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LETTER TO THE EDITORS

Ramsay Hunt syndrome with an unusual clinical presentation in a liver transplant recipient: a case report and literature review

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Dear Sirs,

Reactivation of pre-existing varicella-zoster virus (VZV), a common latent infection in the general population, in cranial nerve neurons or dorsal root ganglia causes herpes zoster (HZ). HZ often presents as unilateral painful cutaneous eruptions along a specific dermatome, especially under stress or conditions of impaired immunity. Ramsay Hunt syndrome (RHS), the most common presentation of HZ in the head and neck region, mainly involves neurons in the geniculate ganglion, but may also be associated with multiple cranial neuropathies. Clinical presentation of RHS includes facial nerve palsy, otalgia, and herpetic auricular vesicular lesions, with or without auditory or vestibular involvement. Because VZV infection of the head and neck may not necessarily be associated with cutaneous lesions and may only present as multiple cranial neuropathies, initial diagnosis of VZV infection or RHS may be missed, delaying treatment. This could be fatal for post-transplantation patients receiving lifelong immunosuppressive therapy.

A 59-year-old man with a diagnosis of hepatitis C-related hepatocellular carcinoma and end-stage liver disease received a living donor liver transplant in 2009. His subsequent hepatic function was normal without any rejection episodes. His immunosuppression regimen included tacrolimus (2.0 mg once daily), sirolimus (2.0 mg once daily), and mycophenolate sodium (360 mg twice daily). Three years after transplantation, he presented to the emergency department with progressive dyspnea and fever up to 39°C for 1 day, a 4-day history of a sore throat with pain radiating to the left ear and occipital regions, dysphagia, and hoarseness. He had visited a local clinic and had received medication for presumed acute pharyngitis. However, despite taking the medication, progressive facial weakness on the left side and vertigo developed, followed by hearing loss 2 days later. Physical examination revealed localized tenderness with erythema and cutaneous eruptive vesicles over the left auricular region and a clear discharge from the external auditory meatus (Fig. 1A). Laryngoscopy revealed several eruptions with white surfaces that spread from the oropharynx region to the laryngopharynx, epiglottis, aryepiglottic fold, and arytenoids, with diffuse laryngeal congestion (Fig. 1B). Laboratory tests showed a white cell count of 15 470/μL, C-reactive protein level of 0.67 mg/dL, and tacrolimus trough level of 1.6 ng/mL. RHS was diagnosed, and we administered a regimen of acyclovir (10 mg/kg every 8 h) and prednisolone (50 mg) immediately following diagnosis. The ongoing immunosuppressive therapy was not modified. The fever subsided gradually, accompanied by laryngeal decongestion, 2 days after acyclovir infusion. On day 7, hoarseness, vertigo, and the pain in the left ear were alleviated. On day 10, facial weakness had improved, and the mucosal lesions in the larynx and pharynx, as well as the skin lesions over the auricular region and external auditory meatus, were healing. On day 14, we discharged the patient who had stabilized and had greatly improved symptoms and signs. The patient's therapy on discharge included oral prednisone taper and valacyclovir (1000 mg three times a day).

HZ is common and causes significant morbidity in solid organ transplant recipients. The incidence of VZV infection is reported as 11.2% at 4 years after kidney transplantation, an incidence that is approximately nine times greater than that in the general population [1, 2]. Herrero *et al.* reported that HZ develops in 12% of liver transplant recipients, a proportion much higher than that of the general population, and HZ development is related to immunosuppressive therapy [3]. Gourishankar *et al.* reported independent organ-specific risk factors for HZ infection, including female gender (liver), mycophenolate mofetil therapy (liver), and antiviral treatment other than prolonged cytomegalovirus prophylaxis (kidney and heart) [4]. However, the exact incidence of RHS in post-transplantation patients remains unclear because none of the population-based studies performed defines the incidence of RHS in adult organ transplant recipient cohorts.

Diagnosis of VZV infection can be based on reports of pain or rash over a dermatome and examination of distinctive lesions. Laboratory methods may also be used, including serologic testing methods such as enzyme immunoassay, latex agglutination, and direct fluorescent antibody staining of scrapings from active vasicular skin

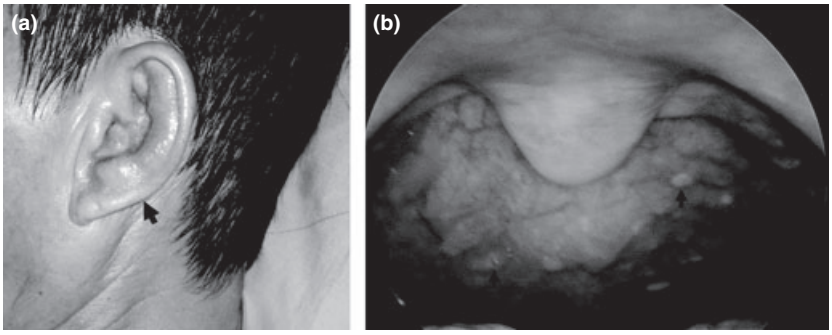

Figure 1 (a) Erythema and cutaneous eruptive vesicles (arrow) over the left auricular region with a clear discharge from the external auditory meatus.(b) Blisters with white surfaces (arrows) that spread from the oropharynx region to the laryngopharynx, epiglottis, aryepiglottic fold, and arytenoids, with diffuse laryngeal congestion.

lesions. However, although these tests are reliable in immunocompetent patients, they may not be as reliable in immunocompromised subjects. DNA hybridization, polymerase chain reaction (PCR) techniques, and cell culture from collected lesion material may also be used for a specific diagnosis. Recent studies suggest that PCR may positively identify the presence of VZV DNA in patient blood before the clinical symptoms develop, facilitating early treatment [5, 6].

In our case, RHS was diagnosed after examining the mucosal lesions of the pharynx 4 days later in the emergency department on the basis of the presence of progressive dyspnea and fever. These symptoms improved gradually after administering antiviral agents and steroids, despite the initial medication for suspected acute pharyngitis. Physicians should be aware that the incidence of VZV infection is increased in organ transplant recipients and that RHS might present without cutaneous lesions, which facilitate early diagnosis, resulting in serious clinical symptoms, including edema of the pharyngeal mucosa or dyspnea, if not properly treated. In addition, PCR for VZV DNA and DNA of other viral entities in blood or in samples collected directly from the suspicious skin lesions should be considered for transplant patients who have upper respiratory tract symptoms to ensure that they receive timely treatment. Finally, organ transplant recipients receiving long-term immunosuppressive medication must be made aware of even the most trivial symptoms they might experience post-transplantation.

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