MELKERSSON ROSENTHAL SYNDROME
(Case Reports and Review of Literature)

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Summary

Melkersson-Rosenthal Syndrome - an extremely rare condition - is described and the literature on the subject reviewed.

Two cases with late onset of the disease - an unusal feature, and migrainous headache are presented. First case represents an incomplete form of the disease showing oedema of the lips and fissured tongue, whereas the second case has the complete form with facial paralysis, facial oedema and fissured tongue.

Melkersson-Rosenthal syndrome is an uncommon condition and comprises of a triad consisting of intermittent non-pitting oedema of the face, fissured tongue, and recurrent facial paralysis. However, it may also manifest in one of the following ways[1] (1) facial paralysis and oedema of lips without a fissured tongue (2) facial oedema and fissured tongue without facial paralysis and (3) facial paralysis and fissured tongue without oedema of lips.

The complete syndrome occurs very rarely. Except for a few reports from Germany, Switzerland and Scandinavian countries, there has been a paucity of reports in the English literature.

Review of literature : The Russian neuro-pathologist Rossolino[2] was the first to describe this condition in 1910, in a woman who also suffered from migraine and related the facial paralysis to the headache. Later in 1928 Melkersson[3] gave a detailed report of a 35 years old female patient with recurrent facial paralysis and angioneurotic oedema. Rosenthal[4] in 1930 described the frequently observed clinical sign of fissured tongue. Rosenthal also pointed out the occasional familial incidence of the triad. Ekbom[5] named this syndrome in 942 after Melkersson, his compatriot who died at an early age. Chronic enlargement of the lips showing non-caseating, tuberculoid or sarcoid granulomata was first described by Meischer[6] in 1945. Later in 1956[7] he reported a case of cheilitis granulomatosa in association with facial paralysis and fissured tongue. The precise relationship of cheilitis granulomatosa and Melkersson Rosenthal syndrome is not clear; Laymon[8] in 1961 emphasized that the two conditions are not necessarily related. Schuermann[9] et al consider the syndrome a generalized disease because of frequent occurrence of symptoms related to other organs and the presence of granulomas in organs other than lips like the tongue, uvula, gums, eyelids etc.

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The cause of the disease is not known - heredity, vascular anomalies, unstable autonomic nervous system, delayed hypersensitivity to virus and bacteria, fungal and spirochaetal infections, have all been considered as possible etiological factors.

Clinical features : Symptoms usually start in adolescence with swelling of the lips and face[10]. In order of frequency the swelling occurs on the upper lip, or lower lip and then in other regions such as ongue, palate, uvula, buccal mucosa, and gums. Extra facial swellings may occur on the scalp[11], hands and feet, and in the lumbar region. The pharynx and the respiratory tract may also show oedema[12]. The swelling is usually of acute onset, non tender and non-pitting. The affected part looks dusky or pale red, or has normal skin colour. Swelling is usually asymmetrical and is soft or elastic to touch. Other manifestations include scaling, fissuring, vesicles and pustules on the vermillion border of lips[13]. Subjective symptoms are usually absent at the beginning, although a feeling of tension or tenderness has been described in rare cases. The initial swelling is transient but keeps recurring periodically until it eventually becomes permanent and fixed.

Facial paralysis is the next common symptom, seen in about 30% of cases and is also prone to recurrence[14]. In most instances its onset is before the age of twenty years. The paralysis may be complete or partial and accompanied by loss of taste in the anterior two thirds of the tongue[15]. Bilateral involvement is not uncommon. The episodes of facial oedema may precede, accompany or follow the facial nerve palsy. Apart from facial nerve palsy, paralysis of olfactory, auditory, glosso pharyngeal and hypoglossal nerve have been reported[16].

Fissured tongue is a usual finding of the triad. It may be found in a third of the cases[1], as compared to a 5% incidence in the general population[15].

The eye manifestations[17] which are not uncommon may include lagopthalmos, blepharochalasia, corneal opacities, and retrobulbar neuritis. Association with a variety of conditions which include leprosy, xanthelasma palpebrarum[12], Ehlers - Danlos Syndrome, leucoplakia, arotic arch arteritis, megacolon[10], otosclerosis[18], craniopharyngioma[10], periodontal and apical dental infections[20] and Hodgkins disease[21] have been reported.

Differential Diagnosis: Diagnosis is not difficult when all the three components of the triad are present. Swelling of the lips should be differentiated from Ascher's Syndrome in which there is also swelling of the face with oedema of the eyelids, hyperplastic labial salivary glands as well as fat deposits in the tissues of all the lachrymal glands, and in the loose skin of these areas. It must also be differentiated from acute swellings due to angio-oedema, trauma and infections of all sorts. Lymphangioma, hemangioma, neurofibroma and sarcoidosis should also be considered. It may be differentiated from Bell's palsy which is a disease chiefly of adult life usually affecting only one side of the face in a single attack. Melkersson Rosenthal syndrome on the other hand begins in most instances before the age of 20 years and sometimes even as early as 18 months shows bilateral involvement of face and is characterised by recurrences[34].

Course and Prognosis: Though long term studies have not been undertaken the course is recurrent and progressive. In some cases after a couple of years the swelling may slowly regress[11]. Schuermann[9] et al suggest that in due course of time lip lesion may turn malignant.

Histopathology : Klaus and Brunsting[1] believe that the microscopic findings are entirely non-specific.

Meischer[6] states that there is an inflammatory reaction consisting of infiltration and oedema throughout the dermis — specially in the papillary region; infiltrate consisting of lymphocytes, a few histiocytes and a few plasma cells. In addition there are round or cylindrical granulomas consisting of epitheloid cells and giant cells of the Langhan's type penetrated and surrounded by lymphocytes. The epidermal changes are unimportant although moderate hyperkeratosis, and vacuolisation have been noted.

Grzybowski and Jablonski in 1949 studied the histopathology in two cases. In both there was a classical histopathological picture of sarcoidosis.

Treatment: Treatment is mainly directed towards the swollen lips. The results of therapy are difficult to evaluate since no one method has been tried in a sufficient number of cases[15]. Of the numerous therapeutic measures employed some improvement has followed surgical excision of the swollen lips, followed by plastic repair[15]. Cerimele and Serri[22] obtained good response after intralesional triamcinolone. New and Kirch used injections of boiling water but their results were not conclusive. Schuppener[23] employed X-Ray therapy, vit. D^2, anti tubercular drugs, atabrine, penicillin, steroids, ultrasound waves, and the application of cold packs with no results. Lowenthal found good results with prednisolone 10 mg. tds subsequently tapering the doses. Hankins and also Kettel[25] recommend surgical decompression of the facial nerve. Dlabalova[26] found good results with gamma - globulin injections.

Case Report

Case No. 1

A 46 years old Hindu male presented with the complaints of swelling of the upper lip and persistent oedematous patch on the cheeks for 5 years. For the same period patient had attacks of severe giddiness and headache associated with nausea and vomiting. Headache was typically of migrainous type and throbbing in nature.

A year after the onset of headache patient noticed his upper lip getting swollen off and on. Swelling was transient and used to disappear (spontaneously) after a few weeks. Except for a feeling of fullness there were no subjective symptoms or associated consitutional disturbances such as malaise, bodyache, fever, running of nose, urticaria or itching over the body. Over a period of five years the fluctuating oedema of the lip became more or less permanent. 2 years prior to the hospital visits patient had noticed two reddish non-tender, non-itchy patches on the cheeks, of about 1 sq. inch size. These patches never disappeared completely, although the swelling and redness used to reduce

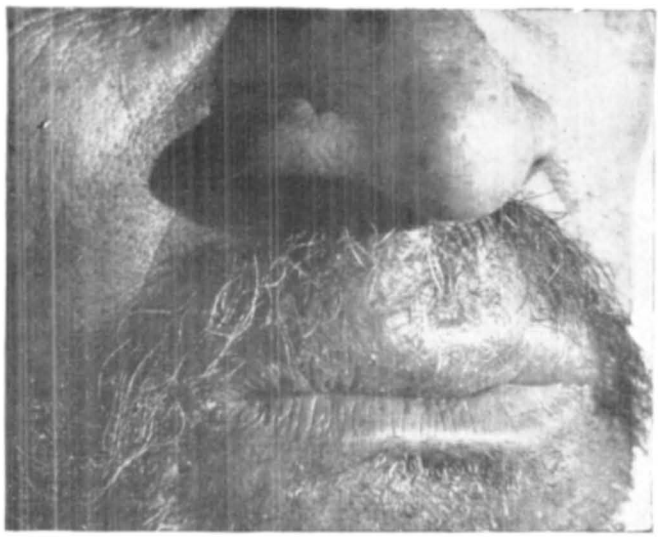

Fig. 1 Showing permanent non pitting oedema of the upper lip.

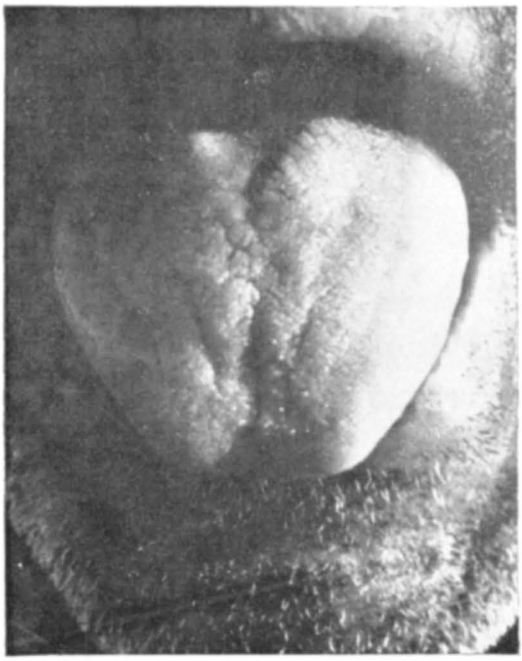

Fig. 2 Showing fissured tongue.

at times. Patient was known to have a fissured tongue since birth. He never had an attack of f·cial paralysis. No one in his family had fissured tongue, facial paralysis or any allergic tendencies. No eye signs and symptoms were present.

Investigations

Routine blood, urine & stool examinations were within normal limits. His blood group was 'A'. Blood VDRL was non reactive. Mantoux test was positive (15 mm). Kveim test was not done. X-Ray skull was normal. Nasal smears for Hansen's bacillus was negative. Lip biopsy showed inflammatory infiltrate in the dermis consisting of lymphocytes, histiocytes and occasional plasma cells.

Treatment:

Prednisolone 10 mg thrice a day was tried with slight improvement on the oedema of the lips. Injections of $B_1 + B_6 + B_{12}$ had no effect. Gammaglobulin in the doses of 3 ml weekly for 4 weeks were given with no benefit.

Case No. 2:

A Muslim female aged 30 years presented with the complaints of left sided facial paralysis, fissured tongue and swelling of the anterior half of the scalp. She was refered to skin clinic by the ENT Surgeon for opinion regarding slight burning and discomfort over a fissured tongue. The fissuring was present since birth. The burning and discomfort were noticed only when the facial paralysis occurred.

In 1972 (February) patient had the first attack of left sided

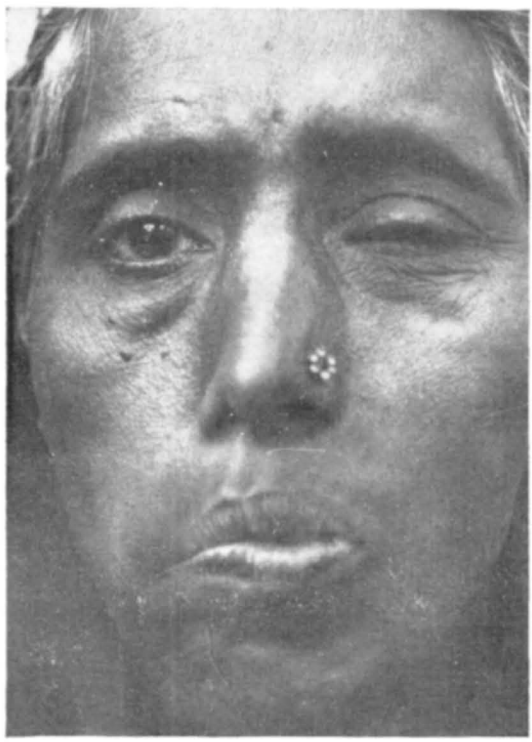

Fig. 3 Showing facial paralysis.

facial palsy from which she recovered within a period of one year. After a lapse of 5 years facial palsy recurred. This time facial palsy was preceded by a severe migrainous headache and a diffuse swelling of the anterior part of scalp and forehead. Headache was accompanied by giddiness, nausea and premonitory visual symptoms. Headache lasted for a few hours and then subsided. Swelling of the scalp was more subjective than obvious although on close observation mild oedema was appreciable. There were no associated consitutional disturbances or history of any allergy. No family history of fissured tongue, oedema lips, facial paralysis or any sort of allergy was obtained.

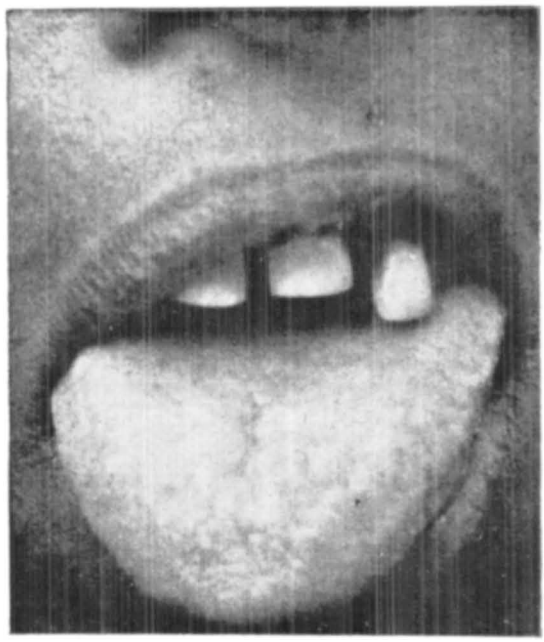

Fig. 4 Showing fissured tongue.

Investigations:

Routine blood, urine and stool examinations were within normal limits except for cysts of Entamoeba Histolytica in stools. Mantoux test was positive (18 mm). Kveim's test was not done. Blood VDRL were nonreactive. Blood group was A.

Treatment

Symptomatic treatment was given for fissured tongue with boro-glycerine paint and B-complex.

Discussion:

With the present state of our knowledge, it is difficult to explain the triad of Melkersson Rosenthal Syndrome on anatomic, physiologic or genetic basis[26]. Usually the onset of the syndrome is in adolescence but in both our cases the onset was late. In the first case the onset was at the age of 42 years and marked by swelling of the upper lip, whereas the second case showed facial paralysis as the 1st sign at the age of 26 years. Congenital fissuring of the tongue was a common denominator in both the cases. Association of migraine in both the cases could possibly indicate a vascular aberration in patients with this syndrome. Rosollino[2] was the first to describe this association. Domonkos[10] states that it is common to have repeated migrainous attacks but very few reports have been published on this association. Other vascular anomalies reported in association with this syndrome are chilblain and erythrocyanosis crurum[27]. Vascular[28] or inflammatory reaction in the region of stylomastoid foramen may itself cause Bell's palsy.

None of our cases showed familial incidence of the full blown syndrome of even isolated components of the triad. Both the patients belonged to blood Group 'A' but two isolated patients are too small a number to draw any conclusion. Carr[29] reviewed relevant medical literature on the subject for evidence of familial incidence. He observed that "the incidence of one or more parts of the triad in family members of the reported cases is higher

than that which would occur by mere chance selection." Fissured tongue is known to be transmitted as an irregular autosomal dominant condition[30]. Ekbom[5] surveyed 103 patients with facial nerve palsy. Among these, 12 had recurrent facial nerve palsies, and 91 had single attacks. Amongst the 12 patients who had recurrent facial nerve palsy, 3 had fissured tongue. The occurrence of fissured tongue in these 3 patients was significant. He concluded that congenital fissuring of the tongue was associated with a predisposition to recurrent facial palsies and perhaps Melkersson–Rosenthal syndrome. The syndrome itself is an autosomal dominantly inherited disorder with variable expressivity. Carr[29] believes that probably there are some inherited abiotrophic changes in the autonomic nervous system which lead to neurological deficits and facial oedema. Hornstein[31] regards Melkersson–Rosenthal syndrome as a manifestation of hereditary instability of the autonomic nervous system which may be stimulated by a variety of external etiological agents. Shasky[12] described a case which showed appearance of swelling during menstrual periods, dental surgery and pregnancy. The association of the syndrome with other disorders like megacolon - a disease caused by absence of autonomic cells in the large intestines – otosclerosis and craniopharyngioma support the neurotrophic origin[10].

Histopathological study of the facial swelling is sometimes suggestive of sarcoidosis and there is also a clinical similarity between the two conditions in that facial paralysis, often bilateral is one of the commonest manifestations of sarcoidosis.[32] Our cases did not show any evidence of sarcoidosis. The Mantoux test was positive in both the cases which again is an evidence against sarcoidosis. Histological picture in case No. 1 showed no evidence of sarcoidosis. In the second case a biopsy could not be done. Evans[27] considered the possibility of Melkersson–Rosenthal syndrome being a form of sarcoidosis in which the facial tissue and their nerves are specifically susceptible because of some hereditary predisposition of which fissured tongue is a manifestation. He, however, concluded that there is no conclusive proof to support this hypothesis. Recurrent facial palsies have not been described in sarcoidosis but Symond[33] reported the case of a 27 years old woman with recurrent cranial nerve palsies in whom many cranial nerves were affected. Biopsy of enlarged spleen in his case revealed microscopical picture of sarcoidosis.

Comments:

The objective of this paper was to create an awareness of the condition – Melkersson Rosenthal Syndrome - which may be quite uncommon but not an extreme rarity, as has been pointed out by some authors. Within a span of 3 years we detected two cases of this syndrome. Any patient presenting with facial palsy, facial swelling or fissured tongue should be examined and questioned concerning the other features of the triad. Joseph suggests a change in the nomenclature of this syndrome preferring to call it a "Rubber lip triad" or lip–tongue–facial paralysis syndrome[26]. Probably these descriptive, non–latin terminology would be preferable.

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