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Reversible Horner's Syndrome and Lyme Disease

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Neurologic manifestations of Lyme disease are common, often debilitating, and potentially treatable. We document a case of *Borrelia* infection of the nervous system manifesting as a reversible Horner's syndrome. The search for Lyme disease should be part of the evaluation of an isolated central or preganglionic Horner's syndrome or any unexplained pupillary abnormality.

Key Words: Lyme disease—Horner's syndrome—Pupillary abnormality.

Lyme disease is a multisystem spirochetel infection caused by *Borrelia burgdorferi* and transmitted by Ixodid ticks (1–3). After infection the characteristic rash, erythema chronicum migrans, and nonspecific constitutional symptoms may ensue. Untreated primary infection may result in various neurologic, cardiac, or joint abnormalities (1–3). The most common neurologic presentations are aseptic meningitis, radiculoneuritis, and cranial neuritis (2–5). This case represents the first report of Lyme disease associated with a reversible Horner's syndrome as its sole neurologic manifestation.

CASE REPORT

The patient was a 30-year-old, previously healthy, right-handed white man who spent most of his leisure time during the month before presentation hunting and skinning deer in southeast Pennsylvania. He felt well until 4 days before evaluation when he discovered a large tick on his neck that he burned with a cigarette and removed with tweezers. The following day he developed a headache, low-grade fever, chills, myalgias, malaise, and stiff neck. Forty-eight hours later, the patient found an erythematous circular "target-shaped rash" on his left calf. That morning he had an episode of lightheadedness while urinating and slumped against the wall. This prompted him to visit a local emergency room, where he was diagnosed with Lyme disease and tetracycline therapy was started at 500 mg orally four times a day. The patient felt better by the next day but noticed that his pupils were unequal and his left lid was drooping. He came to the Hospital of the University of Pennsylvania for further evaluation and was admitted.

On physical examination, the patient appeared

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well developed and well nourished. His temperature was 98.3°F and the remainder of his vital signs were normal. General examination revealed a 16-cm erythematous "target" lesion on his left calf with partial central clearing. It was not vesicular, warm, tender, or indurated. There were no other cutaneous lesions. His neck was slightly stiff and some pain was elicited on full flexion. Results of the cardiopulmonary and abdominal examinations were completely normal.

Neurologic examination revealed the patient to be awake, alert, and oriented to time, place, and person. His mental status was completely intact except for being anxious. Visual acuity was 20/20 bilaterally and his visual fields were full to confrontation. On funduscopic examination, his disks were sharp and flat. There was a 2-mm left ptosis (Fig. 1). In ambient light, the right pupil was 5 mm and reduced briskly to 2 mm on light stimulation. The left pupil size was 3½ mm and, with light stimulation, reduced briskly to 2 mm. When the patient was placed in a dark room, the right pupil dilated to 6½ mm, while the left pupil exhibited a dilatation lag and reached only 4 mm. No afferent pupillary defect was seen. Extraocular motility was full. Facial sensation and strength were symmetric and normal. No abnormalities in hearing were detectable. His palate elevated symmetrically and the gag response was strong. Sternocleidomastoid strength was normal and the patient protruded his tongue in the midline. Muscle bulk, tone, and strength were normal in all extremities. The modalities of light touch, pinprick, temperature, vibration, and proprioception were all intact. Deep tendon reflexes were normal and his plantar responses were downgoing. The patient had a normal gait and there was no dysmetria.

Ten percent cocaine eye solution instilled in both eyes produced a 1½-mm increase in the baseline anisocoria. This confirmed the presence of a left Horner's syndrome. Twenty-four hours later, instillation of 1% hydroxyamphetamine (Paredrine)

FIG. 1. Left Horner's syndrome with ptosis and miosis before treatment.

FIG. 2. Resolving left Horner's syndrome after 10 days of Ceftriaxone therapy. Minimal left ptosis persists.

led to both pupils enlarging to 8½ mm with improvement of the left ptosis. Old photographs were reviewed and did not reveal a prior Horner's syndrome.

Dermatologic consultation advised that the oval erythematous target-like lesion on the patient's left calf was consistent with erythema chronicum migrans. Therapy was initiated with Ceftriaxone 1 g intravenously every 12 h for 10 days.

Laboratory results on admission included normal complete blood count with differential, serum electrolytes, prothrombin time, and partial thromboplastin time. Rapid plasma reagin (RPR) titer was negative. An erythrocyte sedimentation rate was elevated to 27 mm/h. The patient's alkaline phosphatase, γ-glutamyltransferase, alanine transaminase, and aspartate transaminase were all mildly elevated. Chest x-ray, electrocardiogram, and urinalysis results were all normal. Magnetic resonance imaging scans of the patient's head and cervical spine were normal. Cerebrospinal fluid examination showed 1 WBC/mm^3 (all lymphocytes), 3 RBC/mm^3, a glucose level of 72 mg/dl, and a protein level of 28 mg/dl. Lyme IgG and IgM titers from the patient's local hospital were within normal limits. Lyme enzyme-linked immunosorbent assay (ELISA) titer done on admission was 0.74 (normal up to 0.90) and Lyme IgM titer was <1:20.

Two weeks after initial presentation, the patient's Lyme ELISA titer was 2.60 and Lyme IgM titer was 1:64, confirming the diagnosis. Titers from a different laboratory showed a Lyme ELISA of 1.91. A hepatitis screen gave a negative result, and the liver function tests were normalizing. One month after presentation (2 weeks after therapy), reevaluation showed a minimal left ptosis and almost complete resolution of the anisocoria (Fig. 2). There were no new neurologic complaints and the neurologic examination was otherwise unchanged.

DISCUSSION

Although Lyme disease was not recognized in the United States until 1975, its symptoms were

described in Europe as early as 1909 (2). At that time, erythema chronicum migrans was recognized to be a result of tick-mediated infection. Beginning in 1922, neurologic sequelae of tick-borne infections were detailed (2,3). The European syndrome, consisting of dermatologic and neurologic symptoms after an *Ixodes ricinus* tick bite, was known by various names, including Garin-Bujadoux syndrome, Bannwarth syndrome, and tick-borne meningoradiculoneuritis (2–4). The American version of this illness, first called Lyme arthritis, was recognized after identification of a group of children near Lyme, Connecticut, who had been misdiagnosed with juvenile rheumatoid arthritis (1–3). During the following years, it was realized that the illness involved not only the joints and skin but also the central nervous system and heart, and was renamed Lyme disease (2,3).

A number of studies have chronicled the scope and severity of the neurologic manifestations of Lyme disease (2–5). The neurologic signs usually present several weeks after the start of the illness, but may be the presenting manifestation of the disorder. The most common neurologic symptoms are meningoencephalitis, radiculoneuritis, and cranial neuritis (2–5). The meningoencephalitidies may be short-term or chronic, and the cerebrospinal fluid usually has a pleocytosis or lymphocytosis, along with an elevated protein level (2–5). Basal meningovasculitis and occlusion of the basilar artery has been reported in association with *Borrelia burgdorferi* infection (6). Radiculopathies can be motor or sensory, unilateral, or bilateral. Brachial plexitis and mononeuritis multiplex have also been reported (3–5).

The facial nerve is the most commonly involved cranial nerve (2–5) and can be involved either unilaterally or bilaterally. Lesions of every cranial nerve from the oculomotor to the spinal accessory nerve have been documented in patients with Lyme disease (4,7). The optic nerves have not been spared by *Borrelia*. Papilledema has been reported (8). Another case initially thought to show papilledema (9) probably was "optic neuritis with good vision or optic perineuritis" (10) because the cerebrospinal fluid opening pressure on presentation was normal and visual fields revealed "bilateral cecocentral scotomas" (10). In addition, patients have been reported to have had Argyll Robertson pupils (8), iritis, and vitritis (10).

This patient presented with a history of exposure to ticks, and the rash of erythema chronicum migrans. The clinical diagnosis of Lyme disease was serologically confirmed. The patient's neurologic examination was completely normal except for a left Horner's syndrome that was pharmacologically proved using 10% cocaine eye drops. One percent hydroxyamphetamine was used to localize the lesion within the three-neuron oculosympathetic pathway. Because both pupils dilated to 8½ mm after Paredrine instillation the lesion had to be either in the first- or second-order neuron.

A central Horner's syndrome occurs when the first neuron in the oculosympathetic pathway is damaged. The majority of lesions to this neuron are due to brainstem or cerebral vascular insults (11,12). However, intracranial and intraspinal tumors, syringomyelia, multiple sclerosis, and trauma represent other common important etiologies of a central Horner's syndrome (11,12). A preganglionic Horner's syndrome occurs when the second neuron in the oculosympathetic pathway is damaged. Lesions to this neuron are usually the result of tumor involvement or trauma. The most common tumor involving this second-order neuron is bronchogenic carcinoma (Pancoast's tumor). However, breast cancer, sarcomas, lymphoreticular disease, and vertebral column and meningeal tumors have been documented to cause preganglionic Horner's syndrome. Less common causes of preganglionic Horner's syndromes include the pachymeningitis of syphilis, ruptured intervertebral disks, and thoracic aneurysms (11,12).

In this patient there was no evidence of a vascular insult, malignancy, syringomyelia, or multiple sclerosis because both head and cervical spine magnetic resonance imaging scans and chest x-ray films were normal. There had been no history of trauma or recent neck or thoracic surgery. Our patient's Horner's syndrome appeared concurrently with the *Borrelia* infection and resolved with ceftriaxone therapy.

The natural history of Lyme disease may vary considerably and often presents a difficult diagnostic challenge. It has become increasingly evident that the three stages of Lyme disease may overlap, allowing certain features to appear out of sequence or to occur in isolation (13). Given the early onset of this patient's Horner's syndrome and its rapid response to therapy, we believe the most likely pathophysiologic mechanism was direct invasion of the spirochete into the sympathetic pathway. Similar to the facial nerve palsy associated with this disorder (14), a Horner's syndrome may occur in the absence of a cerebrospinal fluid pleocytosis.

In patients with new onset isolated central or preganglionic Horner's syndrome, Lyme disease should be carefully considered. Unlike most cases of Horner's syndrome, it can be treated and re-

versed. The neurologic presentations of Lyme disease are so diverse that serologic tests for Lyme infection are probably essential in the diagnostic evaluation of patients with unexplained pupillary abnormalities.

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