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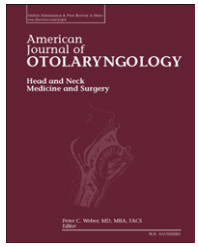

Sudden hearing loss and Crohn disease: when Cogan syndrome must be suspected

Giancarlo Tirelli, MD[a], *Paola Tomietto, MD*[b], *Eliana Quatela, MD*[a,*], *Fiorella Perrino, MD*[a], *Luca Nicastro, MD*[a], *Luigi Cattin, MD*[c], *Renzo Carretta, MD*[c]

[a] *Department of Otorhinolaryngology, Cattinara Hospital, University Medical Center of Trieste, Italy*
[b] *Internal Medicine Department, Rheumatology Out-patients Unit, Cattinara Hospital, University Medical Center of Trieste, Italy*
[c] *Internal Medicine Department, Cattinara Hospital, University Medical Center of Trieste, Italy*

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ABSTRACT

Cogan's syndrome is a rare systemic vasculitis of unknown origin. It is characterized by the presence of worsening audiovestibular and ocular symptoms that may manifest simultaneously or sequentially. No specific diagnostic laboratory tests or imaging studies exist. The diagnosis is clinical and should be established as early as possible so as to initiate prompt treatment with steroids and prevent rapid progression to deafness or blindness and potentially fatal systemic involvement. We report a case of association between Cogan's syndrome and ileal Crohn's disease which we believe deserves attention since, after an accurate review of the literature, we have found approximately 250 reports of patients with Cogan's syndrome, only 13 of whom with concurrent chronic inflammatory bowel disease; of these 13 cases, none experienced improvement after therapy. In the light of the good outcome obtained in our case, we proposed a valid treatment option with boluses of steroids, combined with early systemic immunosuppression and intra-tympanic steroid injections.

1. Introduction

Cogan's syndrome (CS) is a rare disease named after the ophthalmologist David Cogan who first reported its clinical features in 1945 [1]; since then, fewer than 250 cases have been reported in the literature [2].

The classic form of CS affects young Caucasian individuals with an average age of 25 years, and is characterized, according to Cogan's criteria, by the following triad: 1) rapidly progressive bilateral audiovestibular auditory involvement with features similar to Menière's disease (vertigo, tinnitus, ataxia and progressive and fluctuating hearing loss, often leading to deafness) 2) ocular involvement (non-syphilitic interstitial keratitis), 3) less than 2 years' interval between the onset of audio or/and vestibular and ocular symptoms [1].

In addition to the classic form, in 1980 Haynes et al. [3] defined the criteria for an atypical form, namely: 1) inflammatory eye manifestations with or without interstitial keratitis, 2) eye symptoms associated with audiovestibular symptoms with characteristics other than those seen in Menière's disease, 3) more than 2 years' interval between the onset of ocular and audiovestibular symptoms. The atypical form is reported to affect 20% of cases [4]. The vasculitic nature of the syndrome,

* *Corresponding author at:* Hospital of Cattinara, Strada di Fiume 447, 34149 Trieste, Italy. Tel.: +39 347 1864516; fax: +39 040 3994180.
E-mail address: quatela.eliana@gmail.com (E. Quatela).

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hypothesized by Cody and Williams in 1960, is suggested by the finding that 70% of patients have systemic symptoms in addition to the ocular and audiovestibular manifestations [5,6]. In particular, in 15%–21% of cases there may be involvement of the large vessels (Takayasu's-like) and medium-size vessels (polyarteritis-like) resulting in manifestations affecting the cardiovascular system (aortitis with aortic failure), nervous system (hemiparesis and hemiplegia) and gastrointestinal tract (diarrhea, melena, abdominal pain) [2,3,5,7]. Less typical systemic symptoms include headache (40%), joint pain (35%), fever (27%), arthritis (23%), myalgia (22%), and abdominal pain (13%) [4].

The autoimmune nature of the syndrome is also suggested by the fact that in 15% to 30% of cases there is an association with other autoimmune conditions such as interstitial nephritis, chronic inflammatory bowel disease (IBD), hypothyroidism and sarcoidosis [8–11]. The literature to date contains reports of only 13 cases of association between CS and chronic IBD [2,4,12–18].

The diagnosis of CS is exclusively clinical and based on the Cogan or Haynes criteria. Laboratory tests are non-specific whereas in most cases imaging studies (computed tomography, CT, and magnetic resonance imaging, MRI) fail to reveal abnormalities except in advanced or complicated forms [4].

We report a case of a patient who developed CS shortly after receiving a diagnosis of Crohn's disease, and was effectively treated with steroids (intravenous, oral and transtympanic) and azathioprine. In view of the paucity of reports of the coexistence of CS and IBD, we believe that the account of our experience may make a valuable contribution to the diagnosis and treatment of these syndromes.

2. Methods

The study was approved by the local ethics committee and the patient give the informed consent for the treatment and publication of the clinical data.

In addition to the case presented, a literature search (PubMed) of articles published until June 2014 was performed using MEDLINE heading key words "Cogan's syndrome", "hearing loss", Crohn's disease", "Inflammatory bowel disease", "ulcerative colitis", "sensorineural deafness", "interstitial keratitis" in different combinations. We found 13 cases of association between CS and chronic IBD.

3. Case report

A 19-year-old woman, migrainous, smoker, on oral estroprogestin combination therapy and taking mesalazine 1.5 g/day for 2 months for a recent diagnosis of ileal Crohn's disease was referred to the our ENT Division because of the onset, in early January 2014, of dizziness and bilateral tinnitus. Pregnancy test, neurological assessment and unenhanced brain CT were negative. Tone audiometry revealed hearing threshold within normal limits. On clinical vestibular examination the patient reported dizziness without any evidence spontaneous or evoked nystagmus. The patient was therefore discharged with symptomatic therapy.

Two days later, the patient was admitted to the ENT Division because of worsening vertigo and the onset of left aural fullness. She underwent repeat neurological assessment and contrast-enhanced brain stem CT, both of which were again negative. Tonal audiometry showed mild left-sided sensorineural hearing loss, sloping in the high frequencies (Fig. 1), and videonystagmography (VNG) revealed only compensated decreased vestibular response on the left. After improvement of dizziness, the patient was discharged with a diagnosis of vestibular neuronitis and prescribed oral steroid therapy with prednisone 60 mg/day for 14 days tapered by 10 mg/day for an additional 5 days.

On day 16 of steroid therapy (prednisone 40 mg/day) the patient underwent repeat assessment because of migraine and worsened left-sided hearing loss. Sensorineural hearing loss was moderate-to-severe and worse for the high frequencies (Fig. 2), so that oral steroid therapy was increased to 60 mg/day and a consultation was requested for hyperbaric oxygen therapy (HOT). HOT was started and suspended immediately at the first session due to recurrence of dizziness with ataxia and spontaneous nystagmus with rapid component to the left, probably of an irritative nature. Auditory testing showed worsening of sensorineural hearing loss, with a small island of hearing on the left and mild-to-moderate perception falling in the high frequencies on the right (Fig. 3); VNG showed only marked decreased response on caloric tests bilaterally [19].

After 30 days of steroid therapy the patient reduced the steroid dose as per protocol (prednisone 40 mg/day), with subsequent onset of photophobia and intermittent vision loss. The ophthalmologist diagnosed moderate bilateral iridocyclitis and recommended topical corticosteroids. Cogan syndrome was hypothesized and the patient was referred for urgent rheumatological assessment, which confirmed the suspicion. Treatment was initiated consisting of intravenous boluses of methylprednisolone 500 mg/day for 3 days, followed by methylprednisolone 80 mg/day for 3 days and methylprednisolone 60 mg/day for another 7 days and subcutaneous injections of low-molecular-weight heparin 6000 IU. This resulted in bilateral hearing improvement at the end of the therapy (Fig. 4).

Considering partial hearing recovery and positive results obtained in several studies [20–24], we proposed intratympanic injections of steroids. Patient underwent one infiltration daily on each side for 3 consecutive days of methylprednisolone 62.5 mg/ml bilaterally. Tone audiometry performed 7 days after the last infiltration revealed a further improvement with normal hearing on the right and stabilization of the moderate–severe sensorineural hearing loss sloping in the high frequencies on the left (Fig. 5).

In consideration of the patient's young age, her concurrent Crohn's disease and significant response to steroid therapy, she was prescribed maintenance therapy of methylprednisolone 56 mg orally, to be tapered based on stability of her hearing threshold, for a total of 8 weeks. Additionally, treatment was started with azathioprine, as a steroid-sparing agent, at a dose of 2 mg/kg (100 mg/day). After two months of treatment, audiometry showed no change (Fig. 5), there were complete remission of the ocular findings and persistence of the dizziness. The patient underwent rheumatological follow-up at 2-monthly intervals; she is currently taking azathioprine 2 mg/kg since the steroid was discontinued at 6-month