A neuromucocutaneous syndrome of idiopathic aetiology

Melkersson-Rosenthal syndrome associated with Guillain-Barré syndrome

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Summary

Melkersson-Rosenthal syndrome is a rare neuromucocutaneous disorder of idiopathic aetiology. Its presentation has been associated with autoimmune diseases. We present the case of a 56-year-old male patient who developed Melkersson-Rosenthal syndrome associated with Guillain-Barré syndrome. The patient had an excellent response to treatment with plasmapheresis, and physiotherapy and rehabilitation.To our knowledge, this is the first report of an association between Guillain-Barré syndrome and Melkersson-Rosenthal syndrome.

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Introduction

Melkersson-Rosenthal syndrome (MRS) is a rare clinical neuromucocutaneous syndrome of idiopathic aetiology; however, it is attributed to a genetic, allergic, or immune origin [1, 2]. The classic triad consists of orofacial oedema, recurrent peripheral facial paralysis and fissured tongue [1].

On the other hand, Guillain-Barré syndrome (GBS) presents bilateral, ascending motor paralysis with areflexia of unknown aetiology. However, 50% to 70% of cases have been described 2 weeks after an infection or other autoimmune stimulus [3]. This condition occurs as a result of antibodies that generate an immunological response to myelin sheath gangliosides [4].

The relationship between MRS and autoimmune diseases has been documented in sarcoidosis, Crohn's disease, anterior unilateral uveitis and Hashimoto's thyroiditis [2], but there is no report of an association with GBS. We present the case of a 56-year-old man who developed MRS associated with GBS successfully treated with plasmapheresis.

Case report

A 56-year-old man with type 2 diabetes mellitus for 2 years, controlled with diet and metformin 850 mg daily, and grade 1 obesity (body mass index of 31.58 kg/m^2) presented with loss of muscle strength in the lower limbs with a sudden onset and a progressive ascending course, and paraesthesia in hands and feet starting 4 days before admission. On the day of admission (12 December 2019), he had facial diplegia, macroglossia with a fissured tongue, oedema, and paraesthesia of the lower lip (figs 1A and B), loss of strength of the lower

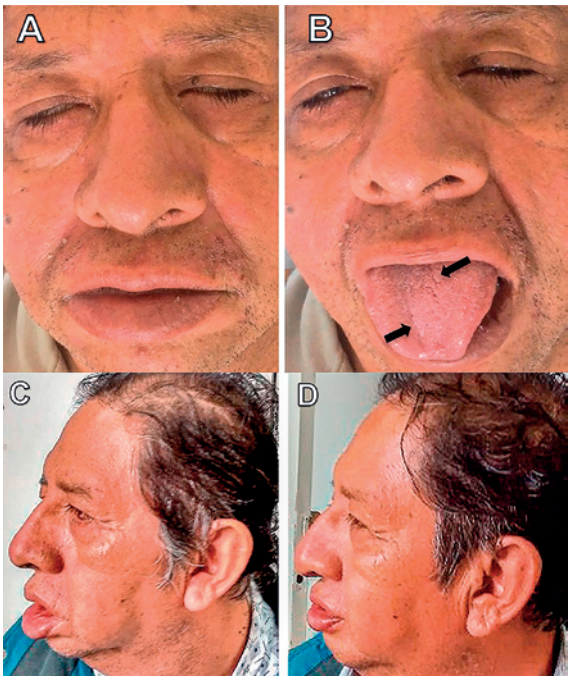

Figure 1: A) Bilateral Bell's sing and lower lip edema. **B**) Bilateral Bell's sing and fissured tongue. **C**) Left lateral view evidence of lower lip edema. **D**) One month after discharge.

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Table 1: Reported cases of MRS associated with some autoimmune disease.

Source	Sex	Age(years)	Clinical presentation	Biopsy (Result)	Associated disease
Scagliusi et al. [2]	F	52	Orofacial edema and facial pain attacks	No	Hashimoto's thyroiditis
Lee et al. [13]	F	9	Right RPFP, fissured tongue, and painless edema of the left zygomatic region and upper lip	No	Hashimoto's thyroiditis
Aksu et al. [14]	F	57	RPFP, persistent edema of the upper lip, and fissured tongue	No	Hashimoto's-thyroiditis
Bouomrani et al. [15]	M	39	Alternating unilateral RPFP, macroglossia, and fissured tongue	Yes (+)	Hashimoto's thyroiditis
Frąckowiak et al. [16]	F	32	RPFP, fissured tongue, and recurrent cheilitis of the upper lip	Yes (+)	Hashimoto's thyroiditis
Lloyd et al. [17]	F	19	Upper lip edema	Yes (+)	Crohn's disease
Ilnyckyj et al. [18]	F	30	Recurrent edema of the lips and genitals	Yes (+)	Crohn's disease
De Aloe et al. [19]	F	23	Recurrent upper lip edema and facial dysesthesia	Yes (+)	Crohn's disease
Ates et al. [20]	M	35	Orofacial edema, RPFP, and fissured tongue	Yes (-)	Anterior unilateral uveitis
Degirmenci et al. [21]	F	23	RPFP, moderate orofacial edema, and fissured tongue	No	Systemic lupus erythematosus
Martins et al. [22]	M	45	RPFP, recurrent lip edema, and fissured tongue	Yes (+)	Celiac disease
Gaudio et al. [23]	F	42	Right RPFP and right facial and upper lip edema	Yes (+)	Psoriatic arthritis
Cabrera-Gómez et al. [24]	F	51	RPFP, fissured tongue, right hemiparesis, and pale optic discs	No	Multiple sclerosis

M: male; F: female; RPFP: recurrent peripheral facial palsy.

limbs up to the thighs (MRC scale: 3), in the upper limbs (MRC scale: 4), and in the chewing and mimicry muscles, and generalised hyporeflexia. He was transferred to the hospital with the diagnoses of type 2 diabetes mellitus, GBS and MRS.

The results of laboratory tests at hospitalisation showed hyperglycaemia, mild hyperbilirubinaemia (predominatly direct) and hypertransaminasaemia. A Study of cerebrospinal fluid showed albumin-cytological dissociation (proteins: 201 mg/dl, cells: 1 leucocyte/mm^3), and Pandy and Nonne-Apelt 2 (+). Needle electromyography recorded voluntary motor units absentin the facial muscles, but present in the lower and upper right limbs. Motor nerve conduction studies showed hypovoltage of motor potentials in the upper and lower limbs and both facial nerves, prolongation of distal latencies, absence of F wave, and a bilateral H reflex. Furthermore, sensory nerve conduction tests revealed absence of sensory potentials in the upper limbs.

The in-hospital clinical evolution did not show warning signs in the first days, so conservative management of GBS was initially preferred. Later, when he developed respiratory distress, two plasmapheresis sessions were performed, conservative management with expectant management of the MRS was chosen, and antihypertensive treatment was initiated owing to a diagnosis of primary arterial hypertension.

The patient was discharged on a low-sodium low-glucose diet, metformin 850 mg daily, and losartan 50 mg daily. Two weeks after discharge, a lower lip biopsy was performed in which nonspecific findings were found. After a 1-year follow-up, the patient was without complications and an excellent response to physical therapy and rehabilitation (fig. 1C and D).

Discussion

This report describes the case of an adult male who presented the complete triad of MRS concomitant with GBS. MRS incidence has been described as 0.08% of the population, mainly in women in the second decade of life, without predilection for race or ethnicity [5]. A complete presentation of the classic triad of MRS is very unusual, found in about 8% to 18% of cases [6]. The most frequent sign is orofacial oedema characterised by being acute, diffuse, painless, and predominantly on the lips (between 50% and 75% of cases) [7]. Due to the frequent oligosymptomatic presentation with oro-

facial oedema, it is recommended to consider sarcoidosis in the differential diagnoses [2], or if it presents with facial diplegia, it should be considered a variant of GBS [8].

There were nonspecific findings in the lower lip biopsy; however, this was taken 2 weeks after discharge. Dhawan et al. reported that histopathological findings can be negative in subacute or chronic stages. In these cases, or when there is no access to a biopsy, the clinical picture is sufficient to make the diagnosis of MRS [9]. On the other hand, the presence of granulomatous cheilitis in the biopsy with one or two clinical manifestations may be sufficient to diagnose monosymptomatic or oligosymptomatic forms of MRS [6].

Although our case had bilateral facial paralysis on just one occasion, described as an unusual manifestation in GBS [10], it should not be ruled out in the differential diagnosis of MRS owing to the other signs of triad, orofacial edema and fissured tongue. In addition, the negative lip biopsy in our case does not rule out the diagnosis of MRS either because the diagnosis can be clinical, as described by Bohra et al. [11].

The relationship between MRS and autoimmune diseases has been documented in Crohn's disease, anterior unilateral uveitis, multiple sclerosis, systemic lupus erythematosus, psoriatic arthritis and Hashimoto's thyroiditis (table 1). The highest number of association reports are for Crohn's disease, with whom it shares the microscopic findings of non-caseating granulomas [12].

There is no standard treatment for MRS; it depends on the severity of the symptoms. The initial treatment is conservative, waiting for a spontaneous resolution followed by physical therapy and rehabilitation. The most widely used therapy is intralesional administration of corticosteroids, which leads to improvement in 50% to 80% of patients and reduces the frequency of relapses in 60% to 75% of cases [9].

Conclusion

To our knowledge, this is the first report of an association between MRS and GBS. Further research is needed to address the relation between MRS and autoimmunity.

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