Cogan’s syndrome: a rare systemic vasculitis

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Abstract
A 4 year old girl presented with keratitis and ataxia. Over the next two months she developed profound hearing loss, arthritis, and polychondritis. A diagnosis of Cogan’s syndrome was made. The importance of early diagnosis to prevent hearing loss is highlighted.

(Arch Dis Child 1994; 71: 163–164)

Non-syphilitic interstitial keratitis with vestibuloauditory dysfunction (Cogan’s syndrome) is an uncommon clinical entity. Although a condition affecting mainly young people, only three children have so far been reported with the condition. In addition to photophobia, redness of the eyes, vertigo, ataxia and hearing loss, there is often systemic involvement as a result of widespread vasculitis. Despite its rarity, it is an important condition to recognise because early treatment may prevent the onset of profound deafness.

Case report
A 4 year old girl developed acute onset of ataxia, rapidly progressive hearing loss, and vomiting. The illness was preceded by intermittent attacks of red eyes and photophobia for several months. Six weeks after the onset of the ataxia she developed polyarthritis affecting knees, hips, wrists, and finger joints. The joint disease resembled juvenile rheumatoid arthritis but without rash, fever, lymphadenopathy, or splenomegaly. During the course of her illness she developed a haemorrhagic polychondritis of the pinnae of both ears leading to considerable destruction of the cartilage and a vasculitic rash on her buttocks that was initially haemorrhagic, then ulcerated, and was slow to heal.

At the most active stage of her illness she had a mild increase of both neutrophils (8·7×10⁹/l), and lymphocytes (6·2×10⁹/l), thrombocythaemia (683×10⁹/l), an erythrocyte sedimentation rate of 90 mm in the first hour, and a C reactive protein of 42 mg/l. Serological studies for a wide range of bacterial, viral, and rickettsial diseases were negative including tests for syphilis. Her Mantoux test was negative. Cultures of blood, urine, and cerebrospinal fluid were sterile. Urea, electrolytes, liver function tests, and tests for muscle enzymes were normal. Immunopathology studies, including rheumatoid factor, antinuclear antibody (by immunofluorescence), smooth muscle antibodies, and mitochondrial antibody were negative. Complement concentrations were in the normal range. Chest radiography, electrocardiography, and echocardiography with Doppler showed normal results. Computed tomography and magnetic resonance imaging of the brain showed no structural lesion. A slit lamp examination of the eyes showed bilateral interstitial keratitis. Pure tone audiometry (using a Kamplex audiometer fully ear proved room) showed a 90 decibel (dB) loss in the left ear and 100–110 dB loss in the right ear. The hearing loss was sensorineural. Cogan’s syndrome was diagnosed on the basis of the interstitial keratitis and vestibuloauditory dysfunction in the absence of syphilis.

Initially she was given a number of non-steroidal anti-inflammatory drugs including ibuprofen and naproxen with little benefit. A dramatic improvement was obtained with steroids. Her balance, polychondritis, vasculitis, ocular, and joint symptoms improved but deafness persisted necessitating the use of bilateral hearing aids.

She has been on prednisolone 5 mg on alternate days for 24 months. Any attempt to reduce this dose has been associated with a recurrence in joint pain and stiffness, polychondritis and the vasculitic rash. There has been no improvement in the hearing loss. Her ability to wear hearing aids is impaired by the destruction of ear cartilage.

Discussion
Using Cogan’s original criteria, Vollertsen et al reviewed all the cases reported in the English literature to date (78 cases). In this series the median age of onset was 25 years with a range of 5–63 years. Our patient is therefore the youngest reported with the condition. While the presence of interstitial keratitis in association with vertigo, tinnitus, or deafness defines the condition, a wide range of systemic findings have been described including all the abnormalities shown by our patient.

Thus, in Vollertsen’s 78 patients, 31 had arthritis or arthralgia, six had skin rashes (three ulcerated), and four had auricular pain or polychondritis. Other clinical manifestations which have been reported, but not so far exhibited by our patient, include systemic vasculitis, aortic valvular disease, gastrointestinal haemorrhage, renal involvement, lymphoreticular disease, and myalgia.

Many systemic illnesses involve both the eye and the audiovestibular apparatus. Of the connective tissue disorders only Sjogren’s syndrome, rheumatoid arthritis, and systemic lupus erythematosus consistently involve the cornea but the picture is of keratoconjunctivitis sicca rather than interstitial keratitis. Rarely ulcerative but not interstitial keratitis may complicate rheumatoid arthritis. The keratitis
of sarcoidosis and tuberculosis are only rarely associated with audiovestibular symptoms. A number of systemic illnesses include vasculitis with eye and audiovestibular symptoms, for example, polyarteritis nodosa, Wegener’s granulomatosis, Takayasu’s arteritis, and Behçet’s syndrome but none show the interstitial keratitis of Cogan’s syndrome.

The association of viral keratitis with middle ear infection or labyrinthitis could cause confusion but the absence of systemic symptoms and the clinical course should clarify the diagnosis.

The presence of interstitial non-ulcerative keratitis in the absence of congenital syphilis, particularly, in conjunction with audiovestibular symptoms, makes the diagnosis of Cogan’s syndrome most likely.

The aetiology and pathogenesis of Cogan’s syndrome are unknown. The clinical features are in keeping with a form of systemic vasculitis and indeed there is some support for such a mechanism. The pathological findings in patients with Cogan’s syndrome are however extremely diverse and suggest a mixed type of inflammatory response directed at many tissues but with a predilection for vascular involvement.

The interstitial keratitis may, as in our patient, be severe, painful and distressing, but it can be evanescent and require repeated examination for detection. Visual impairment is not usual; it occurred in six of Vollertsen’s 78 patients.

By contrast, hearing loss is very common, rapidly progressive, and usually severe. While the vestibular component is generally reversible, the hearing loss is usually permanent. Administration of corticosteroids within two weeks of the initial presentation may result in improvement.

There is no confirmatory test for Cogan’s syndrome. The diagnosis is clinical but there are few conditions with which it may be confused. Until the full picture is manifest, however, it enters the differential diagnosis of ataxia, keratitis, and polyarthritis.

The clinical course is variable with usually an acute phase lasting for months to years followed by a chronic burnt out phase. Up to 20% of those affected die of aortic valvular disease and vasculitis.

Steroids have a dramatic effect on both the systemic and audiovestibular aspects of the condition. As in our patient, however, intermittent maintenance treatment may be required to prevent relapse. Topical steroids and cycloplegics are required for ocular involvement. Immunosuppression with cyclophosphamide or cyclosporin may be necessary in vision threatening eye disease or large vessel vasculitis.