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INVITED REVIEWS

Cogan's syndrome

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INTRODUCTION

Cogan's syndrome (CS) is a rare inflammatory disorder that was first described by David Cogan in 1945 [1]. It is distinguished by the presence of ocular inflammation (non-syphilitic interstitial keratitis) and audiovestibular dysfunction occurring within a few months. The incidence of CS is unknown. It mostly affects young adults (peak incidence: 20-30 years); there is no known sex or racial predominance [2]. CS can also cause systemic vasculitis, which was included in the "variable vessel vasculitis" category in Chapel Hill Consensus Criteria.

Definition

CS vasculitis is defined as vasculitis occurring in patients with CS, characterized by interstitial keratitis, uveitis, episcleritis, and inner ear disease. Vasculitic manifestations may include arteritis (affecting small, medium, or large arteries), aortitis, aortic aneurysms, and aortic and mitral valvulitis [3].

Clinical Features

The most frequent ocular feature of CS is non-syphilitic interstitial keratitis. Iridocyclitis, conjunctivitis, episcleritis, and retinal scleritis are other common ocular findings of CS. The ear symptoms of CS are characterized by attacks consisting of vertigo, ataxia, nausea, vomiting, and tinnitus, leading to sensorineural hearing loss (SNHL). Symptoms such as fever, weight loss, arthralgia, myalgia, lymphadenopathy, hepatosplenomegaly, and abdominal pain may be seen in 50-80% of patients complicated with systemic vasculitis.

Aortitis is the most frequent vascular involvement in CS, although the size of vessels can be affected. Aortic insufficiency related to aortitis is not a frequent (10%) complication of CS. Limb claudication due to stenotic or occlusive lesions may also be seen in CS with large vessel vasculitis [4,5].

Diagnosis

Characteristic involvement of both eyes and inner ear is essential for the definite diagnosis of CS. Infections, malignancies, and other primary or secondary vasculitides should be excluded, especially in suspected cases. There are no diagnostic autoantibodies or specific radiologic findings for CS vasculitis. Although the ascending aorta is mostly involved in cross-sectional imaging, the entire aorta can be affected, and aneurysmal dilatation may develop.

Differential diagnosis

The different disease spectrums that cause oculovestibular symptoms are included in the differential diagnosis of CS. Sarcoidosis, Voyt-Koyanagi-Harada syndrome, Susac Syndrome, and infections including syphilis, tuberculosis, Chlamydia spp., Herpesviridae, Parvovirus b19, and Lyme disease can be counted among these diseases. Aortitis seen in Takayasu arteritis (TA)

is indistinguishable from CS aortitis, and TA may also rarely cause autoimmune membranous labyrinthitis, uveitis, and scleritis. Granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis may also cause Meniere-like symptoms and sensorineural hearing loss similar to CS. Therefore, these conditions should also be considered in differential diagnosis.

Management

Topical glucocorticoids are the first options for mild ocular disease, although extensive ocular and ear disease usually requires oral glucocorticoids or immunosuppressive therapy. An open-label study of etanercept for immune-mediated cochleovestibular disease did not show significant benefit [6].

There are no controlled trials on the treatment of systemic findings of CS. High-dose glucocorticoids are the initial treatment for systemic vasculitis. csDMARDs such as methotrexate, azathioprine, and cyclosporin A are usually suggested as concomitant therapy. TNF inhibitors, JAK inhibitors, and rituximab may be used in resistant cases [7].

Prognosis

Frequent relapses of eye and inner ear disease may occur during the disease course. Ocular outcomes of CS are usually favorable. Sensorineural hearing loss is mostly irreversible. Nevertheless, improvement with early use of immunosuppressive drugs is also reported [8]. There is insufficient data on the prognosis of CS patients with systemic vasculitis, as a rare vasculitic condition.

CASE PRESENTATION

Twenty-year-old male with a history of pulse steroid treatment due to sudden sensorineural hearing loss in both ears applied to our clinic with blurred vision and left ankle pain ten years ago. Physical examination revealed asymmetric oligoarthritis and redness in both eyes. Eye examination showed nodular scleritis. Cardiovascular examination and thorax MRI angiograph were normal. High-dose methylprednisolone (MP) and methotrexate (MTX) 15 mg weekly were prescribed with the diagnosis of Cogan Syndrome. MTX switched to azathioprine six months later for the persistent disease activity, but no improvement was observed. After the first year of follow-up, the patient was hospitalized with tachycardia and chest pain. He had high pitched aortic regurgitation murmur in physical examination. PET-CT revealed aortitis with involvement of the aortic valve and posterior ascending aorta (SUVmax: 5.2). Rheumatoid factor, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, anti-phospholipid syndrome screening, and VDRL tests were negative. High-dose corticosteroid and TNF-alpha inhibitor treatment (Infliximab 5 mg/kg) were started for remission induction. The patient was admitted with fever, palpitation, dyspnea, necrotic ulcer on the sole, acrocyanosis, and splinter hemorrhages in the third month of follow-up. Echocardiography revealed severe (+3) aortic regurgitation. There were no relevant pathogens on repeated blood cultures. The patient was diagnosed with resistant systemic vasculitis associated with CS and treated with pulse MP for 3 days and cyclophosphamide 500 mg every two weeks for 3 months. Rituximab (RTX) (1 g, 6-12 monthly) was commenced as the maintenance therapy. Remission could be achieved for 5 years of follow-up.

Key messages

CS vasculitis has to be kept in mind in patients with systemic vasculitis who had a current or previous history of inflammatory inner ear disease resulting in hearing loss and inflammatory ocular disease within a certain time period.

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