

A 35 Years-Old Male With Neurosensitive Hearing Loss and Interstitial Keratitis

To the Editor: Cogan's syndrome is an infrequent form of autoimmune disease that presents with ocular and audiovestibular symptoms, to which other systemic manifestations can be added. This syndrome requires an early diagnosis in order to initiate treatment as rapidly as possible and thus avoid serious complications. We presented the case of a patient diagnosed with Cogan's syndrome in our department. A 35 years-old male was sent to our clinic for valuation of immunosuppressive treatment for a case of neurosensorial deafness. Symptoms had begun 16 years before with an episode of right sudden deafness associated to tinnitus from which he did not recover. For 14 years he has been displaying fluctuating episodes that responded to steroidal IV treatment. On the other hand, the patient refers unspecific problems in both eyes of several months, along with corneal leukoma, diagnosed as bilateral annular interstitial keratitis (Figure). At the moment he refers continuous fluctuating tinnitus in the left ear and hypoacusia. Upon ENT examination he presents a bilateral neurosensorial fall in the acute frequencies. We asked for complementary examinations and found the blood chemistry blood count, analyses, ESR, syphilis serology, HBV, and HCV to be normal, or negative. Antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antigen antibodies (ANCA), rheumatoid factor, and complement were normal, or negative. The chest x-ray was normal and the cranial resonance did not show alterations, with normality of both cochleas. The respiratory function tests were normal, as well as the electrocardiogram and echocardiogram. With a diagnosis of Cogan's syndrome the treatment with methotrexate 7.5 mg/week began, increased up to 10 mg/week after 1 month, along with methylprednisolone 1 mg/kg/day. After beginning the treatment, the patient experienced progressive symptomatic improvement, with less auditory oscillations and less tinnitus. After 1 year of treatment with methotrexate 10 mg/week and reducing methylprednisolone (doses of 4 mg/día), the patient is subjectively well, without dizziness nor tinnitus and with

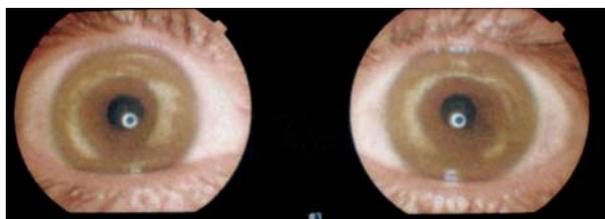


Figure. Corneal leukoma annular secondary to interstitial keratitis.

discreet auditory improvement that is confirmed with audiometry. Cogan's syndrome is a rare disease (less than 250 cases to date) and of unknown origin, described for the first time like an independent entity in 1945 by David Cogan¹ as an association of non luetic and interstitial keratitis, and audiovestibular symptoms that resembles Ménière's syndrome. In 1980, Hayes et al² proposed to extend the definition to include other individuals with different ocular symptoms and audiovestibular symptoms different from Ménière's syndrome. This syndrome usually affects young adults of Caucasian origin and both genders. The interstitial keratitis usually is symptomatic in the form of ocular pain, photophobia or red eye. In these cases, the examination can demonstrate a granular corneal infiltration next to the limb. Other forms of ocular affection are: epyscleritis, scleritis, retinitis, optical neuritis, glaucoma, or papillary edema. On some occasion the ocular affection can lead to amaurosis. In most of the cases, both eyes are affected in the course of illness²⁻⁵ and the ocular symptoms are the first manifestation in 37%-45% of pacientes.⁶ Audiovestibular manifestations include symptoms similar to the Ménière's syndrome (abrupt beginning of nausea, vomit, tinnitus, and vertigo), accompanied by gradual hearing loss. The affection usually is bilateral and, in absence of treatment, the auditory loss becomes irreversible in the course of 3 to 5 years.⁷ Based on the clinical presentation, there are 2 forms,^{2,3} typical Cogan's syndrome (that fulfills the following criteria: nonsyphilitic keratitis without iritis nor conjunctivitis; audiovestibular symptoms similar to those of Ménière's syndrome, and an interval between both manifestations of less than 2 years), and the atypical Cogan's syndrome (that includes patients with ocular manifestations such as epyscleritis, scleritis, choroiditis, thrombosis of the retinal artery; different audiovestibular symptoms from Ménière's syndrome, and an interval between ocular symptoms and audiovestibular manifestations of over 2 years). Our patient fulfilled criteria of atypical Cogan's syndrome. In addition to these manifestations, (all of them more frequent in the atypical forms of Cogan's syndrome)^{3,4,8} other manifestations have been described: general symptoms (fever, asthenia, weight loss), rheumatic manifestations (arthralgias, myalgias, and arthritis), cardiovascular manifestations (aortitis that can require surgery, Raynaud's phenomenon), gastrointestinal manifestations (abdominal pain, splenomegaly), neurological manifestations (peripheral neuropathy, facial paralysis), cutaneous manifestations (vitiligo, oral ulcers, chondritis), renal manifestations (membranoproliferative glomerulonephritis), and lymphadenopathy. There are no established clinical criteria for Cogan's syndrome, but it requires inflammatory ocular affection and objective vestibuloauditive manifestations with hypoacusia.⁸ Laboratory test findings are usually non-specific and must include blood chemistry and ESR in normal ranges. An infection by *Treponema pallidum* is to be discarded, to which some authors add *Borrelia*.^{3,8} With respect to autoimmune diseases, ANA and ANCA⁸ are recommended, to which it is possible to add rheumatoid factor, complement, and antiphospholipid antibodies^{3,5,6,8}

Imaging tests must include a chest x-ray, and usually a cranial resonance where an increase of the signal in the membrane of the labyrinth has been seen.^{4,8} The arteriography is indicated in certain situations, as in the case of differences in peripheral pulses of the extremities or central nervous system symptoms.^{8,9} Although the etiology of this syndrome is not known, it is included among autoimmune diseases due to diverse findings, such as the presence of antibodies against the epithelial cells of the cornea and membrane of labyrinth.¹⁰ Treatment of this disease usually includes different immunosuppressants, of which systemic steroids are the cutting edge along with ocular topical treatment. The atypical Cogan's syndrome, that usually is more aggressive and has a chronic course, frequently merits other immunosuppressants. Among them, one stands out: oral cyclophosphamide (1-2 mg/kg/day), cyclosporin A (1-2 mg/kg/day), or methotrexate (7.5-10 mg/week). The answer to treatment is variable and often partial.^{3,6} Aortic insufficiency can merit surgery and the auditory affection, of cochlear implants.⁸

Pablo Tutor-Ureta,^a Miguel Yebra-Bango,^a
Susana Mellor-Pita,^a José Ramón García Berrocal,^b
Aitor Fernández,^c and Juan Antonio Vargas^a

^aServicio de Medicina Interna,
Hospital Universitario Puerta de Hierro, Madrid, Spain.

^bServicio de Otorrinolaringología,
Hospital Universitario Puerta de Hierro, Madrid, Spain.

^cServicio de Oftalmología,
Hospital Universitario Puerta de Hierro, Madrid, Spain.

References

1. Cogan DG. Syndrome of nonsyphilitic interstitial keratitis and vestibuloauditory symptoms. *Arch Ophthalmol.* 1945;33:144-9.
2. Haynes BF, Kaiser-Kupfer MI, Mason P, Fauci AS. Cogan's syndrome: studies in thirteen patients, long-term follow-up, and a review of the literature. *Medicine.* 1980;59:426-41.
3. Grasland A, Pouchot J, Hachulla E, Blétry O, Papo T, Vinceneux P. Typical and atypical Cogan's syndrome: 32 cases and review of the literature. *Rheumatology.* 2004;43:1007-15.
4. García Berrocal JR, Vargas JA, Vaquero M, Ramón y Cajal S, Ramírez-Camacho RA. Cogan's syndrome: an oculo-audiovestibular disease. *Postgrad Med J.* 1999;75:262-4.
5. Orsoni JG, Zavota L, Pellistri I, Piazza F, Cimino L. Cogan's syndrome. *Cornea.* 2002;21:356-9.
6. Baumann A, Helbling A, Oertle S, Häusler R, Vibert D. Cogan's syndrome: clinical evolution of deafness and vertigo in three patients. *Eur Arch Otorhinolaryngol.* 2005;262:45-9.
7. Cundiff J, Kansal S, Kumar A, Goldstein DA, Tessler HH. Cogan's syndrome: a cause of progressive hearing deafness. *Am J Otolaryngol.* 2006;27:68-70.
8. Gaubitz M, Lübber B, Seidel M, Schotte H, Gramley F, Domschke W. Cogan's syndrome: Organ-specific autoimmune disease or systemic vasculitis? A report of 2 cases and review of literature. *Clin Exp Rheumatol.* 2001;19:463-9.
9. Alabayram MS, Wityk R, Yousem DM, Zinreich SJ. The cerebral angiographic findings in Cogan's syndrome. *Am J Neuroradiol.* 2001;22:751-4.
10. Arnold W, Pfaltz CR, Altermatt HJ. Evidence of serum antibodies against inner ear in the blood of patients with certain sensorineural hearing disorders. *Acta Otolaryngol.* 1985;99:437-44.

Erratum

In the original article "Spanish Registry of Adverse Events of Biologic Therapy in Rheumatic Disease (BIOBADASER): Situation Report, January 26, 2006", published in *Reumatol Clin.* 2007;3(1):4-20, it has been noted that a mistaken omission in the listing of members of the BIOBADASER study group has taken place. The omitted member is:

M. Isabel Rotés Mas (Hospital San Rafael).