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

Case Report DOI: 10.6003/jtad.1373c1

Overlap-Syndrome: Association of Olygosymptomatic *Melkersson-Rosenthal* Syndrome due to Recurrence of HSV-infection and Raynaud's Syndrome in Young Woman with Chronic Eczema of Palms. A Review of the Literature and Case Report

Irina Alexandrovna Amirova,[1] MD, Ilkin Zafar oglu Babazarov,[2*] MD

Address: [1]Department of Dermatology and Sexually Transmitted Diseases of Azerbaijan Medical University, Baku, Azerbaijan, [2]Department of Dermatology of Shirvan Central City Hospital, Shirvan, Azerbaijan

E-mail: babazarov@gmail.com

** Corresponding Author:* Dr. Ilkin Zafar oglu Babazarov, Department of Dermatology of Shirvan Central City Hospital, Shirvan, Azerbaijan

Published:
J Turk Acad Dermatol 2013; **7 (3)**: 1373c1
This article is available from: http://www.jtad.org/2013/3/jtad1373c1.pdf
Key Words: *Melkersson-Rosenthal* Syndrome, *Raynaud* syndrome, overlap-syndrome, dishydrotic eczema, HSV-infection

Abstract

Observations: *Melkersson-Rosenthal* Syndrome (MRS) is a rare or rarely recognized chronic relapsing systemic granulomatous disorder, usually involving lips (relapsing granulomatous cheilitis), facial nerve (recurrent palsy or paresis) and tonque (lingua plicata). However this disorder has three forms: classical (complete) form of MRS presenting with characteristic triad but there is also olygosymptomatic (presence of two symptoms macrocheilitis and one of another symptoms) and monosymptomic form presenting only as macrocheilitis, known as granulomatous cheilitis of *Miescher*. The authors describe the olygosymptomatic MRS in young women 23 year old due to recurrence of HSV-infection in association with Raynaud syndrome and dishydrotic eczema of right palm. To the best of author's knowledge this is a first case of association *Melkersson-Rosenthal* Syndrome and *Raynaud* syndrome. The authors hope that this article will be helpful for physicians in daily practice.

Introduction

Melkersson-Rosenthal Syndrome (MRS) is a rare or rarely recognized chronic relapsing systemic granulomatous disorder, usually involving lips (relapsing granulomatous cheilitis), facial nerve (peripheral recurrent palsy or paresis) and tongue (lingua plicata). This is a classical (complete) form of MRS presenting with characteristic triad but there is also incomplete - olygosymptomatic and monosymptomic form presenting as only macrocheilitis. The most frequent monosymptomatic form is granulomatous cheilitis (GC) [**1**], described by *Meischer* in 1945, which is defined as painless chronic isolated enlargement of one or both lips due to granulomatous inflammation with a recurrent to gradually persistent course. Histopathologic examination reveals focal non-

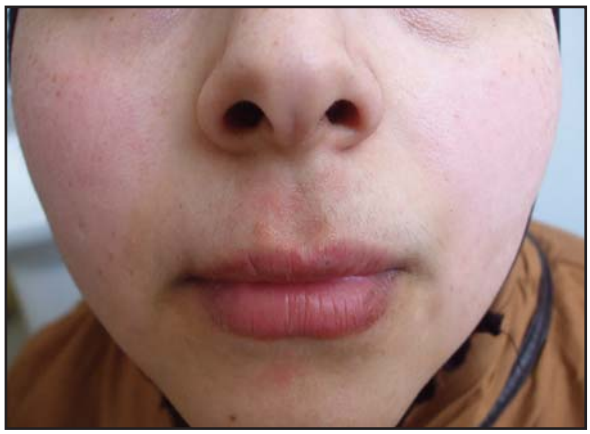

Figure 1. Swollen lips

Figure 2. *Raynaud*'s syndrome

caseating epitheloid cell granulomas with lymphocytes and plasma cells.

But classical MRS is very rare entity, instead mono- and olygosymptomatic MRS is more frequent. Therefore, diagnosis of this incomplete presention of MRS is difficult.

The presence of two or one of the manifestations mentioned above, with granulomatous cheilitis in the biopsy, is sufficient to make the diagnosis of oligosymptomatic or monosymptomatic form of MRS [**2, 3, 4, 5**].

Case Report

We present the case of 23 years old white Caucasian female seller with *Raynaud*'s syndrome complained of a non painful swelling of the upper and lower lip, that had persisted nearly for two years (**Figure 1**). During this period, the symptoms had recurrent-remittent course, but there is no complete remission. She also marks manifestations of the *Raynaud*'s syndrome in a kind change of coloring of fingers

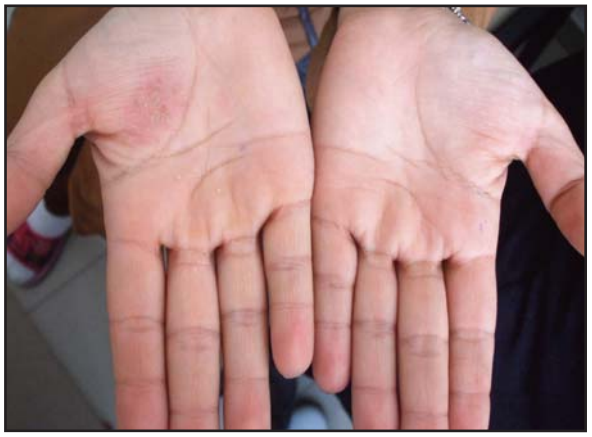

Figure 4. Plaque with scale and crusted surface

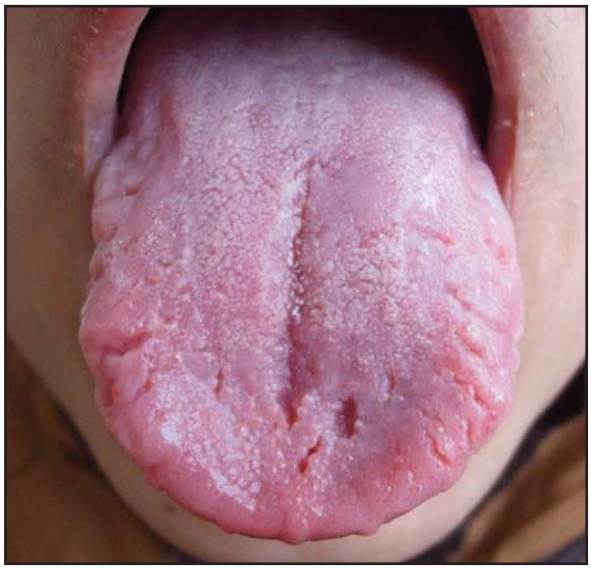

Figure 3. Fissured tongue

(blanching replaced by reddening) under the influence of a cold and emotional stress (**Figure 2**).

Physical examination revealed swollen erythemathous upper and lower lip, herpetic eruption on upper lip, fissured tongue (**Figure 3**), plaque with abrupt margins, scale and crusted surface within right palm (**Figure 4**). Mild cervical lymphadenopathy was also revealed. In other the physical examination revealed no pathologic signs.

Careful analysis of anamnesis morbi revealed the episodes of eyelid, buccal and lip edema, which sometimes were isolated or combined with edema of other sites. Patient denied any allergic disease and reaction, drug allergy, trauma, or past history of any injuries and any bowel pathology. Familial anamnesis revealed no similar condition or hereditary pathology in family members.

A blood work up including a hemoglobin, hemotocrit, RBC, WBC and blood biochemistry resulted (glucose, ALT, AST, ALP, GGT, serum creatinine, urea) in the normal ranges. An acute phase markers slightly elevated: ESR 30 mm/h and CRP (+++). P-ANCA, C-ANCA, ANA, RF, cryoglobulins were all negative. A serology for sexually transmitted diseases, viral hepatitis (VDRL, TPHA, HBsAg, Anti-HBc, anti-HIV, anti-HCV), TORCH, antibodies against streptococcus, EBV (*Epstein-Barr* virus) and *Write* reaction for brucellosis were negative. But only anti-HSV-1-IgG is positive and retesting in a two weeks revealed 5 times increasing anti-HSV-IgG titers. A urine analysis revealed no changes. PPD (purified protein derivative) was negative. Abdominal ultrasound and chest X-ray examination revealed no pathology.

Unfortunately the patient has disagreed carrying out a biopsy.

Based on anamnesis, clinical, radiologic and laboratory data, we diagnosed this case as overlap-syndrome: incomplete olygosymptomatic MRS, Raynaud's syndrome, exacerbation of HSV-infection, chronic eczema of palms.

Patient admitted acyclovir 200 mg five times daily, unguentum acyclovir 5 times daily. Roxythromycine 150 mg twice daily. Pentoxifilline 200 mg three times a day. Lymphomyosot on one injection every other day. Group B vitamins. Placenta compositum on one injection every other day. Against treatment the symptoms gradually regressed and did not renew during 9 monthly period of observation.

Discussion

Melkersson syndrome was described in 1928 as peripheral facial nerve palsy (FNPP) and swelling of the lips [**6**]. *Rosenthal*, in 1930, observed 5 patients with association of persistent macrocheilia, peripheral facial palsy and fissured tongue included the presence of a fissured tongue, completing the triad which defines the syndrome [**7**]. In 1945, *Meischer* described a variant of MRS - presence of granulomas of lip with marked lip swelling as cheilitis granulomatosa [**8**].

MRS is a systemic neuro-mucocutaneous granulomatous disease. Because of noncaseating, sarcoidal character of granulomatous inflammation viewing histologically MRS is placed in the same group of granulomatous diseases such as sarcoidosis and *Crohn*'s disease [**2, 4**].

MRS begins abruptly usually from macrocheilitis of granulomatous origin, which is cardinal symptom of this disorder. Generally, the first and most common manifestation of MRS (75% of the cases) is a non painful swelling of the upper lip, with increase in consistency and without pruritus. The lower lip is less frequently involved [**4, 5**]. The first episode of labial edema often resolves within a period of a few hours or a few days, raising the problem of differential diagnosis with angioedema. Subsequent episodes of edema appear at more irregular intervals and may become persistent [**2, 4**].

The interested lip may present fissures in the central part (central cheilitis), at the corners of the mouth (angular cheilitis/ angular stomatitis) or in other sites [**5**]. In this condition edema usually becomes painful.

Many clinical variations of MRS with different localization of granulomatous inflammation with edema of different severity were described. Other than the lips, the disease can involve eyelids, cervix, auditory channel resulted in hearing loss, the oral cavity, gingival, upper airways, gums, tongue, palate, pharynx and larynx, and these may present erythema, erosions, ulcerations or small pustules [**4, 9, 10**]. The buccal mucosa may also swell, folding itself to give a "cobblestone" aspect [**9**]. Some authors affirm that these manifestations precede those at the orofacial region by many weeks [**9, 10**]. Intermittent swelling of the auditory channel can be a cause of hearing loss [**11**].

Although orofacial swelling is most common manifestation of MRS, several cases of combined or isolated eyelid involvement described in the literature. MRS presented with painless, nonpitting, bilateral asymmetric upper eyelid edema was described [**12**]. MRS should be considered in patients presenting with eyelid edema of unknown etiology and biopsy performed [**13**].

Familial cases of MRS has been also described by *Goto* et al [**14**].

In usually cases FNPP is the second sign of the triad characterizing MRS. It occurs in 30-35% of cases and is indistinguishable from *Bell*'s palsy [**15, 16**]. Although FNPP is able to be a first symptom of MRS extremely rare. It is initially intermittent, but may later become permanent. It may be unilateral, bilateral, partial or complete. This paralysis is due to granulomatous infiltration of the nerve and its sheath or to its compression by tissue edema as the nerve passes through the facial canal within the temporal bone [**5, 11**].

The third sign of MRS is the presence of a fissured tongue or "lingua plicata". It is observed in 20-70% of adult cases [**4, 10**], whereas in pediatric age this symptom is present in only 30% of the cases [**10**]. It can be associated with a burning sensation and dysgeusia (if affects 2/3 of the anterior part of the tongue). Resolution is spontaneous in about 10% of the cases [**2, 5**]. However, lingua plicata has been described as a common anomaly in the general population, making it less significant in the diagnosis of MRS [**4**].

Different associations of MRS with other conditions were described in literature, such as the macrocheilia of MRS associated with Down syndrome or with Ehlers-Danlos syndrome [**17, 18**].

Conclusion

To the best of our knowledge this is a first case of association *Melkersson-Rosenthal* syndrome and *Raynaud*'s syndrome.

Because of its rarity, the syndrome is usually ignored and misdiagnosed; however, the syndrome should not only be considered in the classic perioral presentation but also in the rare periocular form, which may be confused with orbital tumors and orbital pseudotumors [**19**]. We hope that this article will help our colleagues with their daily medical practice.

References

1. Greene RM, Rogers RS 3rd. Melkersson-Rosenthal Syndrome: A review of 36 patients. J Am Acad Dermatol 1989; 21: 1263-1270. PMID: 2584463
2. Ziem PE, Pfrommer C, Goerdt S, Orfanos CE, Blume-Peytavi U. Melkersson-Rosenthal syndrome in childhood: a challenge in differential diagnosis and treatment. Br J Dermatol 2000; 143: 860-863. PMID: 11069473
3. Camacho-Alonso F, Bermejo-Fenoli A, Lopez-Jornet P. Miescher's cheilitis granulomatosa. A presentation of five cases. Med Oral Pathol 2004; 9: 425-429. PMID: 15580120
4. Van der Waal R, Shulten E, Van de Scheur MR,Wauters I, Starink TM, Van der Waal I. Cheilitis granulomatosa. J Eur Acad Dermatol Venereol 2001; 15: 519-523. PMID: 11843210
5. Sciubba JJ, Said-Al-Naief N. Orofacial granulomatosis: presentation, pathology and management of 13 cases. J Oral Pathol Med 2003; 32: 576-585. PMID: 14632932
6. Melkersson E. Ett fall av recidiverande facialispares i samband med angioneurotisk odem. Hygiea 90: 1928; 737–741.
7. Rosenthal C. Gemeinsames Auftreten von (rezidivierender familiarer) Facialislahmung, angioneurotischem Gesichtsodem und Lingua Plicata in Arthritismus-Familien. Zentralbl ges Neurol Psychol 1931; 131: 475–480.
8. Abha P.R. Orofacial granulomatosis: A case report with review of literature. J Indian Soc Periodontol 2012; 16: 469–474.
9. Leao J, Hodgson T, Scully C, Porter S. Review article: orofacial granulomatosis. Aliment Pharmacol Ther 2004; 20: 1019-1027. PMID: 15569103
10. Mignogna MD, Fedele S, Lo Russo L, Lo Muzio L. Orofacial granulomatosis with gingival onset. J Clin Periodontol 2001; 28: 692-696. PMID: 11422592
11. Ziemssen F, Rohrbach JM, Scherwitz C, Denk PO. Plastic reconstructive correction of persistent orofacial swelling and swelling of the eyelids in Melkersson-Rosenthal syndrome. Klin Monbl Augenheilkd 2003; 220: 352-356. PMID: 12766825
12. Akarsu C, Atasoy P, Erdoğan S, Koçak M. Bilateral upper eyelid edema in Melkersson- Rosenthal syndrome. Ophthal Plast Reconstr Surg 2005; 21: 243-245. PMID: 15942506
13. Cockerham KP, Hidayat AA, Cockerham GC, Depper MH, Sorensen S, Cytryn AS, Gavaris PT. Melkersson-Rosenthal syndrome: new clinicopathologic findings in 4 cases. Arch Opthalmol 2000; 118: 227-232. PMID: 10676788
14. Goto A, Kume Ai Aiba I, Yasuda T, Murakami N. A case of typical Melkersson-Rosenthal syndrome with possible autosomal dominant inheritance. Rinsho Shinkeigaku 1999; 39: 1020-1024. PMID: 10655762
15. Rogers RS. Melkersson-Rosenthal syndrome and orofacial granulomatosis. Dermatol Clin 1996; 14: 371-379.
16. Gerressen M, Alitreza G, Stockbrinck G, Riediger D, Zadeh MZ. Melkersson-Rosenthal syndrome: case report of a 30-year misdiagnosis. J Oral Maxillofac Surg 2005; 63: 1035-1039. PMID: 16003636
17. Greco M, Fiorillo MA, Ribuffo D, Corona A, Vitagliano T. Melkersson-Rosenthal syndrome associated with Down syndrome. European Review for Medical and Pharmacological Sciences 2010; 14: 639-642. PMID: 20707255
18. Casken H, Cesur Y, Tombul T, Uner A, KirimiE, Tuncer O, Odabas D, A case of Melkersson- Rosenthal syndrome associated with Ehlers-Danlos syndrome. Genet Couns 2002; 13: 183-186. PMID: 12150220
19. Shapiro M, Peters S, Spinelli HM. Melkersson-Rosenthal syndrome in the periocular area: a review of the literature and case report. Ann Plast Surg 2003; 50: 644-648. PMID: 12783021