Cogan Syndrome: Autoimmune-Mediated Audiovestibular Symptoms And Ocular Inflammation

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Background: Cogan syndrome is an uncommon disorder that presents with symptoms involving the eyes and ears. At its onset, it can mimic many common entities. Family physicians should be aware of Cogan syndrome because it can be successfully treated if it is recognized early in its course. It is one of the few treatable causes of deafness.

Methods: MEDLINE files were searched from 1982 to the present for “Cogan’s syndrome.” Additional references were obtained by cross-referencing bibliographies from available articles.

Results and Conclusions: As first defined in 1945, Cogan syndrome includes nonsyphilitic interstitial keratitis and attacks of vertigo, tinnitus, and hearing loss. Although it usually begins with only one symptom, most patients have both auditory and ocular findings within 1 year of the onset. If untreated, most patients become deaf within 36 months. Blindness occurs in about 5 percent of patients, but ocular symptoms relapse during a period of years. The disease eventually involves other organs with clinical and pathologic findings that suggest vasculitis. Aortic insufficiency, the most serious complication, develops in 15 percent of patients. The cause of Cogan syndrome remains unknown, but several studies suggest an autoimmune-mediated process. Many reports document an improvement in symptoms with immunosuppressive therapy, particularly if started early in the course of the illness. Family physicians should include Cogan syndrome in their differential diagnosis when a young adult seeks care with audiovestibular symptoms or ocular inflammation. (J Am Board Fam Pract 1993; 6:577-81.)

In 1934 Mogan and Baumgartner\(^1\) reported a patient with the Meniere triad — tinnitus, vertigo, and hearing loss — plus recurrent interstitial keratitis. Eleven years later Cogan\(^2\) described a syndrome consisting of nonsyphilitic interstitial keratitis associated with vestibulovestibular symptoms. Since then, many similar cases have been reported, suggesting that this syndrome is a systemic illness also involving other organs and leading to deafness, blindness, and death.\(^3\) Because the illness can be treated successfully, its early recognition is crucial.\(^4\) Although most patients with Cogan syndrome have their condition diagnosed and treated by ophthalmologists and otolaryngologists, family physicians also should become aware of it when young adult patients seek care with vestibulovestibular or ocular symptoms. This article reports a patient with Cogan syndrome and presents a brief clinical review of this uncommon but devastating illness.

Case Report
A 37-year-old woman complained about nasal congestion and a feeling of pressure and decreased hearing in both ears. She denied fever, cough, nausea, and vertigo. Her examination revealed only nasal congestion, mild pharyngeal edema, and mucoid postnasal discharge. Her conversational hearing seemed normal. A diagnosis of viral upper respiratory tract infection was made and symptomatic treatment recommended.

One month later she returned complaining about fluctuating hearing in both ears. Her examination again showed only nasal congestion, and she was thought to have a persistent upper respiratory tract infection with eustachian tube dysfunction. Two months later she returned with tinnitus, decreased hearing, and impaired balance.

History
The patient had uncomplicated measles, mumps, and varicella in childhood but denied hyperten-
sion, diabetes, rheumatic fever, meningitis, tuberculosis, diphtheria, seizures, connective tissue diseases, and sexually transmitted infections. She had never been pregnant and stated that she never had sexual intercourse. There was no foreign travel or known exposure to Lyme disease. She denied unusual noise exposure, ear trauma and infections, central nervous system infections, and use of ototoxic drugs.

She was not taking prescription medications but had used over-the-counter decongestants and antihistamines. Several years before she took oral contraceptives for irregular menstrual bleeding. At the age of 33 years she had a cholecystectomy for cholelithiasis. She did not use tobacco, illicit drugs, or alcohol.

There was no family history of deafness, degenerative neurologic disorders, tuberculosis, syphilis, connective tissue disease, or genetic disorders.

**Physical Examination**

The patient weighed 250 pounds; her height was 5 ft 8 in. She was afebrile and blood pressure and pulse rates were normal. She could not hear a whisper at 15 feet. Pinnae and ear canals were normal. Otoscopic examination showed normal tympanic membranes. A Rinne test demonstrated air conduction to be better than bone conduction bilaterally. The Weber test indicated laterality to the left ear. There was no nystagmus, and except for the 8th, the cranial nerves were normal. There were no peripheral sensory or motor deficits. Reflexes were normal and symmetric; however, the patient was unable to do the Romberg test and could not walk toe to heel without falling. The neck showed no lymphadenopathy or thyromegaly, and examinations of the chest, abdomen, and extremities were unremarkable.

**Consultations**

An otolaryngologist performed an audiogram that confirmed bilateral sensorineural hearing loss, mild in the right ear and moderate in the left. No cause for hearing loss could be found. A complete blood count, chemistry panel, thyroid profile, and erythrocyte sedimentation rate were all within normal values.

The patient's hearing loss was then evaluated by the otolaryngology service of a university teaching hospital. Laboratory studies were again within normal limits, except for a positive rapid plasma reagin, and the patient was referred back to her family physician for treatment of presumed neurosyphilis.

A repeat rapid plasma reagin and fluorescent treponemal antibody absorption test, however, were nonreactive. Complete blood count, erythrocyte sedimentation rate, and tests for antinuclear antibodies and rheumatoid factor were all reported to be in the normal range.

**Clinical Course**

The patient continued to have a progressive hearing loss and eventually required a hearing aid. She had frequent intermittent episodes of vertigo with nausea and vomiting.

Thirty-three months following her original complaint, the patient experienced red, itchy, and inflamed eyes with photophobia. An ophthalmology consultant discovered bilateral interstitial keratitis, but her serologic tests for syphilis remained nonreactive. Her condition was diagnosed as Cogan syndrome, and her eye symptoms resolved with topical prednisolone drops. Prednisone, 1 mg/kg/d, by mouth, was prescribed, but she experienced no improvement in her hearing.

She was referred to another university otolaryngology service, where the diagnosis of Cogan syndrome was corroborated. Corticosteroids, as well as cyclophosphamide and methotrexate, were recommended to the patient, but she declined treatment, fearing the side effects of these agents.

One year later she experienced an excruciating, throbbing pain in her left eye. Her ophthalmology examination and a computerized axial tomography scan of her head were unremarkable. The erythrocyte sedimentation rate was elevated to 50 mm/h. There was no temporal artery tenderness. Vasculitis was suspected, and the patient was treated with prednisone, 1 mg/kg/d, with rapid resolution of her symptoms.

The prednisone dosage was slowly tapered and discontinued. She has continued to use topical prednisolone for her eyes and has remained asymptomatic. Her last audiogram showed a profound hearing loss in the left ear with a moderate loss in the right ear. Because her hearing is very impaired even with bilateral hearing aids, she is being considered for cochlear implants.

**Cogan Syndrome**

In the syndrome that Cogan defined and named in 1945, symptoms were limited to the eyes and
ears. The eyes showed interstitial keratitis, previously described in patients with syphilis, but Cogan's patients tested negative for syphilis. Cogan's original criteria included nonsyphilitic interstitial keratitis associated with attacks of vertigo, tinnitus, and hearing loss.2

By 1953 this syndrome was recognized to have manifestations other than the eye and ear findings,3 and it became apparent that Cogan syndrome was a systemic illness, sometimes including many organs, although the first symptoms usually involved the eyes and ears.4 The eye findings were also varying. Some authors make a distinction between typical Cogan syndrome with nonsyphilitic interstitial keratitis and atypical with conjunctivitis, episcleritis or uveitis, but without nonsyphilitic interstitial keratitis.7,8

Cogan syndrome is rare. Only about 130 cases have been reported in the world literature.5 It usually affects white adults between the ages of 20 to 40 years. The median age of onset is 25 years, ranging from 2 to 63 years.5 The distribution between sexes is equal.3

The illness is characterized by an acute phase lasting several months to years, followed by a low-grade chronic phase that can last indefinitely.7 Initially Cogan syndrome usually affects either the eyes or the ears, but in a few patients it begins simultaneously in both the eyes and the ears.3,4 Most patients have both eye and ear involvement within 1 year of onset.3

Attacks of vertigo generally precede hearing loss.10 There are usually relapsing episodes of vertigo and fluctuations in hearing acuity.6 A progressive hearing loss eventually develops in one or both ears, and most patients become deaf within 36 months.3

With eye involvement, patients complain of redness, blurred vision, and photophobia.9 The ocular symptoms also follow a relapsing course with periodic attacks occurring within a span of years.6 Blindness occurs in about 5 percent of cases.3

Systemic complications develop in about 70 percent of patients.11 Common systemic findings include fever, weight loss, fatigue, headache, arthralgias and myalgias, rashes, and gastrointestinal symptoms.3,12 Although systemic complications are more likely to occur in patients with atypical Cogan syndrome, they have also been reported in patients with typical Cogan syndrome.13,14

Vasculitis occurs in about 20 percent of patients.11 Generally the condition is present early in the course of the illness, usually within the first year, but it has been reported 12 years after the initial diagnosis.12

Neurologic problems reported in 10 to 50 percent of patients include headaches, neuropathies, seizures, strokes, and coma.11 Recent case findings from magnetic resonance imaging suggest that most neurologic disorders might be caused by vasculitis.15

The most serious complication is aortic insufficiency, which can develop in 10 to 15 percent of patients.3,11 Usually associated with vasculitis, aortic insufficiency has been a cause of death in patients with Cogan syndrome.3,16

Etiology
The cause of Cogan syndrome is unknown, although the clinical and pathologic findings suggest an infectious or immunologic cause.12 An upper respiratory tract infection frequently precedes the onset of the syndrome. Many viral and bacterial agents have been implicated, but none has been identified as the actual cause of the illness.3 Because the keratitis is similar to syphilitic eye disease, some researchers have suggested "seronegative" syphilis or Lyme borreliosis as the cause, but this connection has not been firmly established.9,12 Although many etiologic agents have been proposed, no specific infectious agent, vaccine, or toxin has been confirmed.3

The extremely diverse gross and histologic abnormalities in patients with Cogan syndrome suggest a mixed inflammatory response to immune-mediated damage.3,13 Lymphocyte and plasma cell infiltrates have been found in cornea, sclera, and labyrinth tissues.6,13 Patients have also had antibodies against inner ear and corneal membranes.13 Immunologic testing with inner ear and corneal antigens has suggested cell-mediated autoimmunologic reactivity against these tissues.6,13,17 A case report of a patient who developed Cogan syndrome following splenectomy suggests that circulating immune complexes might be involved.18 The often-associated vasculitis and improved condition following corticosteroid treatment further imply an autoimmune mechanism.6,17

Diagnosis
No laboratory tests or clinical findings are pathognomonic of Cogan syndrome. The diagnosis
is based on the simultaneous eye and ear findings that are specific to this syndrome. Non-specific markers of inflammation, such as elevated erythrocyte sedimentation rate, complement levels, cryoglobulins, immunoglobulins, and C-reactive protein, might also be associated with this disease.\(^3,13,19\)

A false-positive serologic test for syphilis has been reported in approximately 8 percent of patients with Cogan syndrome.\(^3\) A few patients have had serologic evidence of *Borrelia burgdorferi*, prompting some researchers to recommend that all patients diagnosed with Cogan syndrome be tested for Lyme disease.\(^12\)

The erythrocyte sedimentation rate is often elevated and has been observed to return to normal after treatment.\(^9,14,18,20\) This test could be useful to mark relapsing disease activity and to indicate a successful response to treatment.

**Treatment**

Although no controlled studies on the treatment of Cogan syndrome have been conducted, an improvement in symptoms with immunosuppressant therapy has been reported in many cases.\(^6\) The ocular symptoms can be successfully treated with topical corticosteroid medications.\(^3,12,16\) Relapsing eye symptoms can be controlled and vision loss can be prevented.\(^12\)

Audiovestibular symptoms have also improved with systemic corticosteroid treatment; however, the treatment must be started early in the disease process to improve hearing and prevent deafness.\(^3,6,7,9,13,17,18\)

Corticosteroids must be used in high doses, equivalent to 1 to 2 mg/kg/d of prednisone, for treatment to be successful.\(^3,7,10,14,21\) The systemic complications and vasculitis of Cogan syndrome also respond to early treatment with high-dose corticosteroids.\(^3,14,21\) In patients who are refractory to corticosteroid treatment, azathioprine, methotrexate, cyclophosphamide, and cyclosporin A have been reported to be helpful.\(^5,10,11,14,22\) There is a single case report of a patient whose ocular symptoms and fevers improved with Cromolyn-cate eye drops and capsules.\(^23\) Aortic insufficiency, the complication responsible for most deaths in this syndrome, has been successfully treated with aortic valve replacement with good long-term results.\(^3,16\) Cochlear implants offer a possible opportunity to return hearing to those patients who become deaf.\(^3\)

**Conclusion**

Cogan syndrome is a disease that affects the eyes, ears, and eventually many other organs. Although its cause is not known, it appears to be an autoimmune disease. The diagnosis is made from clinical findings. No laboratory tests are pathognomonic of this illness, but many abnormalities can be noted. It can be treated with corticosteroids and other immunosuppressant agents. Although Cogan syndrome is one of the few treatable causes of deafness, it must be recognized and treated early to prevent hearing loss.

The syndrome is rare or perhaps underrecognized and underreported. As illustrated in this case report, this uncommon disease can initially be confused with more common conditions. Family physicians should be aware of this disorder and include it in their differential diagnosis when treating a young adult patient with audiovestibular symptoms, ocular inflammation, or both.

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