CASE REPORT

Cogan's syndrome: achievement of complete resolution of auditory deficit with steroids

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SUMMARY

Cogan's syndrome is a rare inflammatory disorder predominantly affecting ocular and audiovestibular apparatus. The typical ocular picture is that of a non-syphilitic interstitial keratitis, while audiovestibular features resemble Meniere's disease. The hearing deficit often does not adequately respond to systemic steroids, which are the mainstay of therapy. Cochlear implants may ameliorate this deficit, but may not be readily available because of financial constraints in the Indian subcontinent. A high index of suspicion and multispecialty coordination will help in the early initiation of therapy and reduce long-term morbidity. We report a case of this rare entity where the recovery of deficits was dramatic on initiation of high-dose steroids.

BACKGROUND

Cogan's syndrome is characterised by non-syphilitic interstitial keratitis and sensorineural hearing loss. It is an inflammatory disorder of unknown aetiology and primarily affects young adults. The clinical presentation is usually with audiovestibular dysfunction such as ataxia and decreased hearing. Other group of patients may present with predominant ocular involvement. Occasionally, systemic features like fever, arthritis and vasculitic phenomena may also be observed. The disease tends to run a waxing and waning course with relapses most frequent within initial 2 years of presentation. Treatment with systemic steroids has been advocated. However, the resolution of ocular involvement and systemic features is invariably accompanied by residual hearing loss, and a substantial number of patients do suffer from moderate to severe hearing deficit. The residual hearing deficit may have significant socioeconomic, vocational and psychological impact. In our experience, the response to steroid therapy was monumental with a complete recovery of auditory function and this was probably attributable to the early diagnosis and treatment.

CASE PRESENTATION

A 14-year-old adolescent girl presented with fever for 20 days, along with acute redness of eyes for 4 days and a sudden hearing loss for 2 days. The patient had received oral antibiotics from a primary healthcare provider for clinical suspicion of enteric fever, but was not relieved of fever and subsequently she had developed redness of the eyes, followed by hearing loss. Redness of the eyes neither associated with gritty sensation or pain in the eyes, nor was there any discharge from the eyes or any

restriction of movements. There was no complaint of diminished vision or diplopia. Also, the patient had an acute onset of severe hearing loss for 2 days which was not associated with any ear discharge or pain. There was no history of tinnitus/similar symptomatic bouts. There was no history of intake of any ototoxic drugs like aminoglycosides, antimalarials (quinine) or chronic diuretic or salicylate intake. There was no history suggestive of any other cranial nerve deficits/seizures/acute confusional state. There was no history suggesting any connective tissue disorder or primary vasculitides.

A physical examination revealed circumciliary congestion of eyes with preserved visual acuity and bilateral severe sensorineural hearing loss. There was no nystagmus (spontaneous or induced) or squint. There was no evidence of other cranial nerve or focal neurological deficit. Rest of the systemic examination was within the normal limits except for existence of low to moderate grade fever. Ophthalmological opinion was sought for slit-lamp examination which confirmed bilateral uveitis while pure tone audiometry showed bilateral severe sensorineural hearing loss.

INVESTIGATIONS

Significant findings in laboratory investigations included raised erythrocyte sedimentation rate (ESR, 122 mm in the first hour) and C reactive protein levels (166 mg/l), while rest of the routine metabolic profile was essentially within the normal limits. Serum studies for Cytoplasmic antineutrophil cytoplasmic antibody, antinuclear antibodies, HIV, hepatitis B surface antigen and anti-hepatitis C virus IgG were negative, while serum calcium (9.2 mg/dl) and ACE inhibitor levels (43 U/l) were within the normal range. MRI of the brain and chest, and paranasal sinuses did not reveal any significant abnormalities. A tuberculin skin test (purified protein derivative (test) was also negative. In this clinical context and after an extensive search of literature, we realised the possibility of Cogan's syndrome. As a result, a serum Venereal Disease Research Laboratory (VDRL) test as well as serology for chlamydia were performed, but both were negative.

DIFFERENTIAL DIAGNOSIS

Considering the working diagnosis for febrile illness with bilateral uveitis and bilateral sensorineural hearing loss in an adolescent girl, the possibility of some multisystem autoimmune connective tissue or vasculitic disorder, like sarcoidosis, polyarteritis nodosa and Wegener's granulomatosis, was

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considered. At the same time, keeping in view the high prevalence in the region, we also entertained the remote possibility of infections like tuberculosis. With a normal screening chest x-ray and a normal MRI of the brain carried out on urgent basis, the likely diagnosis favoured an autoimmune disorder.

TREATMENT

After collecting blood and urine samples for laboratory studies, the patient was started on systemic steroid therapy within a few hours of presentation for the concern lest the patient should develop permanent hearing loss. The patient was treated with pulsed methylprednisolone (15 mg/kg body weight) for an initial 3 days and thereafter transferred to oral prednisolone (1 mg/kg).

OUTCOME AND FOLLOW-UP

Within 3 days of therapy, ocular signs and symptoms resolved, while it took around 2 weeks for the auditory deficit to improve from severe-to-moderate sensorineural hearing loss. Over the next 2 months, the patient had a complete recovery from auditory deficit as documented with pure tone audiometry. Steroid therapy was gradually tapered down and withdrawn over for the next 4 months. There was no recurrence of symptoms. The patient developed mild side effects of steroid therapy like acneiform eruptions over the face and trunk and mild weight gain; both resolved after the withdrawal of steroids. The patient has been under regular follow-up since 1 year and there has been no relapse.

DISCUSSION

An association between audiovestibular deficit and non-syphilitic interstitial keratitis was first recognised in 1934 by Mogan and Baumgartner. Subsequently, the disease was named after David G Cogan, who described four additional cases in 1945.^{1 2} Haynes *et al* in 1980 broadened the definition to include cases of 'atypical Cogan's syndrome' where ocular manifestations were non-keratotic such as uveitis, scleritis or episcleritis or the typical ocular manifestations were temporally separated from the audiovestibular deficit by two or more years.² Atypical Cogan's syndrome often has systemic manifestations like fever, arthritis, neurological deficits (other than audiovestibular), association with other rheumatological disorders and a less favourable prognosis.²⁻⁵ Our case report has merit that, in spite of being a case of atypical Cogan's syndrome (fever and uveitis), it responded remarkably with complete recovery from near-total deafness. Also, the majority of cases reported so far have been from Caucasian descent and to the best of our knowledge, only three cases of Cogan's syndrome have been reported from India so far.⁶⁻⁹

Although the exact aetiopathogenesis of Cogan's syndrome is still speculative, accumulating evidence and recent experiences point towards an autoimmune process as suggested by its association with other autoimmune disorders, histological findings of lymphoplasmocytic infiltration of the cornea and spiral ligaments on temporal bone biopsy, the presence of autoantibodies to inner ear proteins or epithelial cells and the response to immunosuppressive therapy.¹⁰⁻¹²

Clinical presentation of Cogan's syndrome includes ocular, audiovestibular and systemic features in variable combinations. According to a recent retrospective review at Mayo Clinic, the most common isolated presenting symptoms (47% patients) were audiovestibular, for example, ataxia, vertigo and acute bilateral sensorineural hearing loss; while 33% patients presented with only ocular symptoms, for example, acute red eye,

photophobia and blurred vision. Only 5% of patients had coexistent ocular and audiovestibular symptoms, as was the scenario in the present case.¹³ This singularity of target organ damage and resultant symptoms (either ocular or audiovestibular) at the time of presentation may hinder the consideration of the actual diagnosis of Cogan's syndrome and lead to a delayed treatment and consequent permanent hearing loss. Pollard *et al*¹⁴ reported three such cases where a delay in reaching a final diagnosis of Cogan's syndrome resulted in permanent hearing loss and all three of them received cochlear implants. Systemic features were encountered in 19% of cases and included headache, arthralgia, fever, arthritis, vasculitic rash and peripheral neuropathy. However, the most serious systemic complication appears to be aortitis which can result in aortic aneurysm and acute aortic regurgitation, often necessitating urgent surgical intervention.

The clinical diagnosis of Cogan's syndrome is largely based on the clinical finding of audiovestibular symptoms, ocular inflammation and a non-reactive serological test for syphilis. Since no laboratory or radiological investigation is diagnostic of Cogan's syndrome, it is essentially a diagnosis of exclusion. The disorders that may mimic this entity and need to be ruled out are congenital syphilis, Vogt-Koyanagi-Harada syndrome (associated poliosis, alopecia and vitiligo), Meniere's disease (usually unilateral fluctuating hearing loss, prominent complaint of vertigo and tinnitus and associated ear ache), sarcoidosis (predominant involvement of lungs, skin and lymph nodes and high serum ACE inhibitor levels) and Wegener's granulomatosis (predominantly affects the lungs and upper airway, characteristic histopathology).

The laboratory evaluation of a case of Cogan's syndrome may reveal anaemia, raised ESR, leucocytosis, thrombocytosis—all identified as poor prognostic factors according to Vollertsen *et al*.¹⁵ Further, the existence of low complement levels and mixed hyperglobulinaemia may suggest a chronic inflammatory pathology. Pure tone audiometry usually shows bilateral sensorineural hearing loss. Radioimaging (CT or MRI) of the brain is often non-contributory, but may show hyperintense signal in the region of inner ear probably owing to haemorrhage from inflamed blood vessels of the stria vascularis.⁵

While the establishment of the diagnosis of Cogan's syndrome is challenging, so is its treatment. Most of the patients have been treated with systemic steroids while occasional reports of the use of other immunosuppressive agents like methotrexate, leflunomide and cyclophosphamide for steroid-refractory or steroid-dependant cases have also been published.¹³ The treatment strategy is often compounded by the fact that auditory prognosis is not optimistic in spite of treatment. For those presenting with complete deafness, systemic steroid therapy does not help, whereas some response is observed only in 50% of cases from those having partial deafness at presentation.² Further, nearly 90% of the patients suffer from severe bilateral hearing loss eventually, but ocular sequelae are rare.²

From the previous studies, we get the impression that it may not be the mere inherent progression of the disease to have such poor auditory prognosis. In fact, it may be the outcome of delay in reaching the diagnosis and administration of a definitive therapy. Although our patient had multiplicity of poor prognostic factors such as atypical presentation with uveitis, systemic features of fever, anaemia, raised ESR and most importantly profound bilateral hearing loss at presentation itself, our patient still responded favourably to the systemic steroid therapy in an unexpected manner with a complete recovery of auditory function.

The authors concluded that poor auditory prognosis may be a result of delay in initiating definitive therapy. Despite a

predicted poor auditory prognosis, with timely initiation of treatment in the present case, the dramatic response was gratifying.

Learning points

- ▶ Cogan's syndrome is a rare cause of acute bilateral sensorineural hearing loss in young adults; clinical diagnosis is performed by maintaining a high index of suspicion, after excluding common aetiologies.
- ▶ In patients with sudden hearing loss, sometimes the diagnosis may be clinched by ophthalmological examination, especially, assessing for keratitis and uveitis.
- ▶ Early therapy based on strong clinical suspicion may prevent devastating sequelae like permanent deafness.

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Competing interests None.

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