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CASE SERIES

Isolated eyelid edema in Melkersson–Rosenthal syndrome: a case series

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Abstract

Purpose **To report the clinicopathologic features of a series of patients with Melkersson–Rosenthal syndrome (MRS).**
Methods **Patients in this clinicopathological case series were identified through retrospective review. Five Caucasian patients (2 women and 3 men; age range, 46 to 73 years) with isolated eyelid swelling presented over an 11-month period to two Canadian tertiary Oculoplastic referral centres. All underwent clinical examination and had tissue biopsies.**
Results **The patients presented with non-pitting, non-pruritic, painless and recurrent eyelid swelling. None had evidence of cranial nerve palsy or fissured tongue. The duration of symptoms before referral was between 1–5 years. Histopathological examination showed granulomatous inflammation in four patients. Granulomatous folliculitis was a novel finding in three patients.**
Conclusions **Monosymptomatic patients with MRS require a high index of suspicion. Histopathological confirmation is vital for the diagnosis.**
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Keywords: Melkersson–Rosenthal syndrome; eyelid diseases; histopathology

Introduction

Melkersson–Rosenthal syndrome (MRS) is a rare, granulomatous disease characterized by facial palsy, facial edema, and fissured tongue.[1] However, the complete triad is seen only in 25% of cases.[2] Isolated eyelid edema in MRS is uncommon and poses a diagnostic dilemma. We present five patients with isolated lid swelling of varying duration who were diagnosed with MRS.

Case reports

Case 1

A 73-year-old man presented with bilateral upper-eyelid swelling for 2 years (Figure 1a). Examination revealed painless, non-pitting edema bilaterally, but it was otherwise normal. On histopathological examination, the superficial dermis appeared edematous, and there were mild perivascular lymphocytic aggregates (Figure 1b). Numerous small, non-caseating granulomata were also seen in the dermis. Many were in close proximity to lymphatic channels, and histiocytes were present within some of the lumina. Several superficial granulomata were seen adjacent to intact hair follicles (Figure 1c). Some discrete granulomas, which expressed CD68, were seen within dense connective tissue in the anterior orbit (Figures 1d and e).

Case 2

A 71-year-old man presented with painless, longstanding, and recurrent right upper-eyelid swelling that interfered with his vision (Figure 2a). Histopathological examination disclosed scattered, non-caseating granulomata adjacent to lymphatic vessels, consistent with MRS (Figure 2b). He underwent unilateral skin reduction and then developed bilateral disease 6 months later.

Case 3

A 59-year-old man had a 1-year history of painless, unilateral swelling of the upper and

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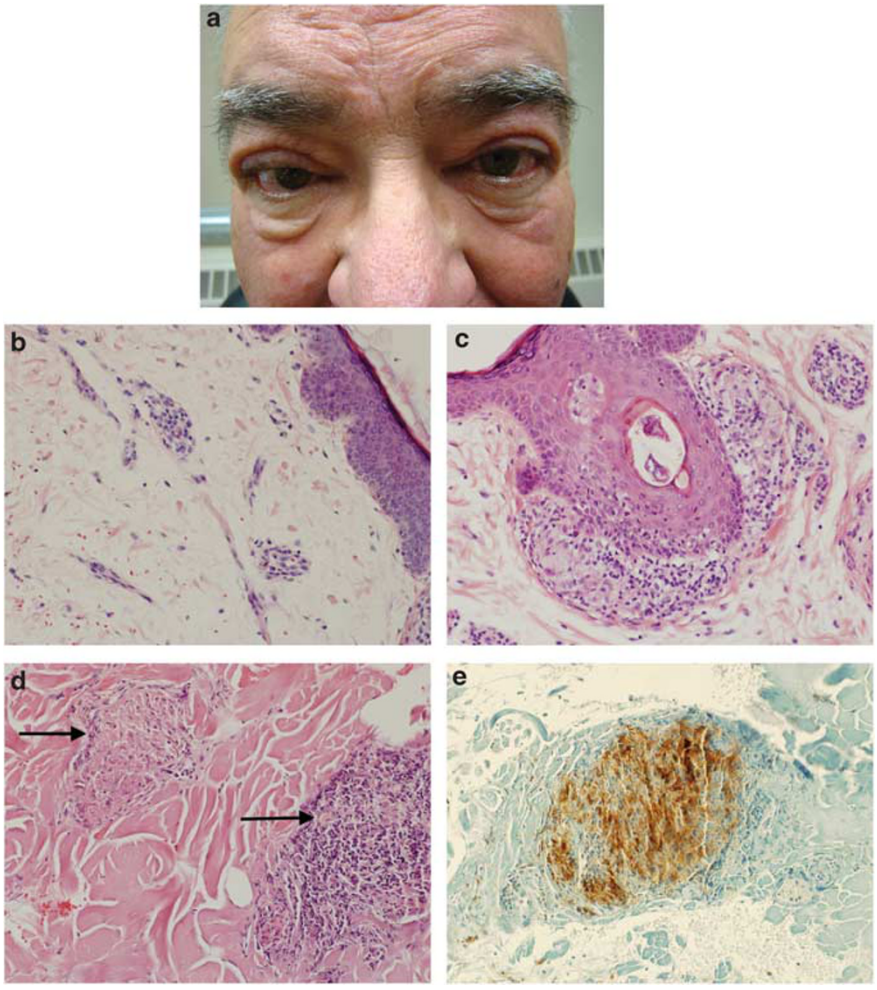

Figure 1 (a) Case 1: 73-year-old male with bilateral, painless, non-pitting, upper-eyelid swelling for the past 2 years. (b) Histopathology of this case showing dermal edema and perivascular lymphocytic aggregates. (hematoxylin-eosin; original magnification $\times 20$). (c) Granulomatous inflammation adjacent to pilosebaceous appendage. (hematoxylin-eosin; original magnification, $\times 40$). (d) Circumscribed granulomas (arrows) located within the orbit. (hematoxylin-eosin; original magnification, $\times 40$). (e) Granuloma with immunoreactivity for CD68. (immunoperoxidase; original magnification, $\times 40$).

lower eyelid. Thyroid profile and rheumatologic work-up were negative. He did not respond to a trial of oral Prednisone. Biopsy of the upper eyelid revealed non-caseating granulomata around blood vessels and lymphatic channels, and within the orbicularis muscle (Figure 3a). Aggregates of histiocytes were visualized within the dilated lymphatics (Figure 3b).

Case 4

A 52-year-old female, with intermittent, painless, bilateral upper eyelid swelling for 5 years, was assessed. She had isolated eyelid edema, greater on the left side. Her eyelid biopsy revealed a lymphocytic infiltrate in the superficial dermis, and dilated lymphatic vessels with an occasional intraluminal macrophage. A focus of granulomatous folliculitis was also noted.

Case 5

A 46-year-old female had a 2-year history of painless, non-pruritic swelling of the left upper eyelid. Eyelid histopathology revealed perivascular lymphocytic aggregates but no evidence of granulomata.

Discussion

MRS is a rare condition of unknown etiology with no sex predilection. It generally presents in adolescence but may be seen in childhood or in patients over the age of

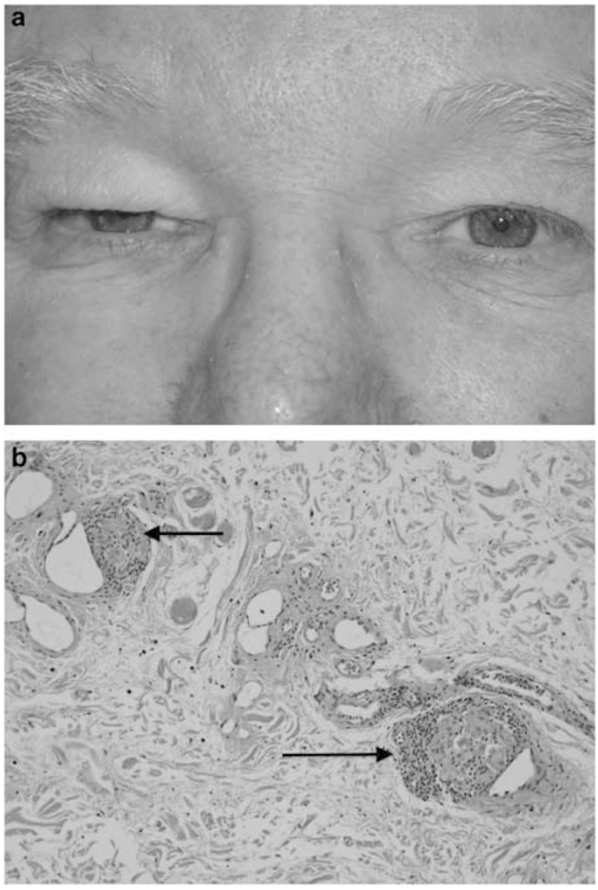

Figure 2 (a) Case 2: 71-year-old male presented with painless, longstanding, and recurrent right upper-eyelid swelling that interfered with his vision. (b) Eyelid biopsy with dermal edema and foci of perivascular granulomatous inflammation (arrows). (hematoxylin-eosin; original magnification, $\times 20$).

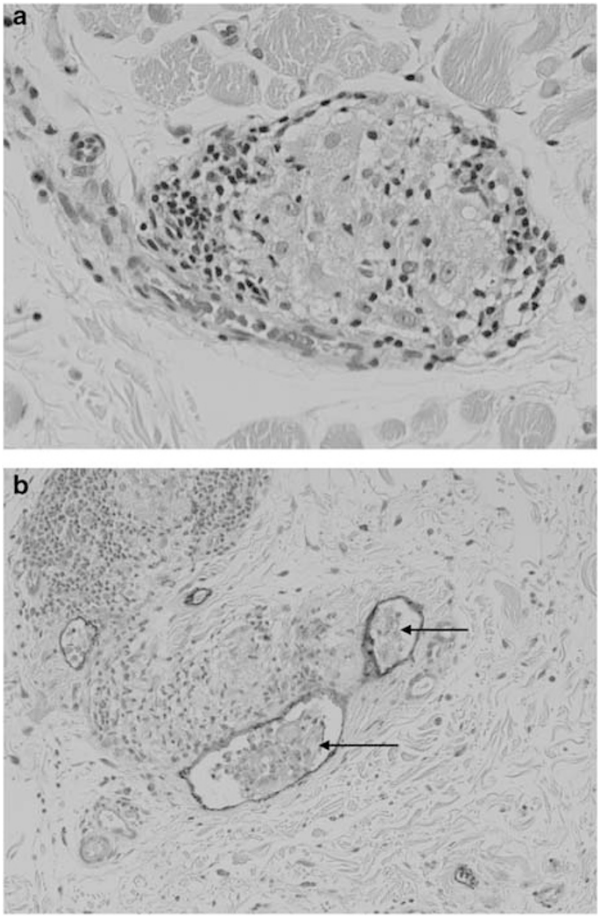

Figure 3 (a) Case 3: Granuloma within orbicularis muscle. (hematoxylin-eosin; original magnification $\times 40$). (b) Granulomata adjacent to lymphatics with histiocytic aggregates within lumen of lymphatic vessels (arrows). (D2-40; original magnification, $\times 20$)

50 years.[3] It is characterized by recurrent orofacial edema, relapsing facial paralysis and fissured tongue. Orofacial swelling is the presenting sign in 86% of cases, while lingua plicata is always congenital.[1] MRS has a chronic course of remissions and relapses, with occasional spontaneous resolution.[4]

In this series, the duration of symptoms before diagnosis was between 1 and 5 years. All patients had isolated eyelid swelling and did not demonstrate the complete triad of MRS. Isolated eyelid edema in MRS is uncommon, painless, non-pitting, and of insidious onset.[4] The two major entities in the extensive differential diagnosis are thyroid orbitopathy, which may need to be excluded by laboratory tests and orbital imaging, and blepharochalasis.[5] There was no history of thyroid disease in any of our patients, although only case 3 was formally investigated for thyroid dysfunction.

The characteristic histopathology of MRS is a granulomatous angiitis with perivascular inflammatory cells and variable dermal edema. The granulomas are seen both within and around the lymphatics and blood vessels and are sparsely distributed in the edematous dermis. They can be found within the skin, orbicularis, and levator muscles.[6] There is no caseation, and microorganisms are not demonstrable. In three of our cases, the skin biopsies contained foci of granulomatous inflammation within and around the epithelium of intact hair follicles. None of the granulomas in or around the follicles contained remnants of Demodex mites or other foreign material. Granulomatous folliculitis has not been linked to MRS before and it remains unclear whether this is truly part of the inflammatory process or merely an incidental finding. In the early stage of the disease, granulomas may be absent, but this should not preclude the diagnosis; serial sections of the biopsy specimen may provide histopathological confirmation.[7] Our patients demonstrated a spectrum of findings: three had widespread granulomas; three had evidence of

granulomatous folliculitis; and one had no granulomata but lymphangiectasia and perivascular lymphocytic infiltrates. Given the non-specific pathological changes in this last case, the diagnosis of MRS in this patient is based primarily on clinical findings at this time.

This condition is often refractory to treatment. The mainstay of therapy consists of corticosteroids administered topically, intralesionally, or systemically,[6] but eyelid skin reduction may be indicated,[8] if the swelling is visually significant, cosmetically unacceptable or unresponsive to medical therapy.

MRS requires a high index of suspicion and should be considered in the differential diagnosis of eyelid edema; definitive diagnosis requires histopathological confirmation.

Summary

What was known before

- Melkersson-Rosenthal syndrome (MRS) is characterized by a triad of facial palsy, facial edema and lingua plicata. These patients may present with isolated eyelid edema, which poses a diagnostic dilemma.

What this study adds

- The presence of granulomatous folliculitis is a novel histopathologic finding in this case series.
- MRS should be included in the differential diagnosis of eyelid edema and requires histopathologic confirmation.

Conflict of interest

The authors declare no conflict of interest.

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