Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report

Paraneoplastic Pemphigus Accompanying Nerve Sheath Sarcoma: A Case Report

Hossein Kavoussi*, MD, Hamid Madani**, MD,
Seyed Mohammadali Hesami***, MD, Ali Ebrahimi*, MD

Address: *Assistant Professor of Dermatology , Kermanshah University of Medical Sciences
**Associate Professor of Pathology; Molecular Pathology Research Center, Kermanshah University of Medical Sciences
***Assistant Professor of Thorasic Surgeon, Kermanshah University of Medical Sciences
E-mail: hkawosi@kums.ac.ir
** Corresponding Author:* Dr Hossein Kavoussi, Golestan Blvd, Hajdaie Dermatology Clinic, Kermanshah, Iran

Published:
J Turk Acad Dermatol 2011; **5 (4)**: 1154c4
This article is available from: http://www.jtad.org/2011/4/jtad1154c4.pdf
Key Words: Paraneoplastic pemphigus, erythroderma, nerve sheath sarcoma

Abstract

Observation: Paraneoplastic pemphigus is a rare immunobullous disease which is associated with an underlying neoplasm. Herein, a case of paraneoplastic pemphigus induced by nerve sheath sarcoma as a rare underlying neoplasm is presented. Our patient had an unusual clinical course and his neoplasm developed 26 months after mucocutaneous disease. In addition to vesiculobullous, erosive and lichenoid lesions, the patient showed erythroderma, which is a very rare cutaneous manifestation of paraneoplastic pemphigus.

Introduction

Paraneoplastic pemphigus (PNP) is an immunobullous disorder which is almost exclusively associated with an underlying malignancy. PNP is diagnosed on the basis of clinical, histopathological and immunofluorescence specific findings as well as detection of antibody against autoantigen [1].

Patients with PNP experience severe painful erosions in oral cavity besides other cutaneous findings, ranging from erosions to targetoid lesions and lichenoid eruptions [2].

The most common hisopathologic finding is suprabasal acantholytic vesiculation with dyskeratosis besides vacuolar interface dermatitis with or without lichenoid inflammation [3].

Direct immunofluorescence study of perilesional skin and mucosa shows IgG in squamous intercellular space along with deposition of immune reactant at dermal-epidermal junction. Granular deposition of complement is most commonly seen at dermal-epidermal junction [4].

Although indirect immunofluorescence study on murine bladder epithelium is enough for PNP screening, sensitivity and spe-

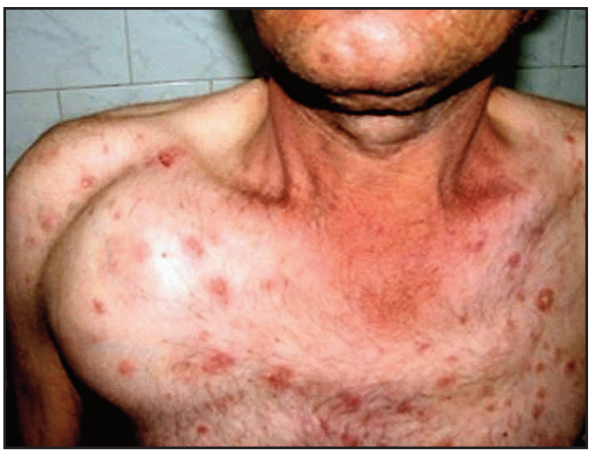

Figure 1. Tumoral mass in right side of chest wall besides generalized erosion

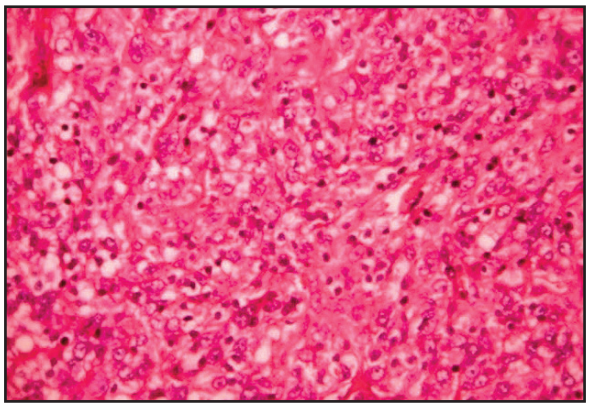

Figure 2. Pleomorphic epithelioid-like cells with large nucleoli (H&E, X400)

cificity of this test are about 75% and 83% respectively [**1**].

Target autoantigens of PNP include cytoplasmic protein of the plakin gene family, desmosomal cadherins, bullous pemphigoid antigen2 and an undetermined 170-kD transmembrane antigen [**5**].

Herein, we report a case initially diagnosed as pemphigus vulgaris based on clinical manifestations, histopathologic features, direct and indirect immunofluorescence findings and detection of anti-desmoglein 1, 3. However, a sarcoma with nerve sheath origin in right chest wall, erythroderma and lichenoid lesion diagnosed as PNP was detected in this case 26 months later.

Case Report

The patient was a 49-year-old man who was admitted 30 months ago to the dermatology ward for

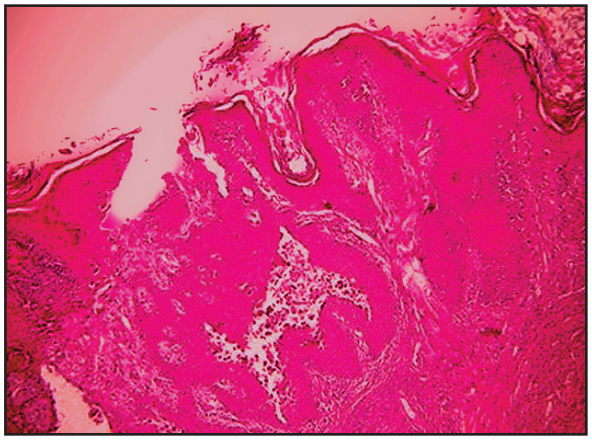

Figure 4. Intraepidermal blister and villi formation (H&E,X100)

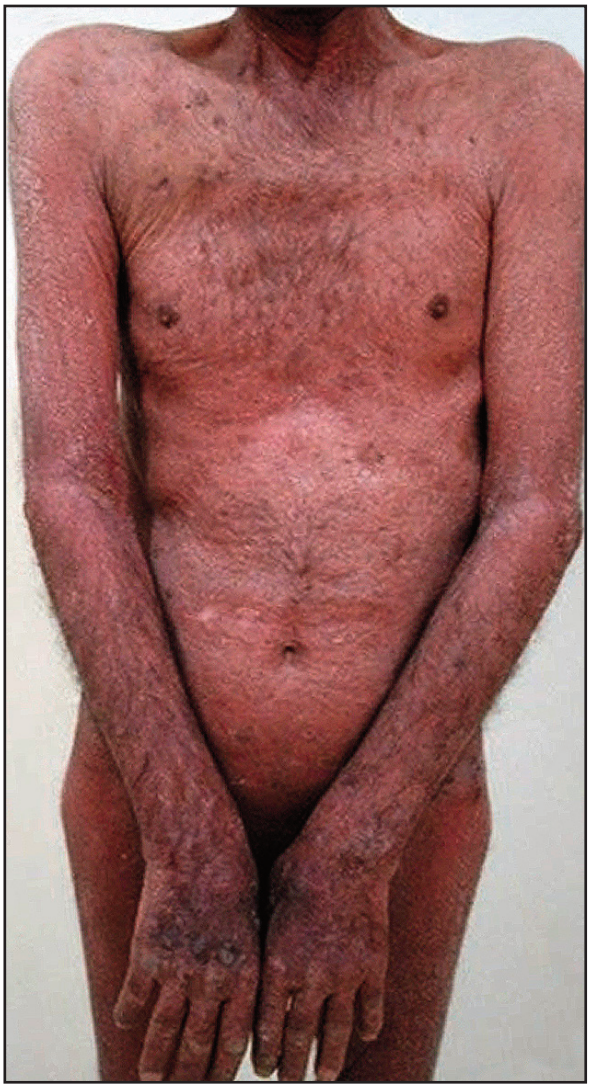

Figure 3. Erythroderma and lichenoid lesions in dorsum of hands

definite diagnosis two times. In spite of the preferred treatment, his disease was uncontrolled and presence of a malignancy seemed possible. According to the recorded information in hospital file, his disease was diagnosed as pemphigus vulgaris at first, based on clinical, histopathological and immunofluorescence findings as well as ELISA positivity of anti-desmoglein 1,3 antibody.

During treatment with high dose prednisolone and azathioprine oral erosions did not show complete improvement. On the other hand, when prednisolone was tapered (below 30 mg daily), disease relapsed with cutaneous new lesions. Nonetheless, laboratory and paraclinical assesments did not show any malignancy.

Four months ago he noticed a mass in front of the upper right side of the chest wall (**Figure 1**). In

magnetic resonance imaging (MRI) it was revealed to be a soft tissue mass with homogenous density and without any pleural connection. Biopsy was taken from tumor and histopathology findings were compatible with malignant soft tissue sarcoma (**Figure 2**). Immunohistochemistry findings were mostly in favor of nerve sheath origin of the tumor cells (EMA: negative, cytokeratin: negative, vimentin: positive in tumor cells, desmin: negative, SMA: positive in small number of tumor cells, S100: positive in nucleus and cytoplasm of the most of tumor cells, CD34: negative in tumor cells).

Three months later, he gradually showed other cutaneous manifestations such as lichenoid lesions on the dorsum of hands and lips, and generalized erythematous scaly patches that became gradually confluent and converted to erythroderma (**Figure 3**).

Histopathologic findings of lichenoid lesion of dorsum of hand showed typical intraepidermal blister containing acanthocytes. Dyskeratotic keratinocytes were also present and villi forms from the underlying dermal papillae typically projected into suprabasal cavity that was compatible with PNP (**Figure 4**). However, histopathologic examination of erythrodermic skin of abdomen showed hyperkeratosis and slight acanthosis with scattered perivascular lymphocytes.

Patient gradually complained of breath shortness and progressive dyspnea. He and his family did not allow further assessments and evaluations because of his disability and severity of disease. Besides, advanced laboratory techniques such as immunoblotting and immunoprecipitation for detection of plakin family of epithelial protein and other autoantiabodies did not exist in this area. Death occurred out of hospital and we suspect that the cause of mortality was respiratory failure.

According to our findings and the data recorded in hospital files, our patient suffered most probably from PNP in association with nerve sheath sarcoma.

Discussion

The PNP reported herein is interesting because of its unusual clinical course, and being associated with a very rare malignancy and erythroderma.

PNP occurs usually at the presence of an existing neoplasm. Indeed, the neoplasm is diagnosed after presentation of the mucocutaneous disease only in one-third of PNP cases [**6**].

Our patient was admitted two times to the dermatology ward 30 months ago for making a definite diagnosis and finding the probable underlying disorder. Although careful evaluation to detect a probable underlying disorder was negative, association of a malignancy was shown later.

In a previous study which included 163 PNP cases and was performed between 1990 and 2003, 84% of patients had hematologic related neoplasms or disorders that non-Hodgkin lymphoma (38.6%) as the most frequent and non-hematologic neoplasm comprised 16% of all cases. Sarcoma comprised 6.2% of all cases that consists of one case as nerve sheath sarcoma [**7**] and in very rare case no identified neoplasm [**8**].

Underlying disorder in our patient was malignant nerve sheath tumor confirmed by histopathological and immunohistochemical studies. This malignancy is a rare underlying neoplasm associated with PNP.

To date, only two cases of PNP associated with erythroderma have been reported and both cases had anti-desmoglein 1 antibody [**9, 10**].

Our patient initially showed generalized blistering and erosion of skin and oral cavity. Various other cutaneous findings such as lichenoid lesion in dorsum of hands and lips, generalized erythematous scaly patches that became confluent later and converted to erythroderma were also observed.

In conclusion, PNP is a heterogenic autoimmune disorder that has different clinical presentations related to stage of disease, underlying disorder, type of autoantibody and other unknown factors. Therefore, it seems that erythroderma is seen in a special type of PNP and hence, PNP can be considered as one of the causes of erythroderma.

References

1. Anhalt GJ, Nousar CH. Paraneoplastic pemphigus: In: Fitzpatricks dermatology in general medicine. Wolf K, Lowell AG, Goldsmith LA, Katz SL, Gilcherest AS, Leffell DJ, eds. 7th ed. New York: McGraw Hill, 2008; 468-474.
2. Billet SE, Grando SA, Pittelkow MR. Paraneoplastic autoimmune multiorgan syndrome: review of the li-

terature and support for a cytotoic role in pathogenesis. Autoimmunity 2006; 39: 617-630. PMID: 17101506

3. Wu H, Branding-Bennett HA, Harrist TJ. Noninfectious vesiculobullous and vesiculopustular disease: In: Lever's histopathology of the skin. Elder DE, Elenitsas R, Johnson BL, Murphy GF, Xu X, eds. 10th ed. Philadelphia: Lippincott Williams& Wilkins, 2009; 235-278.
4. Anhalt GJ, Kim SC, Stanley JR, Korman NJ, Jabs DA, Kory M, et al . Paraneoplastic pemphigus: an autoimmune disease associated with neoplasia. N Engl J Med 1990; 323:1729. PMID: 2247105
5. Preisz K, Karapati S. Paraneoplastic pemphigus. Orv Hetil 2007; 148: 979-983. PMID: 17513251
6. Robinson ND, Hashimato T, Amagai M. The new pemphigus variants. J Am Acad Dermatol 1999; 40: 694-671. PMID: 10321591
7. Kaplan I, Hodak E, Akerman L, Mimouni D, Anhalt GJ, Galderon S. Neoplasm associated with paraneoplastic pemphigus: a review with emphasis on non-hematologic malignancy and oral mucosal manifestation. Oral Oncol 2004; 40: 553-562. PMID: 15063382
8. Ostezan LB, Fabre VC, Caughman SW, Swerlick RA, Korman NJ, Callen JP. Paraneoplastic pemphigus in the absence of a known neoplasm. J Am Acad Dermatol 1995; 33: 312-315. PMID: 7622665
9. Fukumoto T, Shiroyama Y, Niizeki H, Koboyashi N, Sada H, Ishii N, et al. Paraneoplastic pemphigus as erythrodermic lichenoid dermatitis with concomitant feature of pemphigus foliaceus. J Dermatol 2007; 34: 645–649. PMID: 17727368
10. Martel P, Gilbert D, Labeille B, Kanitakis J, Joly P. A case of pareneoplastic pemphigus with antidesmoglein 1 as determined by immunoblotting. Br J Dermatol 2000; 142: 812–813. PMID: 10792239.