Journal of Clinical Neuro-ophthalmology 10(2): 83–87, 1990.

Cogan's Syndrome and Seroreactivity to Lyme Borreliosis

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We document the case of a young woman with bilateral nonluetic, interstitial keratitis, vestibuloauditory problems, and bilateral recurrent facial palsies, who had strongly positive serologic tests of Lyme borreliosis. To our knowledge, this is the first reported case of positive serologic tests for *Borrelia burgdorferi* in a patient with Cogan's syndrome.

Key Words: Cogan's syndrome—Deafness—Interstitial keratitis—Lyme borreliosis.

We report the first case, to our knowledge, of positive serologic tests for Lyme borreliosis in a patient with Cogan's syndrome of bilateral nonluetic, interstitial keratitis and profound hearing loss.

CASE REPORT

A previously healthy 22-year-old black woman was admitted to the hospital on January 13, 1989 because of acute total deafness. She had had a left Bell's palsy 2 years earlier, which resolved with oral prednisone. A subsequent recurrence of the left Bell's palsy again cleared after 2 weeks on oral prednisone. For the last 2 years, she had noted bilateral intermittent ocular redness and photophobia that would wax and wane. Topical steroids gave temporary relief of her symptoms. During the last year, she also noted the gradual onset of bilateral hearing loss accompanied by episodes of vertigo and tinnitus. On the morning prior to admission, she awoke totally deaf.

The patient was from Turk and Caicos Island, British West Indies. She denied travel other than to Miami, Florida, and had come on the insistence of her physician to have her hearing loss evaluated. There was no history of fevers, arthralgias, rashes, tick bites, meningeal symptoms, venereal disease, or other medical illness. The family history was negative.

The patient was seen in eye consultation after the corneas were noted to be abnormal in the emergency room. Ophthalmic examination revealed a corrected visual acuity of 20/20 in her right eye and 20/25 in her left. The patient was totally deaf and communication was possible only by writing notes. Bilateral interstitial keratitis was noted, and the diagnosis of Cogan's syndrome was made. The patient was admitted, and intrave-

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nous megadose steroids (60 mg methylprednisolone every 6 h) were initiated.

Laboratory investigations included normal complete blood count and serum electrolytes, and a nonreactive serum rapid plasma reagin (RPR) and fluorescent treponemal antibody absorption (FTA-Abs). Brain computed tomography (CT) scan was normal. Lumbar puncture revealed a normal opening pressure, clear colorless fluid with 1 erythrocyte, 1 monocyte, glucose of 66 mg/dl, and a protein of 35 mg/dl with a nonreactive cerebrospinal fluid (CSF) VDRL. Further work-up included a negative enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV), an anti-nuclear antibody (ANA) of titer 1:160 with a homogeneous pattern, negative ds-DNA, negative cryoglobulins, and normal complement levels (C3 = 160, C4 = 29 mg/dl). Serum protein electrophoresis showed a polyclonal hypergammaglobulinemia consistent with any chronic inflammatory process.

Her initial Lyme ELISA titer was strongly positive at 1.49 (normal 0.0–1.0, from the Microbiology Reference Laboratory, Inc., California). However, Lyme immunofluorescent antibody (IFA) titers for both IgG and IgM against Lyme antigen were negative (<1:16). Therefore, a second specimen was sent, which again reconfirmed a positive ELISA titer of 1.40.

Three days after admission, neuro-ophthalmic consultation revealed a totally deaf woman with flattening of the left nasolabial fold, as well as subtle aberrant regeneration of the facial nerve on the right (Figs. 1 and 2).

The external eye exam displayed normal lids, lashes, and lacrimal systems. The left eye had some mild pingueculitis, and the right eye was white and quiet. The slit lamp exam revealed classic interstitial keratitis (Fig. 3). Both corneas were clear to just above Descemet's membrane, where a bright silvery sheen was present (Fig. 4). Ghost vessels were essentially absent, and no active inflammation was seen in either cornea. The anterior chambers were deep and quiet, and both irides were without nodules. The lens and vitreous were clear bilaterally. Ophthalmoscopy revealed normal discs and fundi. Audiometry confirmed a profound neurosensory hearing loss.

The patient was then started on intravenous penicillin (2 × 106 U/h) and ceftriaxone (1 g/12 h) in addition to the steroids while the Lyme titer was pending. A dramatic improvement of her hearing within 3 days of the treatment was confirmed by her audiometry. Therapy was continued for a total of 14 days. She was discharged on doxycycline,

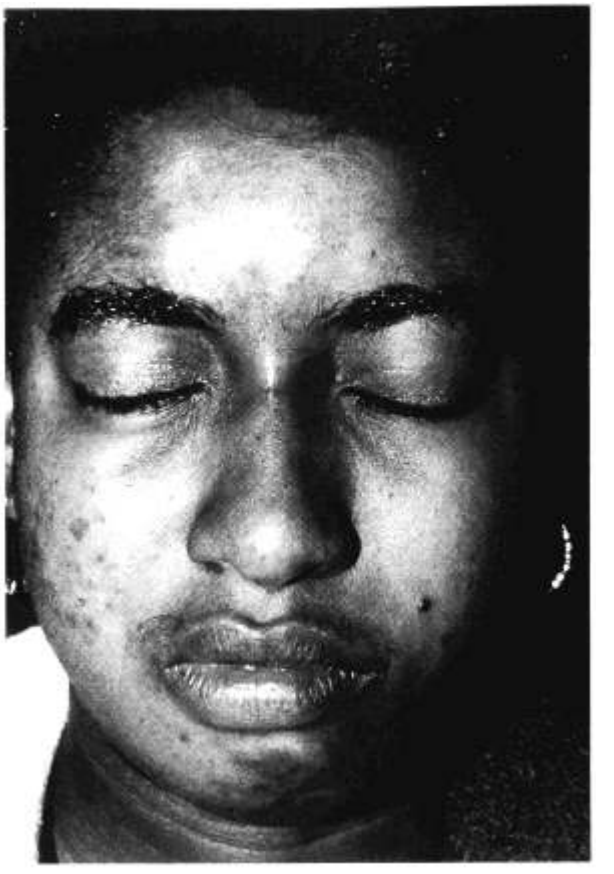

FIG. 1. Patient with eyes closed—minimal facial asymmetry.

100 mg 3 times a day, and 100 mg of oral prednisone every other day. One week later, however, her hearing decreased again leaving her with a profound hearing loss that persisted despite 1 month of oral antibiotics and steroids. A repeat Lyme ELISA titer, after treatment, was normal (0.33). Her clinical status remained unchanged.

DISCUSSION

In 1945, Cogan (1,2) originally described a syndrome consisting of a characteristic type of interstitial keratitis associated with vestibuloauditory symptoms that usually resulted in complete deafness and excellent vision. The ocular signs consisted of patchy deep corneal infiltrates that were followed by deep corneal vascularization if the inflammation persisted. The vestibuloauditory symptoms consisted of the simultaneous onset of vertigo, tinnitus, and deafness. The ocular signs would either precede or follow the hearing loss, generally within 2 months of each other. Rapid progression to complete nerve deafness was the rule. Young adults were particularly susceptible,

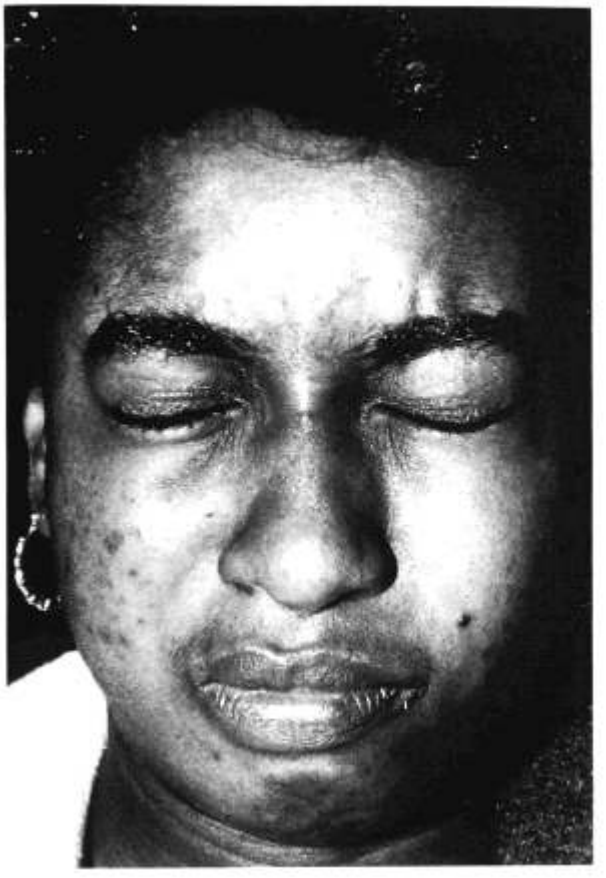

FIG. 2. With more forceful lid closure, left nasiolabial fold flatter than right. Minimal twitch of aberrant regeneration in mentalis on right.

and no evidence of syphilitic infection could be found. Suggestions have been made that the syndrome was a manifestation of polyarteritis nodosa (3,4), temporal arteritis (5), or a postvaccinal involvement (6). Aortic insufficiency and aortitis have been infrequently associated with this syndrome (7). Chlamydia has been recovered from the middle ear drainage of one patient (8) and from the conjunctival sac of another (9). Autoimmunity has been suggested in the etiology of the syndrome as well (10). Fourteen-year follow-up of six of Cogan's eight original patients plus seven additional patients by Norton failed to elucidate the etiology of the syndrome. The majority of the patients remained deaf, but otherwise healthy (11).

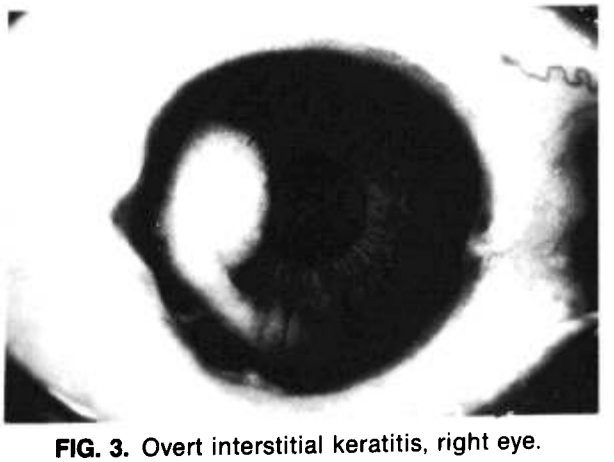

FIG. 3. Overt interstitial keratitis, right eye.

FIG. 4. Slit lamp photo showing silvery sheen at Descemet's membrane.

More recent reviews of this syndrome have described atypical presentations of Cogan's syndrome. These patients have had various ocular inflammations, including episcleritis, orbital pseudotumor, pars planitis, and uveitis associated with vestibuloauditory problems (12,13). Some patients were also atypical because they developed the eye and ear problems more than 6 months apart. However, our case displayed findings that, unlike many of these atypical cases, were consistent with the description of classic Cogan's syndrome.

Successful treatment of the hearing loss in Cogan's syndrome has depended on the prompt initiation of systemic steroids within the first 2–4 weeks of the onset of cochlear symptoms (14).

Other neurologic symptoms have been associated with Cogan's syndrome, including facial palsies, seizures, other cranial neuropathies, headaches, hyper- and hypoactive reflexes, and peripheral neuropathies (15). To our knowledge, no association between Cogan's syndrome and Lyme borreliosis has previously been reported. However, Lyme borreliosis has already been implicated in many ocular disorders, including bilateral interstitial keratitis (16), bilateral diffuse choroiditis and exudative retinal detachments (17), and optic disc edema (18) without any reported vestibuloauditory symptoms. The relationship of specific skin disorders and neurologic and musculoskeletal disorders to the borrelia spirochete has been well established. Neurologic manifestations, including fa-

cial palsies, have been frequently described (19). The importance of Lyme borreliosis as a cause of hearing loss, especially in patients with cranial mononeuropathies, has become recently more apparent. In Sweden, patients with a history of sudden hearing loss, or those associated with facial palsies, were tested for serum antibodies against the *B. burgdorferi* antigen. Seventeen percent of the patients studied had positive serologies, and nearly a third of those showed improvement in their hearing in response to antibiotic treatment (20).

The serologic study of patients using the ELISA technique has been reported by some to be the preferred method because of its high sensitivity and specificity. Lyme disease responsive to therapy has occurred in patients with positive ELISA and negative IFA tests, as was seen in our patient (21,22).

Our patient's serologic tests, without a history of erythema migrans, did not fulfill the present criteria for Lyme disease as established by the Centers for Disease Control (23). However, seronegative Lyme disease has since been documented (24). It remained impressive, however, that Lyme borreliosis has been shown in isolation to cause all of our patient's problems of interstitial keratitis, hearing loss, and facial palsies. Our patient's lack of permanent response to antibiotic therapy may reflect the delay in treatment due to her presentation after her hearing had been deteriorating for an entire year. Previous studies have reported that prompt treatment with steroids was required to avoid profound hearing loss in Cogan's syndrome (14). Steroid therapy may also have interfered with the effective treatment of our patient's late Lyme borreliosis. Failures of treatment of arthritis from late Lyme disease with ceftriaxone were seen most commonly in patients previously treated with steroids (25). It was also interesting that our patient had no response to 3 days of steroids alone, and brief recovery of her hearing did not occur until antibiotic therapy was started.

As Lyme borreliosis has become the most common tick-borne illness in the United States (26), it must be concluded that serologic testing for Lyme disease is advised in all cases of Cogan's syndrome. We recommend a work-up (Table 1) and a trial of antibiotics directed at *B. burgdorferi* in patients with Cogan's syndrome.

TABLE 1. *Work-up of Cogan's syndrome*

Complete history and physical examination with emphasis on
Travel to endemic areas
Tick bites
Skin lesions
Bell's palsy
Arthritis
Palpitations
Aseptic meningitis
Chronic fatigue
Venereal disease
Laboratory studies
Serum RPR or VDRL
Serum FTA-ABS
Serum Lyme ELISA and IFA
If seronegative, consider Western blot and lymphocyte antigen stimulation test for *B. burgdorferi*
Audiometry
Lumbar puncture

Addendum: The patient returned on November 2, 1989 with a recurrent episode of active interstitial keratitis in the left eye. She was still profoundly deaf. Repeat serologic testing that day revealed a Lyme ELISA of 1.00, and the IFA IgM was < 1:16 and IgG was now 1:64. This was considered additional evidence of seroactivity to *B. burgdorferi* in this patient.

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