Ramsay Hunt Syndrome With Atypical Progress in a Renal Transplant Recipient: A Case Report

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Abstract
Ramsay Hunt syndrome is a rare complication of herpes zoster disease in which reactivation of latent varicella zoster virus infection occurs in the geniculate ganglion causing otalgia, unilateral vesicular eruption in a restricted dermatomal distribution, and peripheral facial paralysis. Dermal infections caused by human pathogenic herpes viruses are common in organ transplant recipients. For a transplant surgeon, it is imperative to remember that viral prophylaxis is essential in the follow-up of the transplant patients. Here, we presented a case of renal transplant and Ramsay Hunt syndrome with multiple cranial nerve involvement, with an atypical course. Management and differential diagnosis of this particular case are discussed with a review of the literature.

Key words: Renal transplant, Ramsay Hunt syndrome, Viral infection

Introduction
Ramsay Hunt syndrome is diagnosed in case of relapse of varicella zoster virus infection, and occurs at older ages after the primary infection. Ramsay Hunt syndrome is a rarely encountered cranial polyneuropathy associated with involvement of the seventh cranial nerve. The disease, also referred to as herpes zoster oticus, was first described by James Ramsey Hunt.1 The pathogenesis of the disease is because of the reactivation of latent viruses located in the geniculate ganglion and the spread of these viruses through the facial nerve in a retrograde fashion. It usually occurs in individuals with decreased cell-mediated immunity.2

This clinical entity is more common in immunosuppressed individuals. Here, our case was under posttransplant immunosuppression and is the second reported renal transplant case with Ramsey Hunt. The aim of this paper is to point out the importance of this clinical entity to renal transplant physicians and surgeons.

Case Report
A 27-year-old man who had a renal transplant from a live donor was within his 18th month posttransplant. He was admitted to our clinic with complaints of vertigo, severe right otalgia, fever, nausea, vomiting, and weakness. After 12 days of ambulatory follow-up, he was diagnosed with right facial paralysis. Maintenance immunosuppression consisted of cyclosporine (8 mg/kg/d; the target blood trough levels of cyclosporine in the first 3 months was 200-300 ng/mL for C0 and 1500-1700 ng/mL for C2), mycophenolate mofetil (2 g/d), and prednisolone. The dosage of prednisolone was 30 mg/d during the first 3 months and then was gradually reduced to 10 mg/d by 1 year. In accordance with the protocol, the antiviral therapy (valacyclovir, 1500 mg/d) had been administered for approximately 6 months after the transplant and then discontinued. The dosage of prednisolone was increased to 40 mg/d before 9 days of the onset of facial nerve paralysis.

Symptoms of peripheral nerve paralysis were present on his physical examination. His facial appearance was asymmetric. On the right side, there was no frontal wrinkle observed, and the patient could close his right eye partially. His right nasolabial sulcus...
disappeared, and he could not whistle and show his teeth on the right side. There was a decrease in the sense of taste, as well as a loss of balance. A cranial computed tomography, temporal bone computed tomography, and magnetic resonance imaging did not reveal any cranial pathological finding. Consultations from the departments of neurology, ear-nose-throat, and infectious diseases were requested for evaluation of his vertigo.

Nystagmus on the left side and vertical gaze, of which the rapid phase was left-beating, and rotatory nystagmus on right gaze, were demonstrated together with facial paralysis during the neurologic consultation.

Hearing loss on the right side was compared to the left, and vesiculobullous lesions on the internal aspect of the auricle and on the external ear canal were noted during the ear-nose-throat consultation. It was thus suggested that the patient may have Ramsay Hunt syndrome and that he should be evaluated in association with his other clinical findings.

The results of a routine laboratory examination, including a complete blood count, erythrocyte sedimentation rate, and blood biochemistry analyses were within normal ranges, and results of hepatitis markers and HIV serology were negative. The 24-hour urine creatinine clearance was 36.95 mL/min. The serum creatinine and blood urea nitrogen (BUN) levels were 1.7 mg/dL and 33 mg/dL.

The analysis of herpes simplex virus type I (HSV-1) IgG and IgM, as well as type II HSV IgG and IgM, were negative. Herpes zoster virus IgG and IgM were positive. Biopsy was performed from the scabbed lesions located on the auricle for the isolation of herpes virus; however, no viral growth was detected. It was thought that viral growth did not occur because of the scabbed lesions.

In the present case, acyclovir 10 mg/kg/d, IV every 8 hours was initiated. Two weeks after the onset of symptoms, the patient was given acyclovir, 400 mg, orally, 5 times daily, and the oral prednisolone dosage was tapered. The following week, vertigo, the right-sided facial pain, and otalgia regressed, and facial paralysis partially resolved.

**Discussion**

Ramsay Hunt syndrome is an infection of the geniculate ganglion of the seventh cranial nerve caused by the varicella zoster virus, which is a member of herpes virus group. Varicella, more commonly known as chicken-pox, occurs as the result of the primary infection of varicella zoster virus. Ramsay Hunt syndrome appears years after the primary infection of varicella zoster virus infection by reactivation of the disease.

Reactivations of varicella zoster virus, mainly occurring in adults, are believed to be induced by the impairment of the host’s cell-mediated immune system rather than a reintroduction of the virus into the host. The disease was first defined in 1907 by J. Ramsay Hunt. There are 3 different clinical types of Ramsay Hunt syndrome according to the severity of the disease. The first and mildest form of the disease is herpes zoster auricularis, which manifests as pain, redness, and the formation of herpetic vesicles in the ear. In the second form of the disease, in addition to the herpetic lesions, facial paralysis occurs, which are located at any site of the head and neck. The third form of the disease is accompanied by signs of eighth nerve involvement, with the above-mentioned symptoms.

Primary infection with varicella zoster virus usually occurs in childhood or adolescence, and remains latent. The pathologic symptoms of the infection appear with reactivation of the latent herpes virus. The mechanism of viral reactivation is not clear. Reactivation may occur as a result of failure of cellular immune defense. Control of viral infections is basically provided by cytotoxic natural killer cells and cytotoxic thymus-dependent lymphocytes. The functional deficiency in such cytotoxic active cells causes reactivation of herpes virus in immunodeficient and immunosuppressed subjects. Human pathogenic herpes viruses are divided into 5 groups as follows: HSV-1, HSV-2, varicella zoster virus, cytomegalovirus, and Epstein-Barr virus serostatus. Dermal infections, caused by these viruses, are common in organ transplant recipients. Primary varicella zoster virus infection is rarely encountered after solid organ transplant; it is frequently detected among the pediatric transplant population. Varicella zoster virus infection occurs in 5% to 15% of the patients, frequently around the sixth month after transplant.

Ramsay Hunt syndrome classically begins with prodromal signs, such as severe and sharp pain around the ear, red and swollen auricle, fever, and weakness. This is followed by the formation of herpetic vesicles on the auricle, external ear canal, and sometimes on the tympanic membranes, tongue, and uvula within 3 to 4 days. Vesicles are generally involved on the affected...
Peripheral facial paralysis exists in 60% to 90% of the patients. Facial paralysis generally appears 2 to 3 days after a vesicular eruption. Appearance of the paralysis may sometimes be prolonged up to 1 week. Vesicles are located on the same side as the facial paralysis. The signs of eighth nerve involvement, such as nausea, vomiting, vertigo, nystagmus, tinnitus, and hearing loss, may be accompanied with the disease. In addition, fifth, sixth, ninth, or 10th cranial nerve involvement may occur in some patients as well.

In the present case, facial paralysis was diagnosed 12 days earlier contrary to the classic progress of the disease, and medical treatment had been started. During the second week of facial paralysis, the patient was hospitalized urgently because of severe otalgia, auricular swelling, redness, tenderness, vertigo, nausea, and vomiting, which are signs of eighth cranial nerve involvement. Vesiculobullous lesions appeared on his auricle and in the external ear canal 3 days after hospitalization (Figures 1 and 2).

The time of onset of vesicles carries a prognostic importance. It is reported that vesicular lesions appeared in 19.3% of cases before facial paralysis; simultaneously in 46.5% of cases, and after facial paralysis, in 34.2% of cases. The onset of vesicular lesions before facial paralysis in our case was considered a good prognostic factor.8, 9

The disease is generally diagnosed with anamnesis and clinical signs. Vesicles, located in the external ear canal and on the tympanic membrane, can be observed via direct inspection or with the aid of an otoscope. Sensorineural hearing loss can be documented by audiometric testing. A complete blood count, erythrocyte sedimentation rate, and serum electrolytes may demonstrate an inflammatory process. Varicella zoster virus may be demonstrated on serologic tests. Varicella zoster virus can be isolated from intravesicular fluid.10 Virus also can be detected via PCR from dermal biopsies, including vesicular lesions. A significant increase in antibody titers is also observed in primary and recurrent infections; IgM is indicative of a primary infection.

In the present case, an attempt was made to isolate the virus via dermal biopsies from the auricle, including the lesions; however, the virus could not be isolated. This was considered to be related to the scabbed lesions, as well as owing to delayed biopsy.

In the present case, vesicular lesions located in the external ear canal and on the auricle were also observed. Sensorineural hearing loss was determined on audiometric testing.

The most-effective method in the treatment of Ramsay Hunt syndrome is still a combination of antiviral medications, used to prevent the replication of varicella zoster virus, and systemic steroids, used for anti-inflammatory and antiedemic effects. The initiation of acyclovir at a dosage of 800 mg/d or valacyclovir, 1 g 3 times daily, or famciclovir 500 mg 3 times daily particularly within first 72 hours, is of great importance for treating herpes zoster virus. In the presented case, acyclovir 10 mg /kg/d IV every 8 hours and prednisolone 1 mg/kg/d were initiated. Two weeks after the onset of symptoms, the patient was given oral acyclovir 400 mg 5 times daily and oral

Figure 1A. Right-sided facial paralysis.
Figure 1B. Typical skin lesions of Ramsay Hunt syndrome on the right auricular area.
Prednisolone dosage was tapered. Early diagnosis is important so that acyclovir and steroid therapy can be initiated as soon as possible to maximize the recovery rate of facial nerve function.

The prognosis of Ramsay Hunt syndrome is good from the point of vitality, whereas it is bad from the point of function. In our case, improvement in facial nerve paralysis was slow and only partial.

In conclusion, it is important to bear in mind that viral infections may cause clinical conditions such as the Ramsay Hunt syndrome in transplant recipients who are at risk for herpes virus infections because of immunosuppressant treatment.

References