Adult Human Parvovirus-B19 Infection Presenting with Hearing Difficulty and Dizziness

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Human parvovirus B19 (HPV-B19), a small and non-enveloped DNA virus, causes erythema infectiosum (EI) in children. In adults, however, it is known to cause a variety of symptoms. A 39-year-old woman visited our hospital because of low-grade fever, diarrhea, bilateral leg edema, and numbness in the right arm, one and a half months after her daughter developed EI. We diagnosed her as HPV-B19 infection after her daughter’s history and positive test for serum HPV-B19 IgM antibody, together with the continued observations. Two weeks later, she developed dizziness and left hearing difficulty. However, we did not give her any medication. HPV-B19 IgM antibody value (2.4) measured after one month of the onset was decreased to 1.7, 1.1, and 0.9 after two, three, and five months of the onset, respectively. Thus, it took 5 months for the IgM antibody value to become negative. Her symptoms gradually improved along with the decrease in HPV-B19 antibody without any medication. Hearing difficulty and dizziness are not categorized as manifestations of HPV-B19 infection, because these symptoms are very rare. The present report indicates that the symptoms related to inner ear dysfunctions should be added to those associated with adult HPV-B19 infection. In conclusion, we should consider HPV-B19 infection when we evaluate patients with causeless hearing difficulty and dizziness.

Keywords: HPV-B19; IgM antibody; immune complex; ear symptoms; erythema infectiosum


Human parvovirus B19 (HPV-B19), a small and non-enveloped DNA virus, belongs to the Erythrovirus genus (Broliden et al. 2006). Humans are the only host for parvovirus B19, and its transmission is person-to-person through the respiratory route (Broliden et al. 2006). HPV-B19 is well known to cause erythema infectiosum or fifth disease, a mild febrile illness with rash, in children. In adults, however, HPV-B19 causes a variety of clinical manifestations, although about 25% of infected individuals are completely asymptomatic and about 50% of patients have non-specific flu-like symptoms (Woolf et al. 1989; Hayakawa et al. 2002). Manifestations in adults include polyarthropathy, polyneuropathy, fatigue, skin rash, and edema (Hayakawa et al. 2002; Kerr et al. 2002). However, ear symptoms (hearing difficulty and dizziness) are not usually categorized as HPV-B19 associated symptoms. Concerning the ear symptoms of HPV-B19 infection, to our knowledge there has been only one report (Cotter et al. 1994).

Inner ear disorders cause symptoms such as hearing difficulty or vestibular function loss (Cotter et al. 1994; Lindblom et al. 2005). These symptoms have been recognized to be induced by autoimmune inner ear disease (Cotter et al. 1994; Lindblom et al. 2005). It is possible that autoantibody formation and circulating immune complex deposition cause the symptoms (Cotter et al. 1994). On the other hand, viral infections are assumed to be the primary cause of hearing loss and vestibular neuritis. These inner ear disorders may occur via an immune-mediated manner or direct viral neuron injury. Many kinds of viruses are reported to cause inner ear disturbances except for HPV-B19 infection (Lindblom et al. 2005).

Here, we describe a woman with HPV-B19 infection, whose daughter suffered from erythema infectiosum one and a half months before, complaining of wheals, a low grade fever, diarrhea, bilateral leg edema, hearing difficulty and dizziness. The present report was aimed to describe hearing difficulty and dizziness associated with HPV-B19 infection because these symptoms are very rare in this infection.

Method

We measured serum HPV-B19 IgM antibody using an enzyme immunoassay kit (Seiken, Tokyo, Japan). We left the first well empty. We added 100 µl of the standard and pre-diluted specimen to the anti-human IgM antibody coated wells. Then, we mixed them well and incubated at room temperature for 1 hour. Next, we removed the
solution and washed the plate by wash solution twice and added 100 µl of viral antigen solution to the wells except for the empty one, and mixed and incubated them as described above. After that, we removed the antigen solution and washed twice, and added 100 µl of enzyme-labeled antibody solution to the wells except for the empty one, mixed and incubated them for 1 hour. Then, we added 100 µl of substrate after removing the enzyme-labeled antibody solution and washing. We mixed and incubated them in the same way. Finally, we added 100 µl of stop reagent to each well including the empty one. Within 30 minutes of adding the stop reagent, we measured the optical density (O.D.) of the wells at a filter wavelength of 430/630 nm with an automatic plate reader after adjusting the instrument to zero-absorbance against the empty one.

The O.D. value for the test specimen is expressed as “a”, and the average of the O.D. values for the standard is expressed as “b”. The IgM antibody index for the specimen as follows:

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\text{IgM antibody index} = \frac{a}{b}
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\(a/b > 1.0\) is determined as positive.

**Clinical Findings**

A 39-year-old Japanese woman noticed wheals on her extremities one month prior to visiting our hospital. In addition, one week after her initial symptom of wheals, she developed low-grade fever, diarrhea and bilateral leg edema. And then, gradually, she experienced a sense of generalized fatigue and numbness in her right arm while the bilateral leg edema had gradually improved (Fig. 1). She visited our hospital because of the persistence of the above symptoms one month after the onset of wheals. She did not have any remarkable past history. However, her 7-year-old daughter had erythema infectiosum a few weeks before she developed wheals.

Physical examination did not reveal any abnormality at the first visit. She was not febrile (36.8°C), the complete blood cell count was normal and there were no significant abnormal findings in serum electrolyte, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), urea-N, creatinine, and thyroid hormones. C-reactive protein and rheumatoid factor were negative, although serum antinuclear antibody was elevated (× 640). IgM antibody to HPV-B19 was positive (2.4) (a value > 1.0 was determined as positive). We diagnosed her as having acute HPV-B19 infection and continued observation. Two weeks later, she visited our hospital again because of left hearing difficulty with dizziness (Fig. 1). Pure-tone audiometry revealed asymmetry in the hearing level at 125 Hz and 250 Hz, although both hearing levels were within normal limits. Her hearing difficulty gradually improved spontaneously along with the decrease in the IgM antibody index of HPV-B19. All of her symptoms including hearing difficulty disappeared 3 months after the onset (Fig. 1).

**Discussion**

The patient’s daughter had erythema infectiosum prior to the appearance of her own manifestations. The familial history contributed to her diagnosis and suggested the importance of droplet infection from a child to its mother. Hayakawa et al. (2002), however, described that 11 out of 21 adult patients with HPV-B19 infection did not have familial histories of HPV-B19 infection. Therefore, HPV-B19 infection is potentially transmissible even without a familial history.

The clinical manifestations associated with HPV-B19 infection are influenced by the infected individual’s age. In adults, HPV-B19 causes a variety of clinical manifestations, although about 75% of infected individuals have non-specific flu-like symptoms or are completely asymptomatic (Woolf et al. 1989; Hayakawa et al. 2002). For HPV-B19 infection, however, since there has been only one report about inner ear symptoms (Cotter et al. 1994), our patient

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**Fig. 1.** Clinical course (39-year-old woman). It took more than 3 months from onset to resolution of the constellation of symptoms, and 5 months before IgM antibody became negative. The presence of IgM antibody greater than 1.0 indicates positive.
may represent a rare case given the hearing difficulty and dizziness. In the present patient, hearing levels were within normal limits by pure-tone audiometry. Probably, her audiibility began to improve at that time. Actually, these symptoms improved along with the decrease in IgM antibody to HPV-B19.

The pathogenic mechanisms of HPV-B19 infection are complex and variable (Barah et al. 2003). One possible mechanism is direct infection. HPV-B19 infection sometimes results in anemia. The mechanism of anemia is direct viral infection of red blood cells because the HPV-B19 cellular receptors are distributed mainly on the surface of erythroid progenitors (Brown et al. 1993). Concerning the ear symptoms of our case, the possibility of direct infection is small because of the viral tissue tropism (Cooling et al. 1995). Another possible mechanism is immune complex deposition. It is known that the formation of antigen-antibody complexes can induced neuronal disorders. Probably, the accumulation of the complexes injures the feeding vessels of the neuron resulting neuronal disorders (Brown et al. 1993). In our patient, the ear symptoms improved along with the decrease in IgM antibody to HPV-B19. This course suggested that viral infection-induced immune reactions, that is IgM antibody, could cause hearing difficulty and dizziness. However, such a mechanism may not account for only left affection of hearing difficulty.

Usually, symptoms associated with HPV-B19 infection resolve spontaneously within a few weeks. However, as in this patient, symptoms can sometimes last for months in some patients (Lindblom et al. 2005). Lindblom et al. (2005) reported that the virus was not rapidly cleared even from immunocompetent individuals. They described that HPV-B19 IgM continued to remain positive in a patient for 90 weeks, though in most patients it is cleared within 17 weeks. In our patient, it took more than 3 months from the onset until resolution of the constellation of symptoms, and it took 5 months for the IgM antibody value to become negative (Fig. 1).

Here, we report a patient of adult HPV-B19 infection showing diverse symptoms including hearing difficulty and dizziness. HPV-B19 can infect apparently healthy adults and cause a variety of clinical manifestations. The infection can induce hearing difficulty and dizziness, although such symptoms are very rare in HPV-B19 infection. Therefore, hearing difficulty and dizziness should be included among the symptoms of adult HPV-B19 infection, and we should consider HPV-B19 infection when we evaluate patients with a causeless hearing difficulty and dizziness.

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Conflict of Interest

We do not have any conflict of interests to declare associated with this manuscript.

References


