association between the human leukocyte antigens genes and the onset age of psoriasis may affect these differences [6].

Table 2. Treatments of the patients

Treatments	n=96
Topical treatments	61 (63.5%)
Conventional treatments	28 (29.2%)
Acitretin	6 (6.3%)
Methotrexate	4 (4.2%)
Phototherapy	18 (18.7%)
Biological treatments	7 (7.3%)
Adalimumab	2 (2.1%)
Infliximab	1 (1%)
Ustekinumab	2 (2.1%)
Secukinumab	1 (1%)
Ixekizumab	1 (1%)

The management of psoriasis may be challenging for physicians in the senior age group due to having several comorbidities and polypharmacy that may lead to adverse events, drug interactions, increased hepatotoxicity, and treatment outcomes may be more unpredictable and complicated [7]. In our study, 72.9% of the patients had comorbidities, and 67.7% used additional medication. However, no severe adverse reactions or side effects have been detected during patient follow-ups.

Some authorities have suggested that geriatric psoriasis should be evaluated as a distinct subtype due to the differences in parameters such as the course and involvement of nails and joints [8]. In this study, a milder clinical course of psoriasis was detected with lower PASI scores and less nail and joint involvement. Therefore, our study may also support the hypothesis which offers elderly-onset psoriasis as a distinct clinical subtype.

Moreover, it is also well known that psoriasis is associated with several comorbidities, such as inflammatory bowel diseases, metabolic syndrome, cardiovascular diseases and stroke. The prevalence of comorbidities such as metabolic syndrome and cardiovascular diseases is considered to be higher in patients with chronic plaque psoriasis when compared with the average population [9]. In our study, DM, HT and CAD were the most common comorbidities, consistent with previous studies.

The role of smoking in psoriasis pathogenesis is a well-known entity and has been shown in several case-control and cohort studies. The immunomodulatory effect of nicotine and its role in releasing pro-inflammatory cytokines may lead to the development of psoriasis [10]. Clinicians should be aware of the patients' smoking habits.

It can also be challenging to decide on systemic and biological treatments in elderly patients and topical treatments are usually indicated as first-line therapy due to the lower risk of adverse effects [11]. In elderly patients, skin atrophy, purpuric eruption, bruising, rebound phenomenon, and tachyphylaxis are the most common long-term adverse effects of topical steroids. Therefore, they should be used carefully [12]. Phototherapy and systemic therapy may be suggested in patients with mild-moderate psoriasis. Although phototherapy is a safe treatment protocol, it may be challenging to perform in those with psoriatic arthritis, debilitation, or stroke in these patient groups [13,14]. Systemic therapies are indicated in patients with severe psoriasis with 10% body surface area involvement of a high PASI score. Acitretin may be the first treatment choice in the management of psoriasis in geriatric age group when the hepatic/renal toxicity risk of methotrexate, HT, and hepatic/renal toxicity risk of cyclosporin have been considered [15-

18]. The dose can be started at a low dose and raised over 4-6 weeks to increase patient tolerance.

Biologic agents seem to be safe in elderly patients who have severe psoriasis, but in the literature, there are still reports of hepatitis flare and tuberculosis reactivation, especially with tumor necrosis factor alpha inhibitors [7]. Ustekinumab is a biological agent with a safe long-term safety profile confirmed by real-world data in the over-65 age group. It has also been reported that secukinumab and ixekizumab show similar efficacy and safety profiles in the elderly and younger age groups. However, real-world data regarding interleukin (IL)-17 and IL-23 inhibitors, which came into use later, are not as numerous as those for ustekinumab [5]. We did not observe any serious side effects in our patients over 65 years of age and using biological agents in this study, compared to other age groups.

Lastly, drug-induced or -provoked psoriasis should be always considered in geriatric psoriasis cases. In this group, drugs such as beta-blockers, lithium, non-steroid anti-inflammatory agents, synthetic antimalarial drugs, imiquimod, and targeted treatments using monoclonal antibodies are the best-known drugs to trigger psoriasis, and these drugs can be used quite frequently in this age group [19]. In our study, almost 67.7% of the patients were using different systemic treatments such as antihypertensive drugs, salicylic acid, statins, and antidepressants. Patients should be referred to relevant clinics for replacement of potentially culprit medications.

Study Limitation

The main limitation of our study is being a retrospective study with a small sample size conducted from a single center.

Conclusion

In conclusion, as supported in this study, clinically, the course of psoriasis is usually milder in geriatric age group. More studies are needed to determine the best management of psoriasis in this patient group. Drug interactions and metabolism should be carefully managed in these patients.

Ethics

Ethics Committee Approval: This study was conducted in the dermatology clinic of a public university hospital and the study protocol was approved by the Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine Clinical Research Ethics Committee (number: 43710, date: 02.03.2021).

Informed Consent: Informed voluntary consent forms were obtained from the patients included in the study to use their information.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.K.U., S.G., B.E., Design: T.K.U., S.G., B.E., Data Collection or Processing: T.K.U., S.G., B.E., Analysis or Interpretation: T.K.U., S.G., A.Ö.E., B.E., Literature Search: T.K.U., S.G., Writing: T.K.U., S.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Tseng IL, Yang CC, Lai EC, Lee CN. Psoriasis in the geriatric population: A retrospective study in Asians. J Dermatol 2021;48:818-824.
2. van Winden MEC, ter Haar ELM, Groenewoud HMM, van de Kerkhof PCM, de Jong EMGJ, Lubeek SFK. Disease and Treatment Characteristics in Geriatric Psoriasis: A Patient Survey Comparing Age Groups. Acta Derm Venereol 2020;100:adv00215.
3. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clin Med (Lond) 2021;21:170-173.
4. Orimo H, Ito H, Suzuki T, Araki A, Hosoi T, Sawabe M. Reviewing the definition of "elderly". Geriatrics & Gerontology International 2006;6:149-158.
5. Di Caprio R, Caiazzo G, Cacciapuoti S, Fabbrocini G, Scala E, Balato A. Safety concerns with current treatments for psoriasis in the elderly. Expert Opin Drug Saf 2020;19:523-531.
6. Chularojanamontri L, Kulthanan K, Suthipinittharm P, Jiamton S, Wongpraparut C, Silpa-Archa N, Tuchinda P, Sirikuddta W. Clinical differences between early- and late-onset psoriasis in Thai patients. Int J Dermatol 2015;54:290-294.
7. Balato N, Patruno C, Napolitano M, Patrì A, Ayala F, Scarpa R. Managing moderate-to-severe psoriasis in the elderly. Drugs Aging 2014;31:233-238.
8. Kwon HH, Kwon IH, Youn JI. Clinical study of psoriasis occurring over the age of 60 years: is elderly-onset psoriasis a distinct subtype? Int J Dermatol 2012;51:53-58.
9. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, Gelfand JM. Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol 2017;76:377-390.
10. Armstrong AW, Armstrong EJ, Fuller EN, Sockolov ME, Voyles SV. Smoking and pathogenesis of psoriasis: a review of oxidative, inflammatory and genetic mechanisms. Br J Dermatol 2011;165:1162-1168.
11. Bakirtzi K, Sotiriou E, Papadimitriou I, Sideris N, Vakirlis E, Lallas A, Vrani F, Ioannides D. Elderly patients with psoriasis: long-term efficacy and safety of modern treatments. J Dermatolog Treat 2022;33:1339-1342.
12. Yosipovitch G, Tang MB. Practical management of psoriasis in the elderly: epidemiology, clinical aspects, quality of life, patient education and treatment options. Drugs Aging 2002;19:847-863.
13. Legiawati L, Astriningrum R, Yusharyahya SN, Chandrakesuma V. Sociodemographic and Clinical Characteristics of Geriatric Patients with Psoriasis Receiving Narrowband Ultraviolet B Phototherapy. Ann Geriatr Med Res 2020;24:290-296.
14. Bulur I, Erdogan HK, Aksu AE, Karapınar T, Saracoglu ZN. The efficacy and safety of phototherapy in geriatric patients: a retrospective study. An Bras Dermatol 2018;93:33-38.
15. Sandhu VK, Ighani A, Fleming P, Lynde CW. Biologic Treatment in Elderly Patients With Psoriasis: A Systematic Review. J Cutan Med Surg 2020;24:174-186.

16. Di Lernia V, Goldust M. An overview of the efficacy and safety of systemic treatments for psoriasis in the elderly. Expert Opin Biol Ther 2018;18:897-903.

17. Kostović K, Žužul K, Čeović R, Bukvić Mokos Z. Psoriasis in the mature patient: Therapeutic approach in the era of biologics. Clin Dermatol 2018;36:222-230.

18. Garber C, Plotnikova N, Au SC, Sorensen EP, Gottlieb A. Biologic and Conventional Systemic Therapies Show Similar Safety and Efficacy in Elderly and Adult Patients With Moderate to Severe Psoriasis. J Drugs Dermatol 2015;14:846-852.

19. Tsankov N, Angelova I, Kazandjieva J. Drug-induced psoriasis. Recognition and management. Am J Clin Dermatol 2000;1:159-165.

ORIGINAL ARTICLE

DOI: 10.4274/jtad.galenos.2023.28290
J Turk Acad Dermatol 2023;17(4):97-102

QuantiFERON-TB Gold Test Results in Patients with Psoriasis Receiving Biologic Therapy

Burhan Engin[1], Turana Mammadova[1], Şermin Börekçi[2], Beril Kara Esen[3]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey
[2]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Pulmonology, Istanbul, Turkey
[3]Republic of Türkiye Ministry of Health, Esenler District Health Directorate, Istanbul, Turkey

ABSTRACT

Background: Psoriasis is a chronic inflammatory disease of the skin, and to a lesser extent of the nails and joints, and has recently been recognized as a complex disease with systemic comorbidities. Recent breakthroughs in the treatment of psoriasis have led to significant improvements in the Psoriasis Area and Severity Index response and Dermatology Life Quality Index, but long-term survival and safety remain controversial. Although the risk of biological agents activating latent tuberculosis (TB) is low, it should not be ignored. This is especially important in Turkey where migration traffic is intense due to its geographical location. The aim of this study was to investigate the safety of biological agents in terms of latent TB infection during the initiation and follow-up of treatment in patients with moderate to severe psoriasis.

Materials and Methods: This retrospective, cross-sectional, single-center, hospital-based study included patients admitted to our department between 24.08.2017 and 24.12.2021 who were started on biological agents.

Results: The study included 187 patients. The mean age was 42.45±12.48 (16-74) years. Patients had a mean disease duration of 12.66 (3-32) years and 88.8% (n=166) were diagnosed with chronic plaque type psoriasis, 10.7% (n=20) with plaque + nail psoriasis, and 0.5% (n=1) patient with palmoplantar type psoriasis. Psoriatic arthritis was present in 17.6% of patients. Adalimumab was used as a biologic agent in 10.7%, ixekizumab in 35.3%, secukinumab in 31.6%, and ustekinumab in 22.5% of the patients. The mean duration of biologic agent use was 36.56 (12-61) months. Among the patients included in the study, 78.6% (n=147) had used methotrexate, 25.1% (n=47) cyclosporine and 15.55% (n=29) acitretin as conventional treatment agents. While the rate of patients with positive QuantiFERON test at baseline was 42.2% (n=79), the rates of those who became positive and negative during follow-up were 5.3% (n=4) and 11.8% (n=9), respectively. In two patients, the QuantiFERON-TB Gold (QFT) first became positive and then became negative again. The rate of patients with positive initial QFT test results was 42.2%, while the rate of patients who became negative during follow-up was 11.8%. There were no active TB cases. Of the 79 patients with positive QFT test results, 27.8% (n=22) had a negative QFT test result over time.

Conclusion: It could not be clarified whether this result of patients who became positive during follow-up but whose initial QFT test result was negative was due to false negativity due to previous immunosuppressive conventional treatment or due to the biological agent used. Recently, there are some confusing results regarding the reliability of QFT test results in latent TB infection screening. It should also be taken into account that seroreversion may be due to false QFT test positivity and that negativity during follow-up may be due both to this cause and to decreased QFT test sensitivity in isoniazid treated individuals.

Keywords: Quantiferon, Tuberculosis, Psoriasis, Biological agents, LTBI

Address for Correspondence: Burhan Engin, Prof. MD., Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology and Venereology, Istanbul, Turkey
Phone: +90 538 011 45 62 **E-mail:** bengin@iuc.edu.tr **ORCID ID:** orcid.org/0000-0002-5140-1926
Received: 21.11.2023 **Accepted:** 28.11.2023

Introduction

Psoriasis is a chronic inflammatory disease of the skin and to a lesser extent of the nails and joints [1]. The incidence of psoriasis varies in relation to age, gender, geographic region, ethnicity, genetic and environmental factors. The prevalence of the disease ranges from 0.27% to 11.4%. Epidemiological studies reported a latent tuberculosis infection (LTBI) prevalence rate of 5-22% in Italy, 10% in United Kingdom, 11% in Taiwan, and 20-29% in Spain, respectively, in psoriatic patients screened for tuberculosis (TB) [2,3].

Moderate to severe psoriasis has recently been recognized as a systemic disease due to its association with systemic comorbidities. It causes a great deal of psychosocial pressure in patients and has a negative effect on Dermatology Life Quality Index. Due to all these features, groundbreaking options have recently emerged in the treatment of the disease. The recent increase in the use of biological therapies is an example of this. Their use is more effective and safe in patients with moderate to severe psoriasis who do not respond to conventional treatments or for whom conventional treatments are contraindicated. Although biologic agents are target-oriented, their immunosuppressive effects should not be ignored. The risk of infectious diseases and TB activation should not be underestimated due to immunosuppressive effects. Patients who are candidates for biologic therapy, especially anti-tumor necrosis factor (TNF) agents, should be routinely evaluated for infections and TB before and during treatment [4]. Screening for TB infection should include a detailed medical history, chest radiography and tuberculin skin test or QuantiFERON-TB Gold (QFT) tests.

It is estimated that one-third of the world's population is infected with LTBI [5]. Although LTBI individuals are not infective, they may play a reservoir role in increasing the number of future TB incidence [6]. QFT test should be the first choice for LTBI screening in psoriasis patients for whom anti-TNF and other biologic agent therapy is indicated [4]. QFT test is more specific for LTBI screening and is not affected by Bacillus Calmette-Guerin vaccination or other atypical mycobacterial variants [7].

Materials and Method

Patients and Study Design

We retrospectively reviewed the electronic medical records of 187 patients who were admitted to our department between October 2016 and December 2022 and started biological agent treatments (adalimumab, ustekinumab, secukinumab, ixekizumab). Patients with active infection, premalignancy or malignancy and patients who did not meet the age criteria were excluded.

Demographic characteristics such as age, gender, personal medical history, disease duration, presence of psoriatic arthritis (PsA) and duration of drug exposure were reviewed. Conventional therapies [methotrexate (MTX), cyclosporine (CYC) or acitretin] used by the patients before the initiation of biologic therapy were recorded.

QFT test results were defined as baseline and follow-up QFT results during biological therapies; patients with positive QFT test or those who became positive later (seroconversion) were consulted to the pulmonology department, and isoniazid (INH) prophylaxis was started for 9 months after checking the results of chest radiography and thorax computer tomography. Biological treatment was stopped during the first month of INH treatment in patients with seroconversion.

This study protocol was reviewed and approved by the Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty Clinical Research Ethics Committee (decision number: 749867, date: 15.11.2022).

Statistical Analysis

SPSS v.21 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables were presented as mean ± standard deviation and median (interquartile range), categorical variables were presented with frequency and percentage. The variables were investigated using visual (histograms, Q-Q plots) and analytical methods (Shapiro-Wilk or Kolmogorov-Smirnov test) to determine whether or not they are normally distrubuted. Comparisons of the groups for continuous variables were made by one-way ANOVA or Kruskal-Wallis test. Chi-squared test was used to analyze categorical variables. Post-hoc analyzes were performed to test significance differences for multiple comparisons. All tests are two-sided and significance level was accepted as $p<0.05$.

Results

The study included 187 randomly selected patients, 75 females and 112 males. The mean age of the patients was 42.45±12.48 years. Patients had a mean disease duration of 12.66 (3-32) years and 88.8% (n=166) were diagnosed with chronic plaque type psoriasis, 10.7% (n=20) with plaque + nail psoriasis, and 0.5% (n=1) patient with palmoplantar type psoriasis. An additional 17.6% (n=9) of patients had PsA (Table 1).

Adalimumab was used as a biologic agent in 10.7% (n=20), ixekizumab in 35.3% (n=66), secukinumab in 31.6% (n=59) and ustekinumab in 22.5% (n=42) of the patients. The mean duration of biologic agent use was 36.56 (12-61) months. Among the patients included in the study, 78.6% (n=147) had used MTX, 25.1% (n=47) CYC and 15.5% (n=29) acitretin as conventional treatment agents (Table 1).

Patients on secukinumab had significantly longer duration of drug use than adalimumab and ustekinumab ($p<0.001$). The change in QFT test results during the follow-up period was not statistically significantly different among patients receiving four different drug groups ($p=0.601$) (Table 2).

The number of patients with a QFT at baseline was in 79 patients, of which 38% (n=30) were women and 62% (n=49) were men (Table 3). The rate of those who became positive during follow-up was 5.3% (n=4) and the rate of those who became negative was 11.8% (n=9). In two patients, the QFT was first positive and then negative again.

When sociodemographic characteristics were analyzed, there was no significant difference in age, gender, disease duration and baseline QFT positivity among patients who used different biologic agents. All patients with a positive QFT received INH prophylaxis and accounted for 46.5% (n=87) of the total patients.

Table 1. Sociodemographic characteristics

Feature n(%)	**n(%)**
Age (mean ± SD)	42.45±12.48
Gender	
Woman	75 (40.1)
Male	112(59.9)
Duration of illness (years) (mean ± SD)	12.66±7.58
Psoriasis	
Plaque	166 (88.8)
Plaque + nail	20 (10.7)
Palmoplantar	1 (5.0)
Psoriatic arthritis	33 (17.6)
QFT positivity	
Baseline (n=187)	79 (42.2)
1st year follow-up (n=187)	82 (43.9)
2nd year follow-up (n=177)	77 (41.2)
3rd year follow-up (n=122)	49 (26.2)
4th year follow-up (n=40)	17 (9.1)
5th year follow-up (n=7)	2 (1.1)
QFT test variation	
No change	153 (81.8)
Negativized	22 (11.8)
Becoming positive	10 (5.3)
Positive and then negative again	2 (1.1)
Biological agents	
Adalimumab	20 (10.7)
Ixekizumab	66 (35.3)
Secukinumab	59 (31.6)
Ustekinumab	42 (22.5)
Duration of use of biological agent (months) (mean ± SD)	36.56±11.03
Medication used	
INH (n=185)	87 (46.5)
MTX	147 (78.6)
Cyclosporine	47 (25.1)
Acitretin	29 (15.5)

SD: Standard deviation, QFT: Quantiferon test, INH: Isoniazid, MTX: Methotrexate

There was no statistically significant difference in terms of age and gender according to the change in the QFT results of the patients at follow-up (Table 4).

Among patients who had used MTX, 39.5% (n=58) had a positive QFT at baseline and 5.4% (n=8) became positive during follow-up. Among patients who had used CYC, 48.9% (n=23) had a positive test at baseline and 4.3% (n=2) became positive during follow-up. In patients who had used acitretin, 48.3% (n=14) had a positive QFT at baseline and 3.4% (n=1) became positive during follow-up (Table 5).

Discussion

TB is one of the infectious diseases with the largest reservoir, which is still persisting after many years. The LTBI's 2014 survey put the global burden of TB at 23%, which corresponds to 1.7 billion people. This figure corresponds to almost a quarter of the world's population [8].

In Turkey, the TB death rate (per 100,000 population) and incidence rate (per 100,000 population) in 2017 were 0.53 and 17, respectively. The total number of TB cases was 12,046 in Turkey in 2017 [9]. Due to such a large reservoir worldwide, it is recommended that patients receiving immunosuppressive treatment should be screened as a priority.

The basis of the pathogenesis of autoinflammatory diseases such as psoriasis is a risk factor for latent TB activation [10]. The discovery and increasingly frequent use of biological agents in the treatment of other inflammatory diseases, especially psoriasis, also poses a risk for LTBI. Therefore, LTBI screening before biologic agent treatment and annual routine controls have been included in the treatment protocol in psoriasis patients.

There are many studies on screening the QFT at the start and follow-up of biological therapy. When the existing studies are reviewed, there is no clear idea about the value of QFT results during follow-up [11].

In a study by Yuan et al. [12], patients with a positive interferon gamma release assay test were divided into 2 groups, those who received anti-TBC treatment and those who did not, and biologic treatment was initiated. In patients who did not receive prophylaxis, adverse events were higher at 24 week follow-up than at 12 week follow-up. In the group receiving prophylaxis, adverse events did not show a significant difference in the 12th and 24th week follow-ups. At the same time, the risk of consecutive active TB in the prophylaxis and non-prophylaxis groups was 13% and 27%. Relative risk=2.045, 95% confidence interval; p>0.05 was considered significant.

In a single-center 9-year retrospective study conducted by Megna et al. [13], QuantiFERON TB-Gold test conversion rates were 6.5% over a mean period of 3.2 years. Anti TNF-α seroconversion had the highest percentage (35.5% n=7). The lowest seroconversion rate was

Table 2. Sociodemographic characteristics according to biologic agents used

	Biological agents				
	Adalimumab	Ixekizumab	Secukinumab	Ustekinumab	p-value
	n=20	n=66	n=59	n=42	
Gender					
Woman	9 (45)	23 (34.8)	23 (39)	20 (47.6)	0.577*
Male	11 (55)	43 (65.2)	36 (61)	22 (52.4)	
Age	40.4±12.65	41.74±12.99	41.98±10.18	45.21±14.39	0.411**
Duration of Illness (years) (mean ± SD)	10.5 (6-19)	10 (6.75-17.25)	13 (8-20)	8.5 (6-14.25)	0.249***
Duration of use of biological agent (months) (mean ± SD)	24 (22.5-42)[a]	36 (27-45.75)[a,b]	39 (36-48)[b]	31 (24-38)[a]	**<0.001*** **
QFT positivity (Baseline)	8 (40)	29 (43.9)	25 (42.4)	17 (40.5)	0.982*
QFT change in follow-up					
Negativization	3 (15)	6 (9,4)	6 (10.2)	7 (16.7)	0.601****
Positivization	0 (0)	2 (3,1)	5 (8.5)	3 (7.1)	
No change	17 (85)	56 (87,5)	48 (81.4)	32 (76.2)	

*Chi-squared test, **One-way ANOVA, ***Kruskal-Wallis test, ****Fisher's Exact Test
Each different letter indicates columns that are statistically significantly different from each other.
The change in QFT test results during the follow-up period was not statistically significantly different among patients receiving four different drug groups (p=0.601). QFT: Quantiferon test, SD: Standard deciation

Table 3. Gender of patients according to baseline QFT result

	QFT positivity (baseline)		
	Negative	Pozitive	p-value*
	n=108	n=79	
Gender			
Woman	45 (41.7)	30 (38)	0.611
Male	63 (58.3)	49 (62)	

*Chi-squared test

Table 4. Age and gender of patients according to QFT change at follow-up

	QFT change in follow-up			
	Negativized	Positivized	No change	Becoming positive and then negative again
	n=22	n=10	n=153	n=2
Age	44.18±12.45	47.4±11.11	41.74±12.53	53.5±10.61
Gender				
Woman	6 (27.3)	5 (50)	63 (41.2)	1 (50)
Male	16 (72.7)	5 (50)	90 (58.8)	1 (50)

Table 5. Prior conventional treatments

	MTX treatment		Cyclosporine treatment		Acitretin treatment	
	Yes	No	Yes	No	Yes	No
Baseline QFT test (+)	58 (39.5)	21 (52.5)	23 (48.9)	56 (40.0)	14 (48.3)	65 (41.1)
Positive in follow-up	8 (5.4)	2 (5.0)	2 (4.3)	8 (5.7)	1 (3.4)	9 (5.7)

QFT: Quantiferon test, MTX: Methotrexate

14.7% (n=18) for anti-interleukin (IL)-17. There was no significant difference between the agents included in the biological classes. The study demonstrated the importance of LTBI screening even in Italy, which has a low rate of active TB.

In a single-center retrospective study conducted in Taiwan, which has a high TB case rate, the seroconversion rate was low (7.3%) in patients using IL-12/23 inhibitors during a 6-year follow-up [14].

In the 2021 World Tuberculosis Report, in a single-center retrospective study conducted in China, where 8.5% of all TB cases in the world and 50% of resistant strains were found, QFT conversion rates were 5.43% and 5.26% consecutively in patients receiving adalimumab and secukinumab as monotherapy at 17.13 months follow-up [15].

The rate of patients with positive QFT results at baseline was 42.2% (n=79), while the rate of patients who became negative during follow-up was 11.8% (n=22). Of the 79 patients with positive QFT results, 27.85% (n=22) had negative QFT results over time. In the first serial follow-up of QFT test results conducted by Akdogan et al. [11]. in Turkey, 34 (39.5%) of 86 patients with positive QFT results before the start of biology treatment showed seroreversion over time. But there was no mention of whether QFT seroreversion rates differed between groups. In the same study, there was no statistically significant difference between biologics in terms of the risk of QFT seroconversion (p=0.09). During follow-up, patients with negative initial QFT results became negative in the follow-up 2 years later and then seroconverted again. The rate of patients with a positive QFT test during follow-up was 5.3% (n=10). There was no statistically significant difference between both seroreversion and seroconversion rates in QFT test results during the follow-up period

in the biological agent groups included in our study (p=0.601). In a retrospective cohort study, it was shown that inflammatory diseases may be a factor in negative results in QFT test [16]. In our study, it was noteworthy that 39.5% (n=58) of patients using MTX were seropositive before the use of biological agents and seroconverted with a rate of 5.4% (n=8) during follow-up; among patients using CYC, 48.9% (n=23) had a positive test at baseline and 4.3% (n=2) became positive during follow-up. In patients using acitretin, 48.3% (n=14) had a positive QFT at baseline and 3.4% (n=1) became positive during follow-up. It could not be clarified whether the positive results during follow-up were due to false negativity in the initial negative QFT due to previous immunosuppressive conventional treatment or to the biological agent used. There were no active cases of TB.

The change in baseline and follow-up QFT results of the patients included in the study did not show a significant difference in terms of age and gender. The duration of drug survival was highest in patients on secukinumab. Although there was no significant difference between the agents, the rate of QFT test positivity was higher in the adalimumab group compared to the others. All patients with QFT results completed 9 months of INH treatment regardless of the biologic agent they used. Although there was no specific protocol, biologic agent treatment was given 1 month after INH initiation.

Study Limitation

Considering the geographical location of our country and the migration rate of immigrants, it is an inevitable result that we are among the endemic countries. Therefore, regardless of the LTBI activation rate of the biological agents used, screening for LTBI in every patient should be performed in a complex manner with detailed anamnesis, physical examination and chest radiography, not with QFT alone. Likewise, questioning of the patients, chest radiography and QFT test results should be performed without omission in the annual follow-up of the patient.

Conclusion

Positive QFT test observed during follow-up should be investigated in detail with the pulmonology department. In addition, it should be kept in mind that there may be false negativity at the beginning due to immunosuppressive conventional treatments used by the patients before the biologic agent. It should also be taken into account that seroreversion may be due to false QFT positivity and negativity during follow-up may be due to both this reason and decreased QFT sensitivity in patients receiving INH treatment.

Ethics

Ethics Committee Approval: This study protocol was reviewed and approved by the Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty Clinical Research Ethics Committee (decision number: 749867, date: 15.11.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.E., T.M., Design: B.E., T.M., Ş.B., Data Collection or Processing: T.M., Analysis or Interpretation: B.K.E., Literature Search: T.M., Writing: B.E., T.M.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM; Global Psoriasis Atlas. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ 2020;369:m1590.
2. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol 2013;133:377-385
3. Akyol M, Alper S, Atakan N, Bülbül Başkan E, Gürer MA, Koç E, Onsun N, Özarmağan G, Şentürk N, Yaylı S. Turkey Psoriasis Treatment Guide-2016. Turkderm-Turk Arch Dermatol Venereol 2016;50:1.
4. Megna M, Ferrillo M, Ruggiero A, Cinelli E, Gallo L, Fabbrocini G. QuantiFERON TB-gold conversion rate among psoriasis patients under biologics: a 9-year retrospective study. Int J Dermatol 2021;60:352-357.
5. Sotgiu G. Diagnosi e trattamento dell'infezione tubercolare latente [Diagnosis and treatment of latent tubercular infections]. G Ital Med Lav Ergon 2010;32:264-268.
6. Bautista J, Banaei N. Sensitivity of QuantiFERON-TB GOLD In-Tube for diagnosis of recent versus remote M. tuberculosis infection. Diagn Microbiol Infect Dis 2012;73:257-259.
7. Mazurek GH, LoBue PA, Daley CL, Bernardo J, Lardizabal AA, Bishai WR, Iademarco MF, Rothel JS. Comparison of a whole-blood interferon gamma assay with tuberculin skin testing for detecting latent Mycobacterium tuberculosis infection. JAMA 2001;286:1740-1747.
8. Houben RM, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. PLoS Med 2016;13:e1002152.
9. Karagoz A, Tutun H, Altintas L, Alanbayi U, Yildirim D, Kocak N. Molecular typing of drug-resistant Mycobacterium tuberculosis strains from Turkey. J Glob Antimicrob Resist 2020;23:130-134.
10. Cantini F, Nannini C, Niccoli L, Iannone F, Delogu G, Garlaschi G, Sanduzzi A, Matucci A, Prignano F, Conversano M, Goletti D; SAFEBIO (Italian multidisciplinary task force for screening of tuberculosis before and during biologic therapy). Guidance for the management of patients with latent tuberculosis infection requiring biologic therapy in rheumatology and dermatology clinical practice. Autoimmun Rev 2015;14:503-509.
11. Akdogan N, Dogan S, Gulseren D, Yalici-Armagan B, Ersoy-Evans S, Elcin G, Karaduman A, Atakan N. Serial Quantiferon-TB Gold test results in 279 patients with psoriasis receiving biologic therapy. Dermatol Ther 2021;34:e14699.

12. Yuan L, Li Y, Lin J, Lin X, Yang B, Man MQ, Wang X. Safety of Biologics for Psoriatic Patients with Latent Tuberculosis. Clin Cosmet Investig Dermatol 2023;16:2333-2336.

13. Megna M, Ferrillo M, Ruggiero A, Cinelli E, Gallo L, Fabbrocini G. QuantiFERON TB-gold conversion rate among psoriasis patients under biologics: a 9-year retrospective study. Int J Dermatol. 2021;60:352-357.

14. Hsiao CY, Chiu HY, Wang TS, Tsai TF. Serial QuantiFERON-TB Gold testing in patients with psoriasis treated with ustekinumab. PLoS One 2017;12:e0184178.

15. Xiao Y, Chen H, Zou Q, Wang Y, Gu Y, Wang J, Yan W, Li W. The Tuberculosis Positive Conversion Rate Among Psoriasis Patients Treated with Adalimumab and Secukinumab: A Single-Center Retrospective Study in China. Dermatol Ther (Heidelb) 2022;12:1493-1500.

16. Santos J, Duarte R, Nunes C. Interferon-Gamma release assay and tuberculin skin test: same purpose different problems. European Journal of Public Health 2018;28(suppl_4):cky218-cky141.

CASE REPORT

DOI: 10.4274/jtad.galenos.2023.85057
J Turk Acad Dermatol 2023;17(4):103-105

Angina Bullosa Hemorrhagica: A Case Report

Osmanege Atliya[1], Mahmut Esat Tanrıbilir[1], İrem Ayşe Karaköse[2], Esra Adışen[1]

[1]Gazi University Faculty of Medicine, Department of Dermatology, Ankara, Turkey
[2]Gazi University Faculty of Medicine, Medical Student, Ankara, Turkey

ABSTRACT

Angina bullosa hemorrhagica (ABH) is a self-limited oral blistering disorder that heals spontaneously within a few weeks. ABH has a benign nature and clinical diagnosis is usually straightforward. However, it should be differentiated from other bullous disorders affecting oral mucosa in some cases. In this case report, we presented a 57-year-old male patient diagnosed with ABH and revisited this rare entity with its diagnostic and clinical features.

Keywords: Oral mucosa, Hemorrhagic blister, Sudden onset, Bullous lesion

Introduction

Angina bullosa hemorrhagica (ABH) is a benign disorder characterized by sudden onset hemorrhagic bullous lesions that heal spontaneously within 1-2 weeks [1,2]. In this paper, we report a case of ABH presented to our clinic with recurrent hemorrhagic blisters in oral mucosa. Informed consent was obtained from the patient for this study.

Case Report

A 57-year-old man presented to our clinic with blood-filled blisters on the left side of his tongue. His lesions appeared as hemorrhagic bullae and slight erythema a few days ago without subjective symptoms. He had experienced similar lesions for the last 10 years, occurring 1-2 times per year and healing spontaneously. His lesions were triggered by hot drinks and smoking in previous episodes. In his past medical history; hypertension, ear eczema and left-sided direct inguinal hernia was present. Dermatologic examination revealed multiple hemorrhagic ulcers on the left side of tongue (Figure 1). To exclude other diagnoses; complete blood count, biochemistry, coagulation parameters, anti-nuclear antibody profile, erythrocyte sedimentation rate, complement levels, urinalysis tests were performed. His laboratory values were within normal range.

Based on his typical clinical history and examination findings, we diagnosed the patient as ABH. We prescribed benzydamine hydrochloride mouthwash twice a day for 1 week and advised him

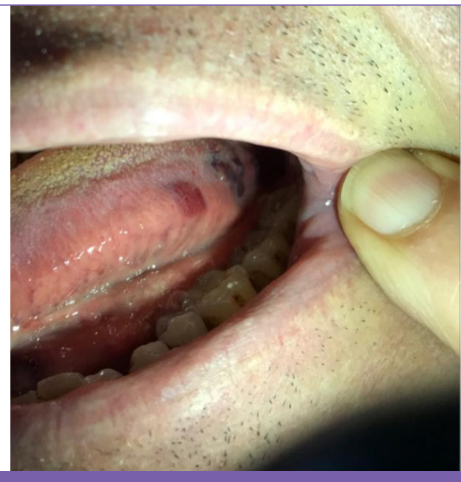


Figure 1. Ruptured hemorrhagic bullae on the left side of tongue

Address for Correspondence: Osmanege Atliya, Asst., Gazi University Faculty of Medicine, Department of Dermatology, Ankara, Turkey
Phone: +90 312 222 61 29 E-mail: osmanegeatliya@gmail.com ORCID ID: orcid.org/0000-0003-2185-6222
Received: 06.06.2022 Accepted: 11.04.2023

to avoid hot, spicy, crispy foods and quit smoking. Ten days later, his lesions healed completely (Figure 2).

Discussion

ABH is a self-limited disorder characterized by sudden onset hemorrhagic bullous lesions. Soft palate is the most commonly affected area; followed by buccal mucosa, lateral side of tongue and lip [1,2,3]. Very rarely, gingiva can be affected [4]. Lesions are usually painless; whereas, secondary to rupture of bullae, ulceration and pain may occur [2,5]. Oral cavity floor, esophagus, pharynx, epiglottis involvement can also be seen [5,6,7]. İncision of blisters may be necessary to prevent airway obstruction [2,8]. ABH is seen mainly in middle-aged people. It is reported almost equally in both genders, mean age of diagnosis is 54 [7,8].

Etiology of ABH is obscure. Loosening of cohesion between epithelium and mucosal dermis, and mucosal vascular abnormalities are proposed to play a role in pathogenesis. Hot, spicy foods; dental trauma, intubation, local anesthesia application, endoscopy, air travel are reported as triggering factors [3,5,7,8]. ABH is also more commonly reported in the premenstruation period of women [7].

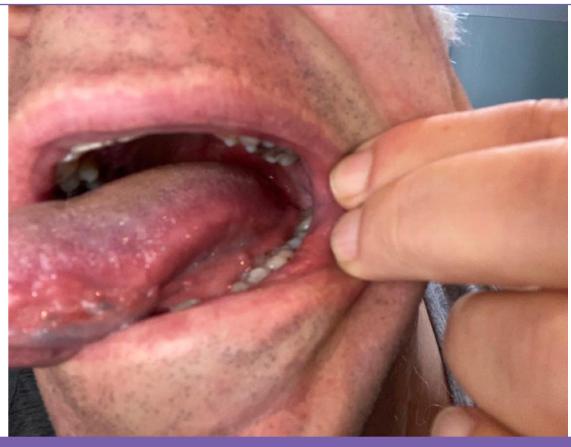


Figure 2. Completely healed lesions

Table 1. Angina bullosa hemorrhagica diagnostic criteria

1	Clinically notable hemorrhagic bulla or erosion with a history of bleeding of the oral mucosa
2	Exclusively oral or oropharyngeal location
3	Palate localization
4	Triggering event or food intake
5	Recurrent lesions
6	Favourable evolution without a scar within few days
7	Painless lesion, tingling or burning sensation
8	Normal platelet count and coagulation profile
9	Negative direct immunofluorescence

To diagnose angina bullosa hemorrhagica, at least 6 of 9 criteria positivity is required, with the presence of both 1st and 2nd criteria positivity are required

Inhaled steroid use (especially more than 5 years), hypertension, diabetes mellitus are major predisposing factors of ABH [7,8]. Long term use of inhaled corticosteroids can disrupt collagen and elastin formation, cause epithelial atrophy; and this can cause weakening and breaking down of capillaries [2,3].

Diagnosis can be made easily by typical clinical history. In some situations, exclusion of other disorders presenting with bullous lesions is necessary. Sudden onset, blood-filled tense blisters in soft palate are very typical findings of ABH. Most of the time, biopsy is unnecessary [1]. In order to diagnose ABH, nine criteria are proposed by Ordoni et al. [3] (Table 1) [9].

If biopsy is performed from blood-filled bulla, most common anatomic localization of detachment is at the subepithelial area. However, intramucosal and intradermal detachments are also reported in the literature [4]. At the surrounding tissue parakeratosis can be shown. In direct immunofluorescence immunoglobulin (Ig) G, IgA and C3 staining is not observed, which is helpful in differentiating from autoimmune bullous disorders [6].

There is no specific treatment of disorder. Mouthwashes or sprays containing chlorhexidine can be used for symptomatic relief. Ascorbic acid and citroflavonoid containing tablets can also be helpful [3,7].

Conclusion

ABH should be considered in patients presenting with sudden onset bullous lesions that heal spontaneously. Although this may be perceived as a fearful condition at first glance for both patient and clinician, ABH has a benign nature and heals spontaneously. Clinicians should be aware of this benign disorder and differentiate it from other oral blistering disorders.

Ethics

Informed Consent: Informed consent was obtained from the patient for this study.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.A., M.E.T., E.A., Concept: O.A., M.E.T., E.A., Design: O.A., M.E.T., E.A., Data Collection or Processing: O.A., M.E.T., İ.A.K., E.A., Analysis or Interpretation: O.A., M.E.T., İ.A.K., E.A., Literature Search: O.A., M.E.T., İ.A.K., E.A., Writing: O.A., M.E.T., E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Horie N, Kawano R, Inaba J, Numa T, Kato T, Nasu D, Kaneko T, Kudo I, Shimoyama T. Angina bullosa hemorrhagica of the soft palate: a clinical study of 16 cases. J Oral Sci 2008;50:33-36.
2. Yamamoto K, Fujimoto M, Inoue M, Maeda M, Yamakawa N, Kirita T. Angina bullosa hemorrhagica of the soft palate: report of 11 cases and literature review. J Oral Maxillofac Surg 2006;64:1433-1436.
3. Alberdi-Navarro J, García-García A, Cardona-Tortajada F, Gainza-Cirauqui ML, Aguirre-Urizar JM. Angina bullosa hemorrhagica, an uncommon oral disorder. Report of 4 cases. J Clin Exp Dent 2020;12:e509-e513.
4. Kurban M, Kibbi AG, Ghosn S. Expanding the histologic spectrum of angina bullosa hemorrhagica: report of one case. Am J Dermatopathol 2007;29:477-479.
5. Beguerie JR, Gonzalez S. Angina bullosa hemorrhagica: report of 11 cases. Dermatol Reports 2014;6:5282.
6. Giuliani M, Favia GF, Lajolo C, Miani CM. Angina bullosa haemorrhagica: presentation of eight new cases and a review of the literature. Oral Dis 2002;8:54-58.
7. Grinspan D, Abulafia J, Lanfranchi H. Angina bullosa hemorrhagica. Int J Dermatol. 1999;38:525-528.
8. Shoor H, Mutalik S, Pai KM. Angina bullosa haemorrhagica. BMJ Case Rep 2013;2013:bcr2013200352.
9. Ordioni U, Hadj Saïd M, Thiery G, Campana F, Catherine JH, Lan R. Angina bullosa haemorrhagica: a systematic review and proposal for diagnostic criteria. Int J Oral Maxillofac Surg 2019;48:28-39.

DOI: 10.4274/jtad.galenos.2023.35220
J Turk Acad Dermatol 2023;17(4):106-108

Lichenoid Drug Eruption Induced By COVID-19 mRNA Vaccine

Tuğcan Yüksek[1], Selda Pelin Kartal[1], Evrim Önder[2]

[1]University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Dermatology, Ankara, Turkey
[2]University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Pathology, Ankara, Turkey

ABSTRACT

Keywords: COVID-19, vaccine, mRNA, lichenoid reaction, drug eruption

Dear Editor,

As the worldwide vaccination campaign is going on rapidly against coronavirus disease-2019 (COVID-19) pandemic, the adverse cutaneous reactions are being studied extensively. While the most common cutaneous side effect is localized delayed injection-site reaction, there are different types of cutaneous reactions with different immunogenic mechanisms reported secondary to various COVID-19 vaccines [1]. Here in, we present a case of lichenoid drug eruption (LDE) in a male patient with no history of lichen planus (LP) occurred following administration of Pfizer-BioNTech (BNT162b2) mRNA COVID-19 vaccine.

A 57-year-old male patient with history of chronic hypertension treated with propranolol for 10 years, approached to our clinic with generalized itchy rash of 3-weeks duration. Detailed medical history revealed that he had the second dose of Pfizer-BionTech COVID-19 vaccine nine days prior to beginning of his complaints. The patient denied any additional medication use and a known history or any supporting symptom for COVID-19 preceding the skin eruption.

On physical examination, the patient was found to have multiple, slightly scaly, brownish-violaceous papules and plaques scattered mainly on the anterolateral sides of the trunk, back, flexural sides of both forearms and bilateral thighs (Figure 1A, B). There was no involvement of genital and oral mucosa or nails. Dermoscopic evaluation of the lesions revealed erythema, dotted vessels and scales whereas Wickham's stria was not observed. (Figure 1C). The differential diagnoses included LDE, LP, pityriasis rosea and secondary syphilis. Routine laboratory tests revealed no pathologic

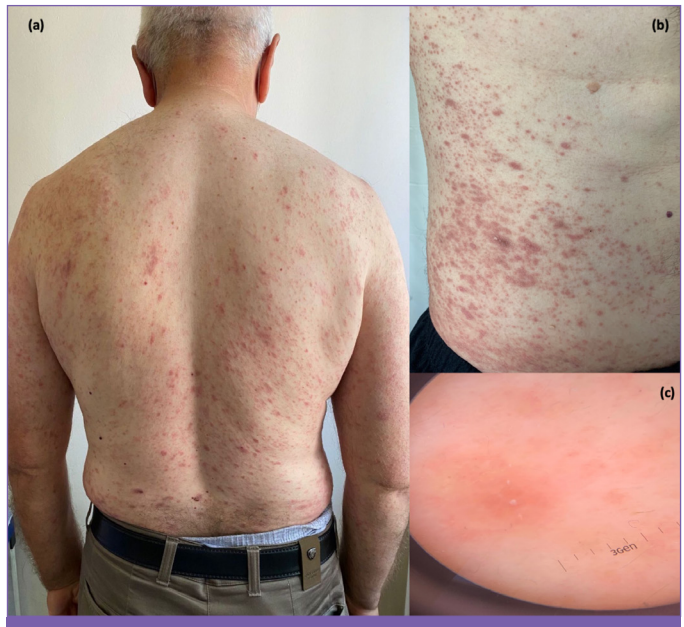


Figure 1. a) Symmetrical arrangement of violaceous papules and plaques on the back. b) Scaly, violaceous papules and plaques on the left flank. c) Dermoscopy: erythema, brownish pigmentation, dotted vessels, scales

Address for Correspondence: Tuğcan Yüksek, Asst., University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Dermatology, Ankara, Turkey
Phone: +90 312 596 12 18 E-mail: tugcanyuksek6@gmail.com ORCID ID: orcid.org/0000-0003-2612-8080
Received: 27.04.2022 Accepted: 29.09.2023

finding. Serology for Hepatitis B, C and human immunodeficiency virus, venereal disease research laboratory test and anti-nuclear antibody were normal. Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) polymerase chain reaction was tested negative.

Histopathological examination showed irregular acanthosis, dense lymphocytic infiltration at the dermoepidermal junction leading to separation of epidermis from the dermis, and few eosinophils (Figure 2A, B).

With clinicopathologic correlation, the patient was diagnosed as LDE triggered by COVID-19 vaccination. He was then administered 40 mg (0.5 mg/kg/daily) methylprednisolone combined with oral antihistamine and topical corticosteroids. Within a two-week period, as the patient's symptoms subsided significantly, methylprednisolone was tapered over 3 weeks. The patient's lesions were healed with post-inflammatory hyperpigmentation. During the 3-months of follow-up, the skin lesions did not recur. Written informed consent was obtained from the patient.

To date, as the mass vaccination against COVID-19 continues, various types of cutaneous reactions have been reported. Although delayed local injection site reactions are the most common type, urticaria, morbilliform rash, pernio/chilblains, pityriasis rosea-like reactions, dermal filler reactions, vasculitis, erythema-multiforme like rash are also well-recognized cutaneous reactions described following mRNA vaccines; Pfizer-BionTech or Moderna [2].

To our knowledge, lichenoid reactions secondary to COVID-19 vaccination is uncommon. Retrospective analysis of the case studies has shown that most of the reported cases were new-onset LP whereas LDE associated with COVID-19 vaccination is rarer (Table 1). In our case, the distribution and the morphology of the lesions,

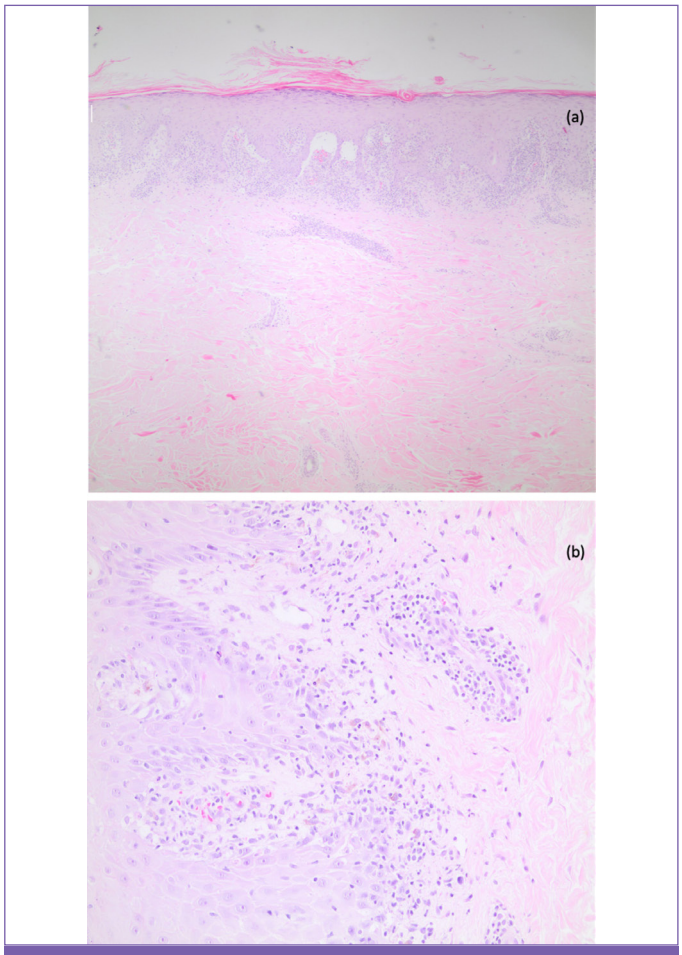


Figure 2. a) Epidermal acanthosis, dense lymphocytic infiltration at the dermoepidermal junction (H&E x40). b) Eosinophils and melanophanges accompanying lymphocytic infiltrate at the dermoepidermal junction (H&E x200)

Table 1. Characteristics of lichenoid reactions reported after COVID-19 vaccines

Patient	Age	Gender	Vaccine	Type of lichenoid reaction	Previous history	Time of onset after vaccination	Treatment given
1[1]	56	Female	BNT162b2	LP	Present	2 days	Topical corticosteroids
2[2]	56	Female	BNT162b2	LP	Absent	7 days	N/A
3[3]	35	Female	N/A	Oral LP[3]	Absent	14 days	N/A
4[4]	59	Female	BNT162b2	LP[4]	Present	14 days	Topical corticosteroids
5[5]	53	Female	BNT162b2	LDE	Absent	12 days	Topical corticosteroids, oral antihistamines, oral prednisone
6[6]	49	Male	Ad26.COV2.S	Oral LP	Absent	6 days	Topical corticosteroids
7[7]	64	Female	BNT162b2	LP	Absent	5 days, recurrence 1 day after second dose	Topical and systemic corticosteroids
8[8]	42	Female	BNT162b2	LS	Absent	3 days	Topical tacrolimus 0.1%
9[9]	65	Female	N/A	Oral LP	Present	N/A	N/A
10[10]	66	Male	AZD1222/ChAdOx1	LDE	Absent	5 days	Topical corticosteroids
11[11]	52	Female	BBIBP-CorV	LP	Absent	10 days	Topical corticosteroids, oral antihistamines

LP: Lichen planus, LDE: Lichenoid drug eruption, LS: Lichen striatus, N/A: Not applicable, COVID-19: Coronavirus disease-2019

absence of mucosal involvement and Wickham's stria and the presence of eosinophils in histopathological specimen led to the diagnosis of BNT162b2-induced LDE rather than LP [3].

LDE has been linked with a diverse group of medications. However, LDE triggered by vaccination is rather rare in literature. There are few cases described after Hepatitis B, influenza, Hepatitis A and human papillomavirus vaccinations [4,5].

Although, the exact mechanism is yet to be clarified, it has been suggested that the BNT162b2 vaccine prompts an upregulation of Th1 response, which increases the levels of proapoptotic Th1 cytokines; interleukin-2, interferon gamma, and tumor necrosis factor alpha that causes a lichenoid inflammation by inducing apoptosis of keratinocytes in the basal layer of the dermis [6].

It can also be postulated that spike protein, which is the target antigen of the SARS-CoV-2 mRNA vaccines have common epitopes with the basal keratinocytes that may cause an immune reaction by activating CD8+ auto-cytotoxic T lymphocytes. Also, it should be noted that, although it is more commonly associated with mRNA vaccines, there are cases of lichenoid reactions described with other types of vaccines including inactivated and vector-based vaccines as well (Table 1). In addition, in literature there are some cases of oral LP following COVID-19 infection. Therefore, it can be suggested that the direct immunogenicity of the viral component of the vaccines rather than a specific ingredient is more likely to be the triggering factor for the post-vaccine lichenoid reactions as there are cases reported with various types of vaccines with different adjuvants.

In conclusion, LDE can be seen as a rare cutaneous adverse reaction of the BNT163b2 mRNA COVID-19 vaccine. However, there are cases of lichenoid reactions associated with vector-based or inactive vaccines as well. Although the exact pathogenesis has not been clearly explained, it is likely that the viral component of the COVID-19 vaccines is the main triggering factor leading to a cell-mediated immune response by T lymphocytes. As the pandemic continues with emerging variants of SARS-CoV-2, sustaining the worldwide vaccination process is still crucial despite the potential side effects. Therefore, dermatologists should be eligible to diagnose and if required, treat the cutaneous adverse reactions related with COVID-19 vaccines. Also, it should be noted that it is important for dermatologists to examine vaccination history besides medication history in patients presented with clinical features of LDE.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.Y., S.P.K., Concept: T.Y., S.P.K., Design: T.Y., S.P.K., Data Collection or Processing: T.Y., E.Ö., Analysis or Interpretation: T.Y., S.P.K., E.Ö., Literature Search: T.Y., S.P.K., Writing: T.Y., S.P.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Niebel D, Novak N, Wilhelmi J, Ziob J, Wilsmann-Theis D, Bieber T, Wenzel J, Braegelmann C. Cutaneous Adverse Reactions to COVID-19 Vaccines: Insights from an Immuno-Dermatological Perspective. Vaccines (Basel) 2021;9:944.
2. McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, Desai SR, French LE, Lim HW, Thiers BH, Hruza GJ, Blumenthal KG, Fox LP, Freeman EE. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. J Am Acad Dermatol 2021;85:46-55.
3. Halevy S, Shai A. Lichenoid drug eruptions. J Am Acad Dermatol 1993;29:249-255.
4. Lai YC, Yew YW. Lichen planus and lichenoid drug eruption after vaccination. Cutis 2017;100:E6-E20.
5. Laschinger ME, Schleichert RA, Green B. Lichenoid drug eruption after human papillomavirus vaccination. Pediatr Dermatol 2015;32:e48-e49.
6. Sahin U, Muik A, Derhovanessian E, Vogler I, Kranz LM, Vormehr M, Baum A, Pascal K, Quandt J, Maurus D, Brachtendorf S, Lörks V, Sikorski J, Hilker R, Becker D, Eller AK, Grützner J, Boesler C, Rosenbaum C, Kühnle MC, Luxemburger U, Kemmer-Brück A, Langer D, Bexon M, Bolte S, Karikó K, Palanche T, Fischer B, Schultz A, Shi PY, Fontes-Garfias C, Perez JL, Swanson KA, Loschko J, Scully IL, Cutler M, Kalina W, Kyratsous CA, Cooper D, Dormitzer PR, Jansen KU, Türeci Ö. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses. Nature 2020;586:594-599.

2023 Referee Index

Algün Polat Ekinci
Bilal Doğan
Demet Kartal
Emine Gökcan
Güldehan Atış
Güllü Gencebay
Gürkan Yardımcı
Muazzez Çiğdem Oba
Özge Askın
Selda Pelin Kartal
Selma Emre
Tuğba Atcı
Tuğba Kevser Uzunçakmak
Tuğba Özkök Akbulut
Ümit Türsen
Zeynep Altan Ferhatoğlu

2023 Author Index

Ayşe Serap Karadağ ... 80
Ayşegül Satılmış ... 27
Ayşegül Yalçınkaya İyidal ... 22
Ayşenur Özdil Eser ... 92
Ayşenur Şam Sarı ... 31
Bengü Çobanoğlu Şimşek ... 80
Beril Kara Esen ... 97
Bilal Doğan ... 83
Bilun Reşit ... 50
Burhan Engin ... 10, 50, 59, 92, 97
Defne Özkoca ... 1, 18, 37
Dursun Dorukhan Altınışık ... 10
Dursun Türkmen ... 35, 46, 69
Esra Adışen ... 27, 103
Esra Fırat Oğuz ... 22
Evrim Önder ... 106
Fatma Bengisu Baran ... 69
Funda Erduran ... 22
Funda Eren ... 22
Gaye Güldiken ... 31
Güldehan Atış ... 31
Herman Saputra ... 54
İlayda İş Kılıç ... 27
İmge Durmaz ... 46
İrem Ayşe Karaköse ... 103
Kübra Nur Özcan ... 46
Mahmut Esat Tanrıbilir ... 103
Meryem Yüvrük ... 76
Muazzez Çiğdem Oba ... 1, 76
Muhammed Yasin Adıgüzel ... 69
Nasim Behkami ... 87
Nazlı Caf ... 18
Nebahat Demet Akpolat ... 83
Nihal Altunışık ... 35, 46, 69
Nyoman Suryawati ... 54
Osmanege Atliya ... 103
Özcan Erel ... 22
Özge Aşkın ... 37, 62
Özkan Sever ... 50
Petek Üstün ... 27
Selami Arslan ... 35, 69
Selda Pelin Kartal ... 106
Selim Gümüş ... 62, 92
Sera Nur Yücesoy ... 41, 59
Şermin Börekçi ... 97
Serpil Şener ... 46
Şıho Hidayet ... 69
Tuğba Kevser Üstunbaş Uzunçakmak ... 18, 41
Tuğba Kevser Uzunçakmak ... 1, 62, 80, 92
Tuğcan Yüksek ... 106
Turana Mammadova ... 97
Yıldız Hayran ... 22
Zekayi Kutlubay ... 18, 41, 83
Zeynep Altan Ferhatoğlu ... 50, 87

2023 Subject Index

Acne ... 10
Adnexal tumors ... 76
Alcohol consumption ... 92
Alopecia areata ... 62
Androgenetic alopecia ... 69
Anti-aging ... 37
Antifungal ... 83
Atopic dermatitis ... 18
Azathioprine ... 41
Balanitis ... 1
Bioelectrical impedance ... 69
Biologic agents ... 80, 92
Biological agents ... 97
Body mass index ... 50
Bullous ... 27
Bullous lesion ... 103
Bullous pemphigoid ... 41
Bullous skin disorders ... 41
Ceruloplasmin ... 22
CIMT ... 69
Clinicopathologic correlation ... 76
Collagen ... 37
Comorbidity ... 92
Conventional treatments ... 92
COVID-19 ... 27
COVID-19 vaccine ... 35
Dermatology ... 80, 92
Dermatology Quality of Life Index ... 87, 106
Dermoscopy ... 54
DLQI ... 87, 106
Dyspareunia ... 1
Dysuria ... 1
EFT ... 69
Facial erythema ... 10
Fissures ... 1
Genital ... 1
Geriatric ... 92
Hair follicle ... 76
Hemorrhagic blister ... 103
Herpes zoster ... 35
Hidradenitis suppurativa ... 50
Histopathology ... 54
Hurley stage ... 50
Immunohistochemistry ... 54
Immunosuppressant ... 59
Inflammation ... 92
Internet ... 62
Lentigo ... 80
Low dose ... 18
LTBI ... 97
Lupus erythematosus ... 10
mRNA vaccine ... 35
Nail ... 46
Nail psoriasis ... 92
Nevus sebaceus ... 31
New ... 27
Onset ... 27
Onychomycosis ... 22, 46
Oral mucosa ... 103
Oxidative stress ... 22
Pemphigoid ... 27
Pemphigus vulgaris ... 41
Phototherapy ... 18, 87, 106
Pilomatricoma ... 76
Premalignant ... 1
Psoriasis ... 35, 80, 92, 97
Psoriatic arthritis ... 92
Pustular psoriasis ... 59
Q-switched Nd:YAG laser ... 46
Quantiferon ... 97
Red face ... 10
Rosacea ... 10
Sebaceous ... 76
Secukinumab ... 80
Smoking ... 50, 92
Social media ... 62
Squamous cell carcinoma ... 1
Sudden onset ... 103
Superficial fungal infections ... 83
Supplementation ... 37
Sweat gland ... 76
Telangiectasia macularis eruptiva perstans ... 54
Temporal triangular alopecia ... 31
Treatment ... 59, 83
Trichoscopy ... 31
Tuberculosis ... 97
UVA-1 ... 18
Vaccine ... 27
Visceral fat ... 69
Vulvar dermatosis ... 1
Vulvar disease ... 1
VZV ... 35
Zona ... 35