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DERMATOLOGIC THERAPY WILEY

LETTER

A case of Melkersson–Rosenthal syndrome successfully treated with hydroxychloroquine

Dear Editor,

A 30-year-old man presented with a 1-year-history of persistent, painless swelling of the lower lip (Figure 1A). His medical history was positive for celiac disease and atopic diathesis. The patient had already consulted other dermatologists that had prescribed topical and oral corticosteroids with only partial benefits and temporary improvements. The thing that most of all caught our attention was that the patient reported seven episodes of facial nerve palsy occurring since he was 17 years old. During clinical examination an important tongue oedema with scrotal appearance was observed too (Figure 1B).

Dermoscopy of lower lip showed a pattern of globular vessels regularly distributed throughout the entire lesion with white lines drawing a sort of negative network (Figure 1C).

A punch biopsy (2.0 mm) was done on patient's lower lip. Histopathological examination showed epithelial acanthosis, hyperplasia, and hyperkeratosis, with oedema, ectatic blood vessels, a dense perivascular lymphomonocytic infiltrate in the dermis, with few non-necrotizing granulomas (Figure 1D). A clinical-pathological consultation (CPC) was organized and a diagnosis of Melkersson–Rosenthal syndrome (MRS) was made.

MRS is a rare disorder of unknown etiology, characterized by the triad of oro-facial oedema, facial nerve palsy, and furrowing of the tongue.[1] This symptomatic triad may not be present simultaneously in MRS, as indeed in our patient (last facial nerve palsy had occurred 1 year before the visit). Differential diagnosis covers sarcoidosis and inflammatory bowel disease, which were excluded by clinical examination, laboratory tests, and endoscopy. Allergic contact dermatitis was ruled out with negative patch test.

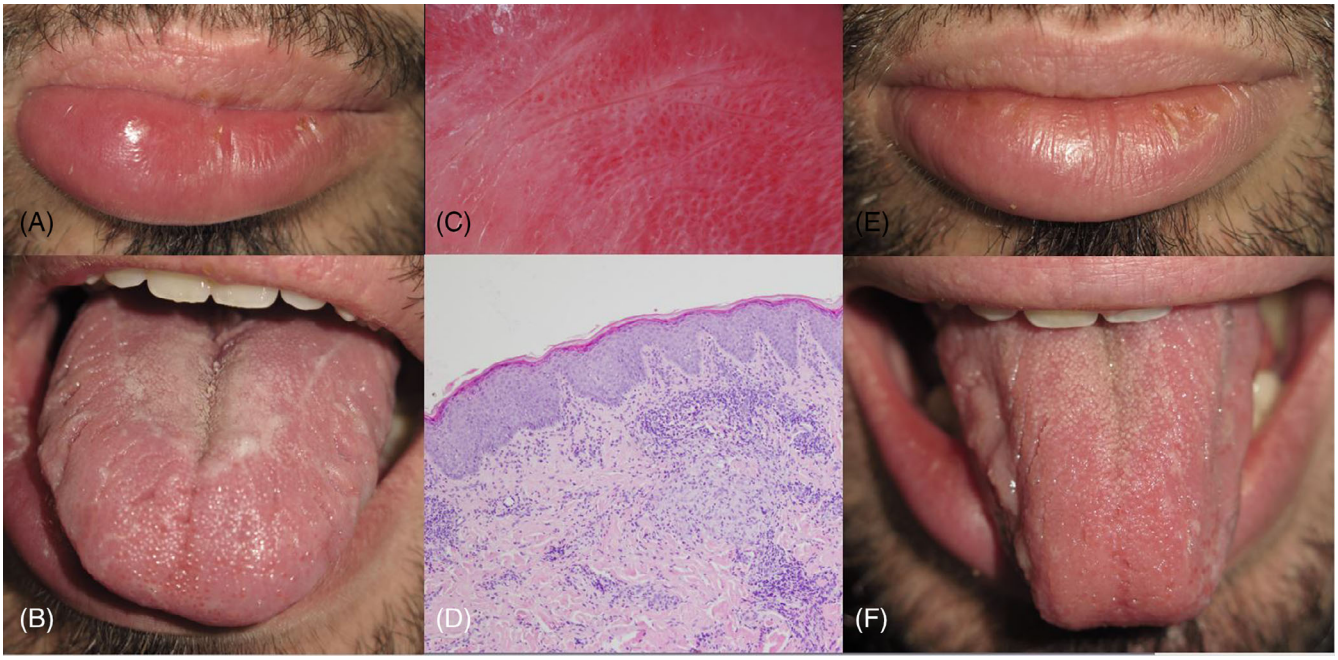

FIGURE 1 Oedema of the lower lip (A) and furrowed tongue (B). Dermoscopy of lower lip, showing a pattern of globular vessels regularly distributed throughout the entire lesion with white lines drawing a sort of negative network (C). Biopsy showed epithelial acanthosis, hyperplasia and hyperkeratosis, with oedema, ectatic blood vessels, a dense perivascular lymphomonocytic infiltrate in the dermis, with few non-necrotizing granulomas—hematoxylin–eosin, ×10, (D). Improvement of patient's conditions after 1 year of treatment with HCQ (E,F)

Being a rare disease, randomized clinical trials have never been conducted; by the way, in literature MRS first-line treatment consists of topical and systemic corticosteroids. Indeed, few data are available about the use of hydroxychloroquine (HCQ) in MRS.[2] Here, we reported a successful use of HCQ in MRS. We started therapy with oral prednisone 25 mg (0.3 mg pro-kg) daily and bromelain with poor results. After 2 months, due to low effectiveness of this therapy, we decided to associate HCQ. HCQ belongs to antimalarials: these drugs, reducing lysosome pH, can prevent the formation of antigenic peptides with major histocompatibility complex's class II molecules, thus suppressing the immune response of CD4+ lymphocytes against autoantigenic peptides.[3]

The patient started to assume HCQ 200 mg daily, associated with prednisone 25 mg. After 2 months, we noticed a progressive improvement of oedema. We chose to decrease progressively corticosteroid therapy and prescribed a topical inhibitor of calcineurin (pimecrolimus) once daily. Nowadays, he is still in therapy only with 200 mg of HCQ with excellent results (Figure 1 E,F).

Moreover, what captured our attention was that the patient, who worked as a greengrocer, revealed that oedema had appeared for the first time following a prolonged sun exposure. Moreover, he noticed an improvement of lip oedema when he started to wear face masks for COVID-19 emergency. Probably, when he started to work in a close space for the pandemics, the reduction of temperature variations helped him to improve during HCQ treatment.

MRS is still an obscure identity and a challenge for clinicians, both for its low incidence and unknown etiology. More studies should be conducted to clarify the causes and define an optimal therapeutic algorithm.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

INFORMED CONSENT

The patient is not identifiable in the pictures; anyhow, an informed consent and releases to publish photographs has been obtained.

AUTHOR CONTRIBUTIONS

Stefano Caccavale, Paola Vitiello, Stefano Badolato: conceptualization; Stefano Caccavale, Vittorio Tancredi, Andrea Ronchi: writing and editing; Stefano Caccavale, Paola Vitiello, Antonello Sica, Renato Franco, Giuseppe Argenziano: methodology.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Wehl G, Rauchenzauner M. A systematic review of the literature of the three related disease entities Cheilitis Granulomatosa, orofacial granulomatosis and Melkersson–Rosenthal syndrome. *Curr Pediatr Rev*. 2018;14(3):196-203. doi:10.2174/1573396314666180515113941
2. Dhawan SR, Saini AG, Singhi PD. Management strategies of Melkersson-Rosenthal syndrome: a review. *Int J Gen Med*. 2020; 26(13):61-65.
3. Fox RI. Mechanism of action of hydroxychloroquine as an antirheumatic drug. *Semin Arthritis Rheum*. 1993;23(2 Suppl 1):82-91. doi: 10.1016/s0049-0172(10)80012-5