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Herpes zoster aseptic meningitis and Ramsay Hunt syndrome in an immunocompetent young adult post mild COVID-19 – A coincidence?

Dear Editor

We report a nearly missed case of Ramsay-Hunt syndrome with aseptic meningitis in a young immunocompetent man post mild Coronavirus Disease-2019 (COVID-19).

A 25-year-old man experienced mild COVID-19 (manifesting as fever and sore throat) at the start of the Omicron BA.2 outbreak in May 2022. He had fully recovered without antivirals and presented three weeks later with sudden onset right facial palsy, headache, dizziness, and vomiting. Upon triage, his body temperature was 36 °C, heart rate 75 bpm, respiratory rate 20 bpm, and blood pressure 125/74 mmHg. The physical examination showed right facial swelling with tenderness but no erythema, Brun nystagmus without ptosis, right face hypoesthesia, peripheral facial palsy, hearing impairment and right mastoid tenderness (Fig. 1A). A diagnosis of acute right peripheral vestibulopathy was made, and high dose prednisolone (1 mg/kg) was prescribed by the neurologist.

However, headache and vomiting persisted so he was admitted the following day. His nasopharyngeal swab for SARS-CoV-2 RNA yielded a cycle-threshold value of 36.36 (Alinity®; Abbott Diagnostics) but reverted to being undetectable two days later. Blood tests showed unremarkable WBC count 6820/μl, hemoglobin 16.4 g/dL, platelets 194 × 10^3/μl, alanine aminotransferase 16UI/l, creatinine 1.0 mg/dL, and C-reactive protein 0.14UI/l. He tested negative for HIV (ARCHITECT®; Abbott Diagnostics) and had normal immunoglobulin (IgG) levels and CD4/CD8/CD19 lymphocyte counts. He was seropositive for varicella-zoster-virus (VZV) IgG.

Brain MRI revealed a right mastoid effusion (sFig. 1A) and CSF analysis confirmed elevated total protein 71.3 mg/dL, pleocytosis with 89 lymphocytes/μl, normal glucose 54 mg/dL, positivity for VZV DNA, and negativity for SARS-CoV-2 virus, *Mycobacterium tuberculosis* and pathogens on the FilmArray Meningitis/Encephalitis Panel (Biofire® ME Panel). He later developed right inner ear vesicles (Fig. 1B). Intravenous acyclovir (10 mg/kg every 8 h) was prescribed for 10 days. Headache, vomiting, and dizziness were alleviated but brain MRI one month later revealed a persistently abnormal signal at his right cochlea and semicircular canals (star) and an abnormal enhancement of his right facial nerve (arrow) compatible with his unresolved facial palsy (sFig. 1B).

Cases of shingles have visibly risen during this pandemic. Reviews of increased incidence of VZV reactivation in association with COVID-19 vaccination and SARS-CoV-2 infection are summarized in the Supplementary Table 1. Most reactivations were cutaneous and self-limited, but in an unusually persistent case of shingles following vaccination, spike protein encoded by the mRNA (BNT162b2) vaccine was found in the skin lesions.[1] In addition, immunocompetent adults developing VZV meningitis following COVID-19 vaccination (not limited to mRNA vaccines) have been reported.[2–5] Neither vaccination nor mild COVID-19 is recognized as an immunocompromising condition, but the perturbations in cellular immunity resulting from the presence of SARS-CoV-2 spike protein warrant further investigation.

Ramsay-Hunt syndrome is shingles affecting the geniculate ganglion of the facial nerve, characterized by painful blisters affecting the ear, ipsilateral facial paralysis, and hearing loss. It is rare in healthy young adults in the absence of immunosuppression or stress. In this case, mild COVID-19 may have been the "stress factor". Although dermatomal pain due to viral induced neuronal inflammation is common, meningitis is rare. PCR analysis of CSF confirmed the VZV infection, and neuroinflammation persisted despite antiviral and steroid therapy.

Facial palsy during the convalescent phase of COVID-19 should prompt investigations before attributing to

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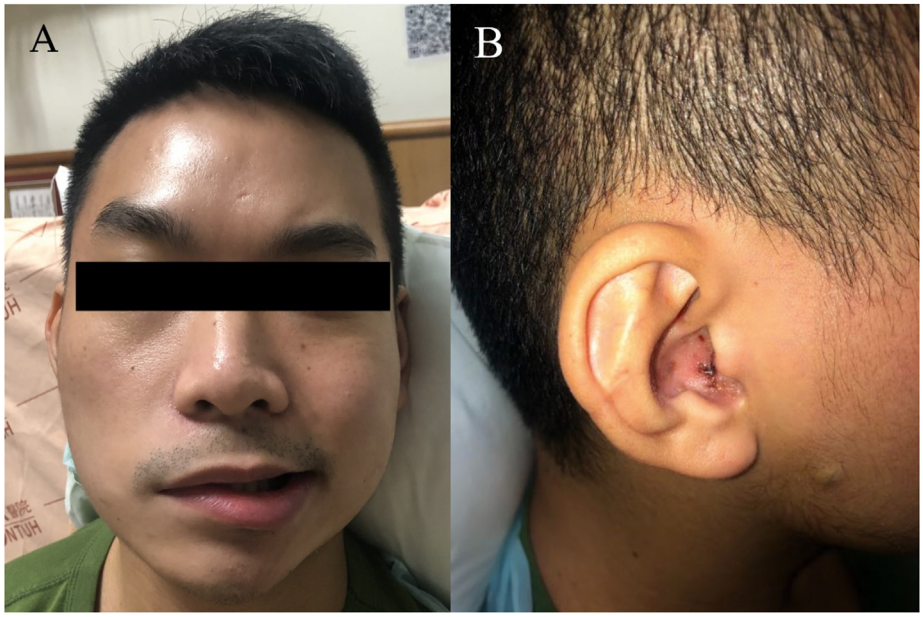

Figure 1. (A) Right face hypoesthesia and right peripheral facial palsy upon admission (B) right ear vesicles appearing three days later.

idiopathic Bell's palsy or long COVID-19. Aseptic meningitis by VZV should be a concern even in immunocompetent patients presenting with Ramsay-Hunt syndrome. SARS-CoV-2 as an agent of latency reversal and persistent neurocutaneous inflammation deserves further mechanistic elucidation.

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Declaration of competing interest

The authors have no conflicts of interests to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2023.04.006.

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