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CONCISE COMMUNICATION

A case of complete Melkersson-Rosenthal syndrome: Possibly associated with *Mycolicibacterium fortuitum* from odontogenic origin

Wenqing Zhang | **Zhimin Yan**

Department of Oral Medicine, Peking University School and Hospital of Stomatology & National Center for Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Research Center of Oral Biomaterials and Digital Medical Devices, Beijing, China

Correspondence
Zhimin Yan, Department of Oral Medicine, Peking University School and Hospital of Stomatology & National Center for Stomatology & National Clinical Research Center for Oral Diseases & National Engineering Research Center of Oral Biomaterials and Digital Medical Devices, No. 22, Zhongguancun South Avenue, Haidian District, Beijing, 100081, China.
Email: yzhimin96@163.com

Abstract

Melkersson-Rosenthal syndrome (MRS) is a neuromucocutaneous disease of unknown pathogenesis. With this communication, we describe a case of a 26-year-old woman with complete MRS in whom *Mycolicibacterium fortuitum* was detected in the swelling lip biopsy by next- generation sequencing. The patient's symptoms were slightly improved after intralesional corticosteroid injection combined with broad-spectrum antibiotics, while they were significantly improved after further treatment of dental caries and removal of the residual root. This case provides insight into the possible microbial infection pathogenesis of MRS, and *M. fortuitum* was speculated to be related to granulomatous and neuronal disorders, most probably from odontogenic origin.

KEYWORDS
cause, infection, Melkersson-Rosenthal syndrome, *Mycolicibacterium fortuitum*, odontogenic

1 | INTRODUCTION

Melkersson-Rosenthal syndrome (MRS) is a neuromucocutaneous disease characterized by recurrent or persistent oral-facial swelling, peripheral facial palsy, and fissured tongue. Until now, the specific cause of MRS is not clear, but several theories have been proposed including heredity, allergies, and microbial infection.[1] *Mycobacterium tuberculosis* complex and *Borrelia burgdorferi* have been supporting a possible involvement in the cause of MRS and orofacial granulomatosis.[2,3]

Mycolicibacterium fortuitum is a rapidly growing mycobacteria commonly found in soil and water, which can infect soft tissue and other sites of human.[4] It was reported that *M. fortuitum* could cause central nervous system (CNS) infections in both patients with HIV and those who are immunocompetent.[5,6] In animals, there are reports of *M. fortuitum* infection leading to the development of granulomatous and neuronal disorders.[7] Here, we present a complete MRS case, with *M. fortuitum* detected in the swelling lip biopsy by next-generation sequencing, which was speculated as a possible association with MRS.

2 | CASE REPORT

A 26-year-old woman presented with a 4-month history of recurrent then persistent upper lip swelling. Moreover, she also experienced facial paralysis for 1 year. The patient had no significant medical history. The physical examination revealed left-sided facial palsy, upper lip swelling with a tough quality, and fissured and geographic tongue (Figure 1a–c). Moreover, a residual root of tooth #16 was observed, and radiographic imaging revealed proximal caries of teeth #11 and #12 (Figure 2). The laboratory investigations of complete blood cell count, comprehensive metabolic panel, γ-interferon release test, angiotensin-converting enzyme, chest x-ray, otolaryngology, abdominal ultrasound, and endoscopy showed no abnormalities. The incisional biopsy was taken on the upper lip and microscopic manifestations in histopathological examination were consistent with orofacial granulomatosis (Figure 1d). Eventually, a diagnosis of complete MRS was made based on clinical, laboratory, and histopathological findings.

Aiming at detecting and identifying the microbial infection, microbial next-generation sequencing of the surface-disinfected biopsy

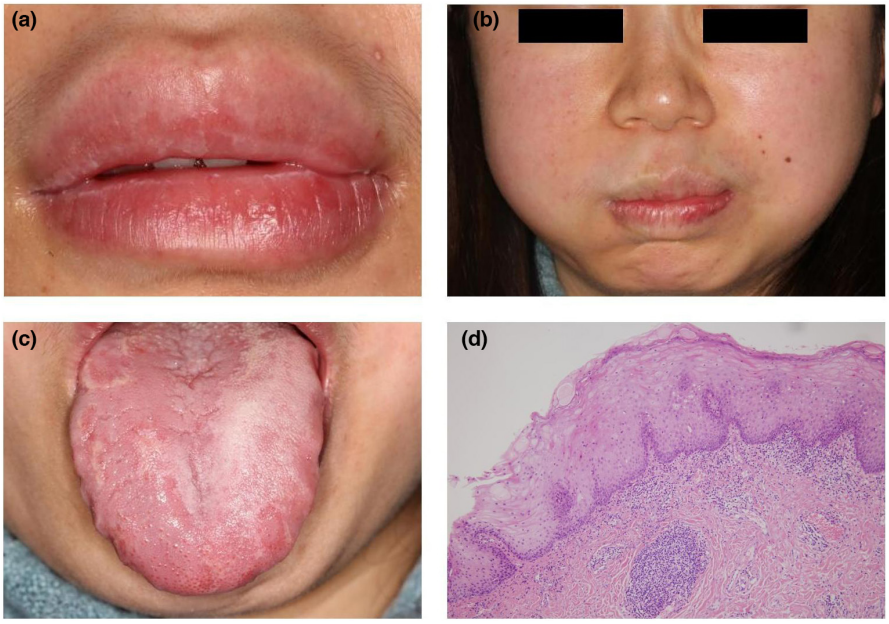

FIGURE 1 (a) Upper lip swelling, (b) left facial palsy, (c) fissures and geographic lesions on the tongue, and (d) histopathologic manifestations of the patient's biopsy showed edema of epithelium and infiltration of perivasculitis cells in lamina propria (hematoxylin and eosin staining, ×10 magnification).

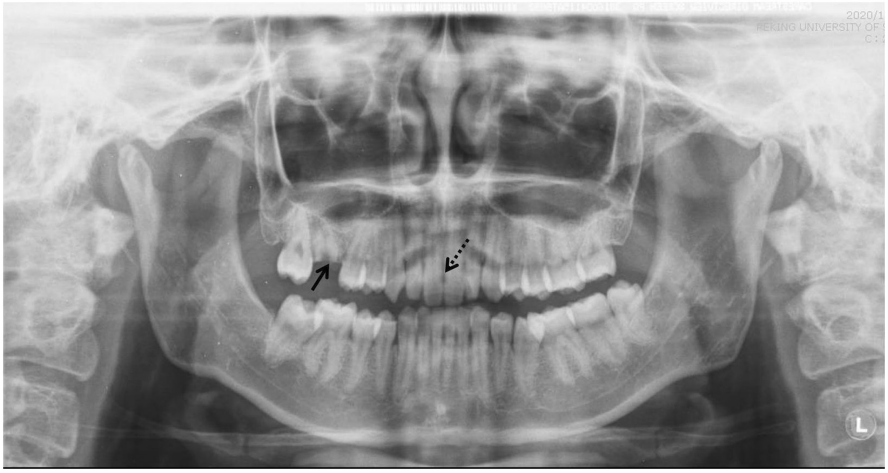

FIGURE 2 Radiographic imaging. The solid arrow represents a residual root of tooth #16. The dotted arrow represents the proximal caries of teeth #11 and #12.

sample was performed (BGI Group). The tissue sample was collected according to standard procedures, and DNA was extracted directly from the sample with a TIANamp Micro DNA Kit (DP316, Tiangen Biotech) according to the manufacturer's recommendation. The DNA libraries were prepared in a OneTouch system by emulsion polymerase chain reaction and then sequenced on an Ion Torrent Proton (Life Technologies) sequencing platform.[8] After removing human sequences, the remaining sequencing data were aligned to the microbial databases, and nucleic acid sequences of *M. fortuitum* were detected.

After treatment of typical intralesional injection with triamcinolone acetonide, which is the mainstay of the current knowledge, combined with broad-spectrum antibiotics (moxifloxacin), the swelling of the upper lip slightly improved with relapse. Since odontogenic infection was suspected as the possible origin, the patient was referred for removal of the residual root and the endodontic treatment of the decay of teeth #11 and #12. The swelling of the upper lip subsided after elimination of the odontogenic infections, and the facial palsy was relieved. There was no recurrence of the symptoms at 6-month follow-up.

3 | DISCUSSION

MRS is a neuromucocutaneous disease of unknown pathogenesis. Previous studies have provided some evidence for microbial infection as the cause of MRS, and the mainly pathogenic microorganisms, *M. tuberculosis* complex and *B. burgdorferi*, were proposed to be associated with the granulomatous reactions.[2,3] However, the relationship and mechanisms between microorganisms and this disease, especially its neurological aspects, are unknown.

In this case, we reported a case of complete MRS with symptoms of facial paralysis, swelling lip, and fissured tongue, and *M. fortuitum* was detected in the lip tissue by next-generation sequencing, which is valuable in detecting low abundance target DNA sequences in tissue samples. In the literature, it was reported that *M. fortuitum* can cause both neuronal and granulomatous disorders. Talati et al.[4] reported 19 cases of primary and secondary CNS infections, with 14 cases caused by *M. fortuitum*. It was also reported that *M. fortuitum* could cause CNS infections in both patients with HIV and and those who are immunocompetent.[5,6] Parti et al.[7] constructed a murine

model infected with wild-type *M. fortuitum* and found that early granuloma could be seen on the 10th day, which were more pronounced and developed on day 25 along with the tubular damage. Johansen et al.[9] used the zebrafish model and found that zebrafish embryos form granulomas from as early as 2 days postinfection of *M. fortuitum*. Therefore, we further speculated that *M. fortuitum* may be related to the phenotype of MRS, such as facial paralysis and lip swelling.

The patient was initially treated with the combination of broad-spectrum antibiotics in addition to conventional injection of corticosteroids, and the symptoms improved but with relapse. We began to consider the association of MRS with microbial infection pathogenesis, and the possible *M. fortuitum* infection from odontogenic origin in this case. There were reports about *M. fortuitum* causing osteomyelitis, and the mandibular osteomyelitis can originate from odontogenic infection such as residual roots,[10,11] which might provide the bridge in between. In this case, the symptoms of the patient improved significantly after thorough treatment of the odontogenic focus further verified this hypothesis.

To summarize, it was speculated that *M. fortuitum* likely from dental origin might be linked with MRS, the rare neuromucocutaneous disease with granuloma and neuronal manifestations. The causal role of this organism in MRS is worthy of further exploration.

4 | CONCLUSION

To the best of our knowledge, this case is the first in the literature to report a complete case of MRS with *M. fortuitum* detected by next-generation sequencing. In addition, *M. fortuitum* was speculated to be related to granulomatous and neuronal disorders. In the future, further clinical and basic investigations are needed to clarify the association between *M. fortuitum* and MRS.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

ORCID

Zhimin Yan https://orcid.org/0000-0002-0751-7374

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