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Melkersson-Rosenthal syndrome: About a Tunisian family and review of the literature

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ABSTRACT

Melkersson-Rosenthal (MRS) syndrome is a rare disorder defined as a triad of recurrent peripheral facial palsy, orofacial edema, and fissured tongue. The etiology of this disease is still unclear. Genetic origin has been postulated. Several theories have been advanced to provide further evidence for a hereditary basis of MRS. We describe a case of 14-year-old girl presented with the classic triad symptoms of MRS. The diagnosis of MRS was made on the basis of history, clinical, histopathological examinations and exclusion of differential diagnosis. The family history showed that some members presented similar symptoms. A chromosome analysis was performed. This observation with familial occurrence of MRS may support the genetic origin theory of MRS. However; present available studies do not provide sufficient evidence to confirm a genetic origin.

1. Introduction

Melkersson-Rosenthal syndrome (MRS) is a rare, non caseating granulomatous disease markedby the triad recurrent orofacial edema,fissured tongue, and recurrent peripheral facialparalysis [1].

The presence of the complete triad of symptoms in MRS is not common, with an incidence varying between 8% and 18% in the literature [2,3]. Many investigators consider mono-symptomatic and oligosymptomatic forms [3].

The cause of MRS is unknown although various theories have been proposed.

The suggestion that MRS might be a hereditary disease has been reported based on several reports of family occurrence.

2. Method

In this paper, we describe a case of MRS with the classic triad of symptoms and with family characters.

An online database search (Pubmed/Medline, scienceDirect, Google Scholar) with no language restriction was performed to analyze family cases of MRS in world literature.

Keywords used included: Heredity, genetic, Melkersson-Rosenthal syndrome, recurrent facial paralysis, fissured tongue.

3. Case report

A 14-year-old girl presented on February2016 to the neurological department of Military Hospital of Tunis, with gradual onset of right-sided facial paralysis. The medical history revealed a recurrent facial paralysis. She had experienced a left-sided facial paralysis less than one year ago.

Her physical examination revealed right seventh nerve paralysis, swelling of the upper lip and a fissured tongue (Figs. 1 and 2).

No clinical sign of intestinal or pulmonary disease was present in our patient and the oral examination lacked any ulceration or cobblestoning of the mucosa. Histopathologic examination by incisional biopsy in the swollen lip revealed plasmocytes and lymphocytes infiltrates without epithelioid granulomas.

Chest X-ray, colonoscopy, cerebral magnetic resonance imaging (MRI) were performed to rule out sarcoidosis, Crohn's disease, and ischemic stroke. The tuberculin skin test (TST), Cytomegalovirus IgG and IgM antibodies, Herpes simplex virus IgG and IgM antibodies were also negative. The patient's laboratory findings were all within normal range. Serological studies for Rheumatoid factor (RF), antinuclear antibodies (ANA),Sjögren's syndrome antigen A (SSA), Sjögren's syndrome antigen B (SSB), anti-neutrophil cytoplasmic antibodies (ANCAs), Angiotensin-converting enzyme (CE) were negative.

The diagnosis of MRS was made on the basis of history, clinical, histopathological examinations and exclusion of differential diagnosis.

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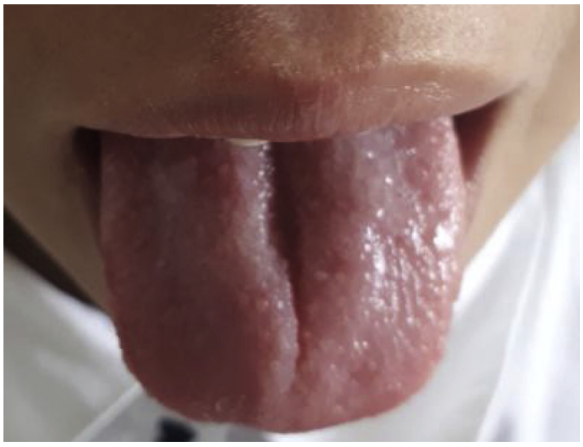

Fig. 1. Fissured tongue.

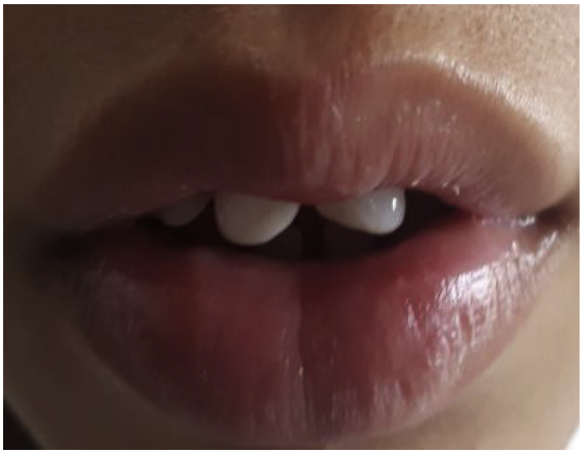

Fig. 2. swelling lips.

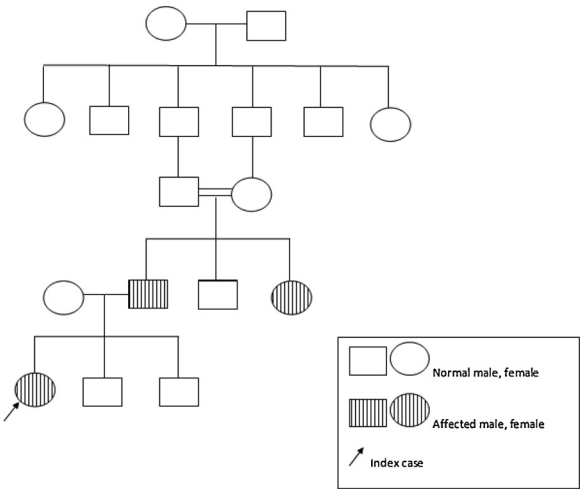

Fig. 3. The pedigree tree of the family presented.

Moreover, family history was significant as shown in the pedigree of the family (Fig. 3).

She is the third child of non-related parents. Among the family members, apart from our patient, two others were also affected (Table 1).

The patient's father who is the son of related parents, when examined showed a residual facial weakness on the left side and fissured tongue. Description of symptoms of the affected paternal aunt was obtained by questioning relativesand revealed a fissured tongue and orofacialedema.

A chromosome analysis revealed a normal female karyotype (46,XX) for our patient and normal male Karyotype (46,XY) for her father.

She was managed with daily oral methylprednisolone 1 mg/kg. Orofacial edema and facial palsy had improved after 30 days of steroid therapy but the fissured tongue showed no improvement.

4. Discussion

MRS is a rare disease that can affect any age group but the usual onset is in adolescence. The rarity of the MRS makes assumptions about incidence difficult [2].Diagnosis is based on clinical features as there is no specific diagnostic test and no established diagnostic criteria. The presence of at least one of this features idiopathic facial paralysis or fissured tongue accompanied by idiopathic orofacial swelling leads to a positive diagnosis [4]. It occurs more often in its incomplete form as seen in our patient's relatives, thus easily neglected making the diagnosis more difficult. Histological investigations may help to establish the diagnosis and rule out other potential causes [5]. Typical MRS histology of a biopsy taken during an acute edema episode, shows lymphoepitheloid granulomas, or small lymphoplasmocytic clusters or mononuclear infiltrates surrounding small vessels [3].However, in the absence of the histological characteristics, the diagnosis of MRS should not be excluded particularly if the full clinical triad is present [6]. In our case, biopsy helped to rule out differential diagnosis of MRS including a variety of disorders : Crohn's disease, sarcoidosis, granulomatosisblepharitis, cheilitis, contact dermatitis, facial trauma, and Bell's palsy [3].

The cause of MRS is still unknown and various theories have been proposed such as infectious agents, allergic reactions to various food additives, autoimmune and genetic factors [7].

By presenting this MRS patient with familial similar cases, this paper's aim is to support genetic origin theory.

Genetic origin was based on some reports of families in which several generations were affected [3,8–10]. Thus, when patients with MRS are encountered, physicians should examine and question other family members.

In this way, diagnosing our case, allowed us to identify undiagnosed generations.

As, the role of a genetic predisposition toward development of the syndrome remains unclear, several theories have been advanced to provide further evidence for a hereditary basis of MRS.

Reviewing the literature we found that some authors suggest a genetic tendency with autosomal dominant inheritance [8,11,11,12]. Others assume that MRS is probably paternal inheritance dominated [11].

The data presented in our case are supportive of these last patterns of inheritance but nothing further can be inferred in our single family report.

Therefore, de novo autosomal reciprocal translocation t(9;21)(pll;pl1) in an isolated patient was found in 1994 [8]. Mutation (c.68C > G, p.Pro23Arg)of a Fatty acid transport proteins robustly expressed in skin (FATP1) was also identified as a causal gene for MRS in a Han Chinese family [13].

But none of these theories have been proven so far.

5. Conclusion

This observation with familial occurrence of MRS supports the notion that genetic predisposition may play an important role. However; present available reports do not provide sufficient evidence to confirm a genetic origin. Further genetic studies of MRS family are necessary to prove the hereditary basis of this rare syndrome.

Table 1
Characteristics of family cases with Melkersson-Rosenthal syndrome.

References	patients (n)	gender	Age of onset (years)	Initial symptom	Facial palsy	Facial edema	Lingua plicata	Histopathologic examination	Familyhistory	symptoms	Geneticresults
LYGIDAK C 1979 [10]	1	F	7	Facial palsy	X	X	X	–	6 affected members Four generations	–	Normal karyotype
Greene RM 1989 [14]	1	M	23	Lingua plicata	X	X	X	–	Brother	Fissuredtongue	–
Smeets E 1994 [8]	1	F	late adolescence	swelling of the upper lip		X	X	–	–	–	de novo autosomalt(9;21) (pll;pll) translocation
Alioğlu Z 2000 [3]	1	F	17	Facial palsy	X	X	X	–	Brother	Fissure tongue	–
	2	F	14	Facial palsy	X	X	X		Mother	Fissuredtongue	
	3	M	8	Facial palsy	X	X	X		Brother	Fissuredtongue	
Hentati H 2007 [9]	1	M	18	upperlipSwelling	X	X	X	Infiltrates without epithelioid granulomas.	Six generations 19 family'smembers	3/19: the triad 16/19 one sign	–
Kanerva 2008 [7]	123	FFF	311043	—–	XX	X	X	Atypical findings.	Father	Facial Palsy	Mutations not found
					X	X	X	Non necrotizing granulomatos.	Mother	Facial edema	
						X			Four siblings	Fissured tongue	
									Sister and grandfather	Fissured tongue	
									uncle	Facial palsy	
Liu R 2013 [7]	12	MM	2244	–	XX	XX	XX	–	brother	Fisuredtongue	–
Feng S 2014 [11]	13	–	–	–	–	–	–	–	–	–	–
X.G. Xu 2016 [13]	1	F	12	Facial palsy	X	X	X	Non-caseating granulomas with mononuclear inflammatory cells.	Mother Maternal uncle	Fissured tongue Fissured tongue	FATP1 mutation
Our case	1	F	14	Facial palsy	X	X	X	Plasmocytes and lymphocytes infiltrates without epithelioid granulomas.	Father Partenal aunt	Fissured tongue Facial palsy Fissured tongue Facial edema	Normal Karyotype

F:female, M: male, -: non-reported, X: present.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical committee of the Military Hospital, Tunis, Tunisia and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

informed consent was obtained from all individual participants included in the study.Patient informed consent of the use of her pictures for this article was also obtained.

Declaration of Competing Interest

We have no conflict of interest to declare.

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