



## Sensorineural Hearing Loss Associated with Kawasaki Disease

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### Introduction

Kawasaki disease (KD) is an acute systemic vasculitis of children characterized by fever, rash, conjunctival hyperemia, oropharyngeal erythema, edema and erythema of the hands and feet, and cervical adenopathy [1]. A variety of other features are also characteristics of this syndrome, including coronary artery aneurysms, urethritis, anterior uveitis, mild hepatobiliary dysfunction, and gallbladder hydrops. Coronary artery abnormalities, including aneurysms and ectasia, occur in approximately 20% of untreated patients [2]. Neurologic involvement is rare. Cranial nerve palsy, especially involving the seventh nerve, has been reported [3], as well as hemiparesis caused by cerebral thrombosis and infarction, and convulsions.

Although about 30% of patients with acute KD in the United States have been reported to suffer mild sensorineural hearing loss (SNHL) [4], only a few such cases have been reported in Japan. On the other hand, in both countries, a few cases of severe or profound SNHL in children who were in the acute phase of KD have been documented [5].

Here we describe a three-year-old Japanese girl with bilateral profound SNHL

associated with acute KD

### **Case Report**

A previously healthy Japanese girl aged three years presented with fever that had persisted for seven days. The patient met all of the following criteria for KD: 1) persistent fever for more than five days, 2) changes in the peripheral extremities, such as erythema and edema of the hands and feet in the acute phase, and membranous desquamation of the finger and toe tips in the convalescent phase, 3) polymorphous exanthema, 4) bilateral nonexudative painless conjunctivitis, 5) oropharyngeal changes including erythema, fissuring of the lips, strawberry tongue and diffuse mucosal infection of the oropharynx. No echocardiographic or electrocardiographic abnormalities were found. The patient was conventionally treated with intravenous gammaglobulin (2 g/kg/day for one day) and aspirin (30 mg/kg/day for 11 days, followed by 4 mg/kg/day for 30 days). Although her clinical symptoms initially resolved, she developed fever again and was treated with gammaglobulin (1 g/kg/day) for one day. She was discharged from hospital two weeks after symptom onset. One month after onset, her parents noticed an absence of response to sound stimuli. Her eardrums were normal and tympanometry revealed normal middle ear compliance and pressure. A play audiometry task and auditory brain-stem response (ABR) (Neuropack<sub>μ</sub>, Nippon Koden, Tokyo, Japan) assessed one month after the onset of KD revealed no hearing response and an absence of waves generated by click stimuli at 105 dBHL on both sides, respectively. The patient was treated with methylprednisolone (starting from 10 mg/kg/day and then tapered), vitamin B12, and adenosine triphosphate disodium intravenously for one week. Two weeks after the treatment, auditory acuity on the right improved to 40-50dBHL, but remained absent on the left in terms of auditory steady state response (ASSR)(the frequency-specific thresholds were recorded by a Bio-logic MASTER system, Mundelein, IL). Figure 1 shows the patient's hearing level at one (A) and six (B) months after onset, as assessed by ASSR.

## **Discussion**

In Japan, only eight patients (mean age 3.2 years, range 0.4 - 4 years) with severe or profound SNHL associated with KD have been reported, and most cases were bilateral. In seven of these patients, hearing loss was permanent to some degree. The time between the diagnosis of KD and the perception of hearing loss ranged from six days to eleven months. Such a delay is related to the difficulty in establishing a diagnosis in younger children, especially those aged less than four years, when parents may fail to identify the perception problem. Most cases of SNHL associated with KD have been treated with steroid. In KD patients who develop sudden SNHL, there may be no alternative therapy to steroid despite a lack of evidence as to its efficacy.

The mechanism of SNHL associated with acute KD remains to be determined. Epidemiologic data suggest that KD has an infectious etiology [6]. The relative rarity of KD in the perinatal period and among adolescents and adults suggests that KD may be caused by an agent to which virtually all adults are immune, and from which most very young infants are protected by maternal antibodies. The SNHL associated with acute KD might reflect infection of the inner ear, analogous to the direct cytopathic effects on the labyrinth and cochlea associated with certain viral illnesses, such as mumps and rubella [7].

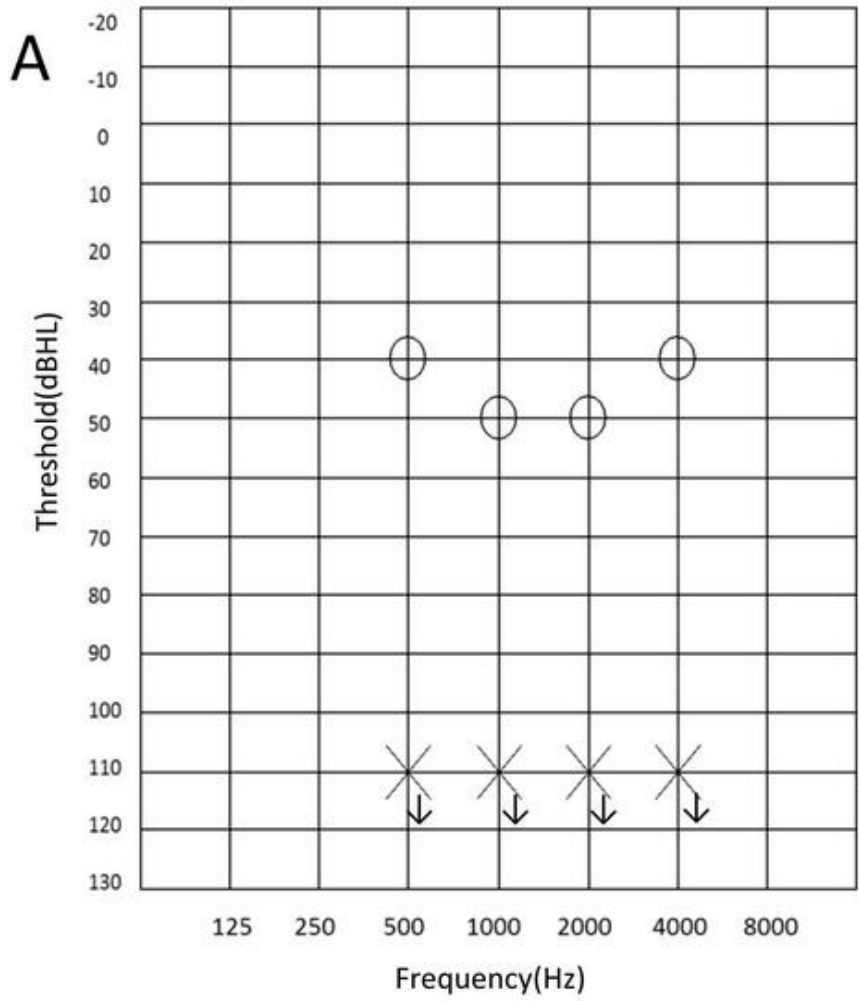
Alternatively, SNHL may be associated with the intense immune activation or elevated levels of circulating immune complexes seen in patients with acute KD [8]. In collagen-vascular diseases, such as Cogan syndrome (nonsyphilitic interstitial keratitis and vestibuloauditory dysfunction) or systemic lupus erythematosus, hearing loss has been ascribed to numerous autoimmune mechanisms, including anticochlear antibodies, lymphocytes reactive to inner ear antigens, and immune complex deposition within the otic capsule [9]. This hypothesis does not contradict bilateral SNHL associated with KD.

Finally, occlusion of cochlear vessels or of the vasa nervorum of the eighth cranial nerve can lead to ischemic damage to the membranous labyrinth or the auditory nerve itself [10].

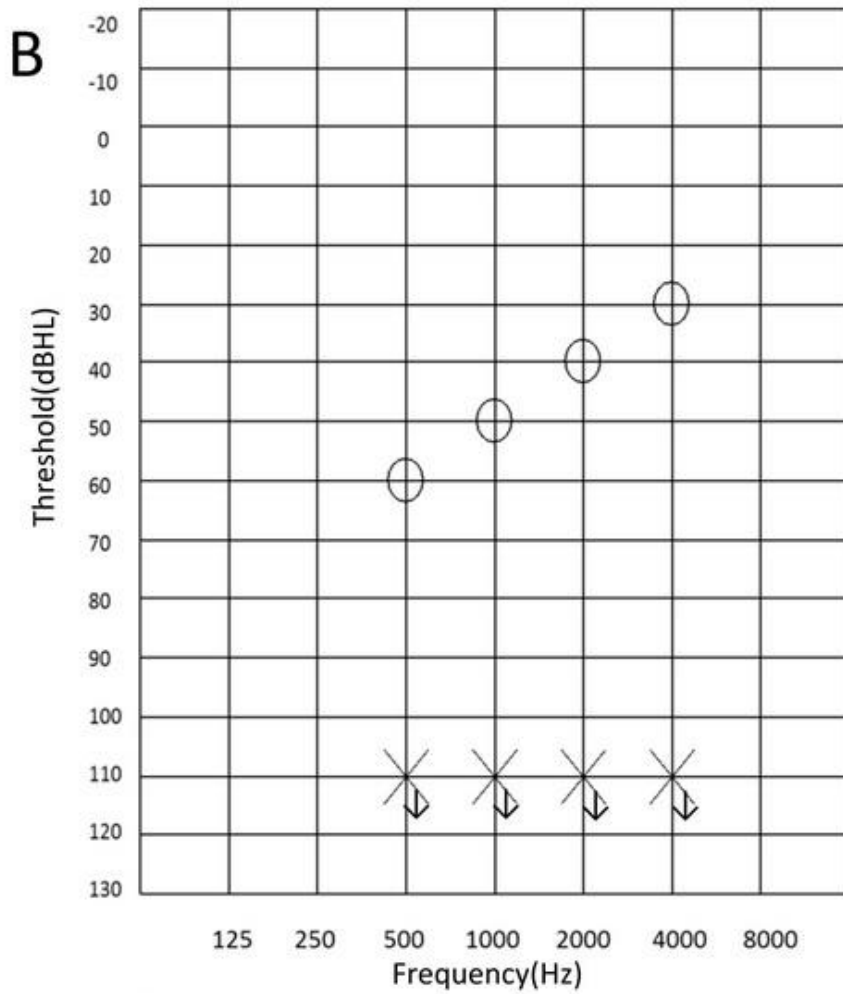
The potential role of aspirin toxicity in SNHL associated with KD requires further study. Many studies have shown that aspirin in high doses causes mild to moderate SNHL that improves to a normal hearing level without any treatment [11]. Higher doses tend to cause more severe hearing loss. Furthermore, aspirin toxicity in adults is reported to be reversible within 72 hours [12]. In Japan, high dose aspirin is never used because of concerns regarding the hepatotoxicity of salicylates. Reports from Japan have documented a few KD patients complicated by severe or profound SNHL. Among

reports from the United States, a prospective study by Knott and Sundel showed that about 30% of KD patients had SNHL, although the SNHL was mild and temporary in most cases [4,13]. Thus, it is possible that Japanese cases of SNHL associated with KD were not triggered by aspirin. In the United States, however, many cases of mild and temporary SNHL associated with KD may have been due to aspirin toxicity, because there the dose of aspirin for treatment of KD tends to be two to three times higher than in Japan [14]. The pathogenesis of mild and temporary SNHL caused by aspirin might differ from that of severe and permanent SNHL, such as that in the present patient.

Children with KD may be referred to an otolaryngologist for a variety of signs and symptoms during their acute illness. However, referral for evaluation of hearing loss may be made long after the signs and symptoms of acute KD have disappeared. Especially, children aged less than four years cannot perform conventional audiometry tests. Parents should be educated about the possible sequelae of unrecognized hearing loss in this age group, as it may lead to speech and language delay, behavioral and social adjustment difficulties, and poor academic performance.



One month after onset (after steroid treatment)



Six months after onset (after steroid treatment)  
round: right air conduction, cross: left air conduction

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