Atypical Cogan’s Syndrome with Aortitis

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Abstract

Cogan’s syndrome is characterized by non syphilitic interstitial keratitis and Meniere’s syndrome-like audiovestibular function disorder, as well as various systemic manifestations, including fever, arthralgia, vasculitis, and aortitis. We report the case of atypical Cogan’s syndrome with aortitis; the patient’s symptoms caused by active inflammation, including inflammatory ocular manifestations, audiovestibular symptoms, and aortitis, were improved by early administration of corticosteroids, however, her reduced visual acuity was not improved because of post-inflammatory change in her left eye.

Key words: atypical Cogan’s syndrome, scleritis, hearing loss, aortitis, corticosteroid

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Introduction

Cogan’s syndrome was defined by David Cogan in 1945, as the case both of non-syphilitic keratitis and Meniere’s syndrome-like audiovestibular function disorder occurring together within 2 years (1). In 1980, Haynes et al suggested that the definition of this condition should be expanded to include patients with ocular manifestations other than interstitial keratitis or audiovestibular function disorder distinguished from Meniere’s syndrome, and proposed the diagnostic criteria for typical and atypical Cogan’s syndromes (2).

Interstitial keratitis is necessary for the diagnosis of typical Cogan’s syndrome; however, various ocular manifestations, including conjunctivitis, uveitis, scleritis, and choroiditis, were reported to be either independent of or associated with interstitial keratitis in atypical Cogan’s syndrome (2). Generally, visual loss is superimposed on Cogan’s syndrome, leading to blindness in a few cases. Audiovestibular manifestations associated with Cogan’s syndrome include sensorineural hearing loss, tinnitus, and vertigo. The vestibular manifestations are severe and definitive hearing loss has lead to deafness in many cases.

In addition to the ocular and audiovestibular manifestations, various systemic symptoms have been reported in patients with Cogan’s syndrome. According to the case review of Cogan’s syndrome, about one-third of the patients had a fever and a loss in body weight and 12.5% had aortitis (3).

Here we report a woman patient with atypical Cogan’s syndrome with aortitis superimposed. Oral administration of corticosteroids improved her ocular inflammatory manifestations, hearing loss and aortitis with no relapse observed to date; however, reduced visual acuity of her left eye remained unimproved due to corneal opacity, synechia formation, and refractive error considered to be post-inflammatory changes. Our findings suggest that early therapeutic intervention for Cogan’s syndrome is essential for the improvement of ocular and audiovestibular symptoms.

Case Report

A 59-year-old woman had pain, erythema, and discharge in her left eye in July 2006. Her ocular symptoms improved temporarily by topical administration of steroid and antibotic drugs. In September, her ocular symptoms were exacerbated, leading the sudden development of bilateral hearing loss, tinnitus, and vertigo. In addition to her ocular and audiovestibular symptoms, she had fever and fatigue, so she consulted a physician of the general hospital. At that time, the laboratory test showed that the white blood cell count was 13,600/μL and the C-reactive protein (CRP) level was...
Figure 1. Pure tone audiogram before (a) and 20 days after the administration of prednisolone (b). The circles and crosses indicate hearing levels by air conduction of the right and left ears, respectively. The left bracket ([) and right bracket (]) indicate hearing levels determined by bone conduction of the right and left respectively.

6.93 mg/dL. Since her diagnosis was not established, she was admitted to our hospital in October.

The medical examination on admission showed that her body temperature was 37.7°C, and bruit was heard on right side of the neck. She lost 8 kg in body weight in 6 months. No abnormal findings were observed in her chest, abdomen, joints, and skin. Audiogram showed moderate, bilateral hearing loss in terms of both air and bone conduction hearings (Fig. 1a). On admission her complaints of vertigo and tinnitus had disappeared with no abnormal sign observed in the vestibular function test. Visual acuity was reduced in the left eye. The ophthalmologist pointed out corneal opacity in bilateral eyes, scleritis and synchia in the left eye (Fig. 2).

The laboratory test results on admission were as follows: white blood cell count; 18,100/μL, hemoglobin level; 10.4 g/dL, platelet count; 74.7×10⁴/μL, erythrocyte sedimentation rate (ESR); 139 mm/hr, and CRP; 13.16 mg/dL. The analysis of blood chemistry revealed that her hepatic and renal functions fell within their normal limits. She was borderline positive for the rheumatoid factor at 44 U/mL and negative for antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA) and syphilis serology. All the blood and urine samples repeatedly collected and cultured were negative.

Since aortitis was suspected of causing fever, neck bruits, and elevated acute-phase laboratory parameters, chest computed tomography (CT) scan was performed. The chest CT scan showed arterial wall thickening in the aortic arch, brachiocephalic trunk, right common carotid artery, and abdominal aorta (Fig. 3a). These findings were assumed to be consistent with those of aortitis. Since her symptoms met only two of six evaluation items defined in American College of Rheumatology (ACR) criteria for the classification of Takayasu’s arteritis (neck bruits and arteriogram abnormality) (4), and only two of five evaluation items in ACR criteria for the classification of Giant-Cell Arteritis (age and elevated ESR) (5), it was impossible to diagnose her with these two diseases. The echocardiogram showed mild aortic valve insufficiency and aortic wall thickening.
Atypical Cogan’s syndrome with aortitis was diagnosed on the basis of bilateral interstitial keratitis, left anterior uveitis and scleritis, and Meniere’s syndrome-like audiovestibular symptoms. The fever and aortitis detected by CT were assumed to be systemic manifestations complicated with Cogan’s syndrome.

Pre-existing remittent fever had persisted even after admission. On admission, sensorineural hearing loss and aortitis were not found, as systemic infection was suspected of causing the fever. Antibiotic therapy was started, however, her symptoms were not improved. Atypical Cogan’s syndrome was diagnosed, and oral prednisolone (1 mg/kg/day) and betamethasone eyedrops were administered. Her bilateral eye pain and general condition improved; the bruits on the right side of her neck disappeared. Her CRP level also decreased gradually. Audiogram taken at 20 days after the administration of prednisolone showed the endpoints of the hearing test were improved (Fig. 1b). Arterial wall thickening in the aortic arch, brachiocephalic trunk, right common carotid artery, and abdominal aorta was improved after the administration of prednisolone (Fig. 3b). However, reduced visual acuity of her left eye was not improved by oral and topical administration of the corticosteroids. This was because corneal opacity, synchiae formation, and refractive error, which were assumed to be due to post-inflammatory change, persisted, though active inflammation of interstitial keratitis, scleritis, and anterior uveitis disappeared after the administration of corticosteroids. This finding suggested that her visual acuity might not be expected to be improved even with concomitantly use of corticosteroids and immunosuppressive drugs. The dose of oral prednisolone was tapered gradually; subsequently no further relapse of ocular inflammation and hearing loss has occurred and no deterioration of general status has been observed.
The cases of Cogan’s syndrome were mainly reported in a young adult Caucasian population. No gender preponderance was observed in the patient group (3). In Japan, about 20 cases of Cogan’s syndrome have been previously reported, however, the incidence in a Japanese population has not been clarified.

Most of the patients have eye redness, photophobia and eye pain associated with interstitial keratitis; usually, both eyes are affected throughout the course of the disease. On examination of patients with interstitial keratitis, irregular, granular infiltration is observed, especially in the posterior part of the cornea, near the limbus. The audiovestibular manifestations associated with Cogan’s syndrome are similar to those of Meniere’s syndrome, with an acute onset of symptoms or the combination of symptoms including vertigo, instability, nausea, vomiting, and tinnitus. Generally, vestibular manifestations are severe and definitive hearing loss may lead to deafness.

Haynes et al suggested that the definition of Cogan’s syndrome should be expanded, and proposed the diagnostic criteria of atypical Cogan’s syndrome (2). According to the criteria defined by Haynes et al, the patients who have one of the following complications developed, may be classified into atypical Cogan’s syndrome group: (i) inflammatory ocular symptoms, including conjunctivitis, uveitis, scleritis and choroiditis, associated with Meniere’s syndrome-like episodes within two years, (ii) typical ocular manifestations, interstitial keratitis, were associated with audiovestibular symptoms distinguished from Meniere’s syndrome-like episodes within a period of two years, (iii) a delay of more than two years between the onset of typical ocular and audiovestibular manifestations. We diagnosed the present case with atypical Cogan’s syndrome on the basis that; she had uveitis and scleritis, which were associated with interstitial keratitis, with Meniere’s syndrome-like sensorineural hearing loss and temporal vestibular dysfunction, and that both her ocular and audiovestibular symptoms occurred almost at the same time.

In addition to the ocular and audiovestibular symptoms, various systemic manifestations in the group of patients with this syndrome have been reported. Aortitis and arteritis of primary branches or large arteries are the most serious complication in the patients with Cogan’s syndrome, because they may cause various cardiovascular involvements, aortic valve insufficiency, rupture of aneurysm, coronary artery stenosis, and so on. Some studies have reported on the case of Cogan’s syndrome patients with aortitis and arteritis of major branches, who were diagnosed on the bases of subclavian arterial narrowing shown by aortic arch angiogram (6), and of abnormal uptake in the aorta ascendens by 2-deoxy-2-[18F]fluoro-D-gucose positron emission tomography/computed tomography (F18-FDG-PET/CT) investigation (7). Grasland et al reported 32 patients with either typical or atypical Cogan’s syndrome from multi centers in France (3). In their report, 17 patients had typical Cogan’s syndrome and the remaining 15 had atypical Cogan’s syndrome. Four patients (12.5%) had aortitis, and no significant difference in frequency of aortitis occurrence was observed between the cases of typical and atypical Cogan’s syndrome. Systemic manifestations other than aortitis included fever, arthritis/arthritis, lymphadenopathy, vasculitis, and neurological disorder. Acute-phase laboratory parameters, CRP and ESR, were elevated in the patients with Cogan’s syndrome; however no prominent abnormality was observed. Although elevated ANCA was reported at diagnosis of Cogan’s syndrome (7, 8), no causal role of ANCA in the development of Cogan’s syndrome was clarified. In the present case, acute-phase parameters were elevated, however ANCA was not detected.

The differential diagnosis of Cogan’s syndrome is made on the basis of various conditions that cause similar ocular and audiovestibular manifestations, such as polyarteritis nodosa, Wegener’s granulomatosis, relapsing polychondritis, and rheumatoid arthritis. If aortitis is associated with Cogan’s syndrome, Takayasu’s arteritis and Giant-cell arteritis should be added as evaluation items for differential diagnosis, because these two disorders may be associated with either ocular or audiovestibular manifestations. However, aortitis of Cogan’s syndrome is indistinguishable from Takayasu’s arteritis, and a case of Cogan’s syndrome with Takayasu’s arteritis was previously reported (6). That case met five of six evaluation items defined in the ACR criteria for the classification of Takayasu’s arteritis.

With the initial administration of corticosteroids for controlling the symptoms of Cogan’s syndrome, prednisolone is orally administered routinely at an initial dose of 1 mg/kg/day and a corticosteroid eye drop is used for the ocular inflammation. The oral corticosteroids are gradually tapered, as the symptoms are alleviated. However, in some cases, hearing loss or ocular inflammation do not respond, or they relapse during tapering of the corticosteroid mono-therapy. Immunosuppressive drugs are generally combined with corticosteroids for these cases. Effectiveness of low-dose methotrexate (9, 10) or cyclophosphamide (6, 11) in treating patients with Cogan’s syndrome resistant to corticosteroid mono-therapy has been reported. Fricker et al reported two cases of the Cogan’s syndrome, who took infliximab, a TNF-alpha blocker, resulting in improved symptoms (12). However, deafness generally remains permanently cureless once occurring, even after the administration of corticosteroid and immunosuppressive drugs. On the other hand, the prognosis of reduced visual acuity is better than that of hearing. According to the review of Grassland et al, among 32 patients, a significant decrease in hearing was observed in 19 patients, while a significant decrease in visual acuity was observed in 9 patients, to whom corticosteroid drugs and some immunosuppressive drugs were administered (3).

The present case had inflammatory ocular and audiovestibular symptoms of Cogan’s syndrome and aortitis. She
achieved a preferable outcome by oral administration of the corticosteroid drug alone; her bilateral sensorineural hearing loss, active ocular inflammation, and aortitis features were improved and the remission was maintained. However, her reduced visual acuity was not improved because post-inflammatory changes persisted. Her clinical course suggests that her visual acuity reduction might have been less if immunosuppressive treatment had been started earlier.

Generally, it is said that early therapy is important for the improvement of reduced auditory acuity associated with Cogan’s syndrome. We think that the administration of immunosuppressive drugs at the earliest stage possible is also very important for the improvement of the reduced visual acuity associated with Cogan’s syndrome. Moreover, aortitis, which may be a fatal disorder in the systemic manifestations of Cogan’s syndrome, should be assessed carefully. Physicians should have such new knowledge of Cogan’s syndrome, although it is a rare disease in Japan, because the early and careful assessment and treatment by an ophthalmologist, otolaryngologist, and physician are essential to achieve a good prognosis.

References