Hansen’s disease, or leprosy, was first identified in patients in 1873 by Dr. Gerhard Armauer Hansen. It is a chronic infectious disease with a multitude of clinical manifestations. Though still a major health concern and leading cause of peripheral neuropathy in the developing world, it is rare in the United States, with only about 150 cases reported each year. Nevertheless, it is imperative that neurosurgeons consider it in the differential diagnosis of neuropathy.

The causative organism is *Mycobacterium leprae*, which infects and damages Schwann cells in the peripheral nervous system, leading first to sensory and then to motor deficits. A rare presentation of Hansen’s disease is pure neuritic leprosy. It is characterized by nerve involvement without the characteristic cutaneous stigmata. The authors of this report describe a case of pure neuritic leprosy presenting as ulnar nerve neuropathy with corresponding radiographic, electrodiagnostic, and histopathological data.

This 11-year-old, otherwise healthy male presented with progressive right-hand weakness and numbness with no cutaneous abnormalities. Physical examination and electrodiagnostic testing revealed findings consistent with a severe ulnar neuropathy at the elbow. Magnetic resonance imaging revealed diffuse thickening and enhancement of the ulnar nerve and narrowing at the cubital tunnel. The patient underwent ulnar nerve decompression with biopsy. Pathology revealed acid-fast organisms within the nerve, which was pathognomonic for Hansen’s disease. He was started on antibiotic therapy, and on follow-up he had improved strength and sensation in the ulnar nerve distribution.

Pure neuritic leprosy, though rare in the United States, should be considered in the differential diagnosis of those presenting with peripheral neuropathy and a history of travel to leprosy-endemic areas. The long incubation period of *M. leprae*, the ability of leprosy to mimic other conditions, and the low sensitivity of serological tests make clinical, electrodiagnostic, and radiographic evaluation necessary for diagnosis. Prompt diagnosis and treatment is imperative to prevent permanent neurological injury.

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we describe the diagnosis and management of a case of pure neuritic leprosy manifesting as ulnar neuropathy at the elbow to demonstrate the potential diagnostic challenges in the modern imaging era and to discuss surgical considerations related to leprosy.

Case Report

Presentation and Examination

An 11-year-old, otherwise healthy male was referred for evaluation of a progressive right ulnar palsy and abnormal MRI. His symptoms began 9 months earlier with hand paresthesias followed by numbness. He also complained of a 5-month history of progressive hand weakness and pain involving his right medial elbow, forearm, wrist, and thumb. He had no history of neck or radicular pain, denied recent trauma or viral illness, and had no family history of neurological disease. He was delivered full-term by cesarean section in India and lived there until the age of 5 years, when he moved to the United States. He had spent 6 weeks in India visiting family several months prior to the onset of his symptoms. His medical history was otherwise unremarkable, and his immunizations were up to date.

Physical examination findings were limited to the right upper limb. The ulnar nerve was palpably enlarged in the medial arm. He had loss of pin sensation in the ulnar distribution of the hand as well as in the dorsum of the hand generally. Motor exam revealed severe ulnar palsy with minimal function of intrinsic hand muscles innervated by the ulnar nerve and significant weakness in the flexor digitorum profundus to the fourth and fifth digits with associated clawing. Median and radial motor function was normal.

Imaging Studies

On MRI studies, the ulnar nerve was thickened diffusely from the midhumeral level into the forearm with a maximal diameter of 12 mm (Fig. 1). It was isointense to muscle on T1 and hyperintense on T2 and STIR sequences. The nerve demonstrated intense contrast enhancement (Fig. 2). There was a questionable additional lesion involving the median nerve versus an enhancing lymph node just proximal to the elbow.

Electrodiagnostic Studies

Nerve conduction studies revealed an absent right ulnar sensory potential and motor potential at the first dorsal interosseous muscle. The ulnar motor potential at the abductor digit minimi muscle was significantly reduced in amplitude at 0.2 mV (left 5.5 mV). The radial sensory potential was also significantly reduced at 2.5 μV (left 75.7 μV). Left-sided responses, right median responses, and right radial motor responses were normal in duration and amplitude. Electromyography studies revealed significant abnormal spontaneous activity and no voluntary motor unit activation in the ulnar-innervated forearm and intrinsic musculature of the hand; otherwise, the studies were normal.

Preoperative Evaluation and Operation

Because the differential included leprosy, the patient was referred to a pediatric infectious disease consultation. The National Hansen’s Disease (Leprosy) Clinical Center was also contacted. As the patient had no clear cutaneous manifestation amenable to slit-skin biopsy and given the relative constriction of the ulnar nerve at the elbow in the face of a severe ulnar palsy, surgical exploration was recommended. At surgery, the ulnar nerve was enlarged and firm. A relative constriction at the cubital tunnel was identified and released. Using electrophysiological monitoring and microscopic dissection, we removed a small nonfunctioning fascicle and sent it for pathological evaluation.

Pathological Evaluation

Sections stained with H & E revealed severe granulomatous and lymphocytic infiltration with little residual nerve visualized (Fig. 3). Fite stains performed at the national Hansen’s disease laboratory revealed moderate acid-fast organisms within the specimen whose frequency led to the patient’s classification in the multibacillary, mid-borderline to borderline lepromatous (BB-BL) portion of the disease spectrum (Fig. 4).

Postoperative Course

After rendering a diagnosis, we started the patient on a 3-drug regimen including rifampin, clofazimine, and dapsone with a planned duration of 2 years. He was also given a 3-month course of steroids. At 8 months postoperatively, the radial distribution numbness had resolved and the ulnar distribution numbness was improving. The clawing had resolved, and the flexor digitorum profundus...
weakness had improved, but the severe ulnar interosseous muscle weakness persisted.

Discussion

General Comments

Leprosy remains a major cause of neurological morbidity worldwide,13,16,22,23 and with a mobile population traveling to and from endemic regions, the disease needs to be considered in the differential diagnosis of neuropathy. Typically, the diagnosis is made by taking a history and completing a physical exam and slit-skin smear or skin biopsy. In a nonendemic region, travel history, rash, and anesthetic skin may not be obvious unless actively sought. In the Americas, including the southern United States, interaction with the wild armadillo, the only other natural host of *M. leprae*, may result in transmission of the disease.28,31 So a travel history within the United States is also valuable.

While only 150 new cases are diagnosed in the United States each year, in 2009 it was estimated that more than 7000 people previously registered with the National Hansen’s Disease Program might still be living in the United States. Because leprosy can be difficult to eradicate even with current multidrug therapy, leprosy patients may present with disease years after the initial diagnosis.17,32

Diagnosis and Imaging

When presented in this case report format, the diagnosis of leprosy seems obvious; however, the pure neuritic form of the disease presenting in a nonendemic area complicated the diagnosis. The patient had emigrated from an endemic region, but his father, who is a physician, noted that the patient had had no known contact with an infected individual. As 95% of individuals have a natural immunity to the microorganism, concern for leprosy was minimalized.1 Electrodiagnostic studies were helpful in delineating the extent of nerve involvement but were not specific to any particular diagnosis. The imaging studies were interpreted as being consistent with perineurioma, and neurological specialists at a nationally recognized institution counseled the family against surgical intervention. This is in keeping with recommendations in recent literature against biopsy of perineuriomas given their classic MRI appearance.20,24 While the sciatic nerve is the most common site of perineurioma involvement, ulnar nerve involvement has been reported.19

In addition to perineurioma, the differential diagnosis of nerve thickening, increased T2 signal, and contrast enhancement on MRI studies is broad and includes neoplastic entities such as nerve sheath tumors and lymphoma, inherited diseases, infectious entities such as leprosy, and inflammatory processes such as inflammatory pseudotumor of nerve.4,5,18,36 In our experience, the T2 signal change and enhancement in our case were more intense than typically seen in perineuriomas and more closely mimicked the T2 signal of a nerve sheath tumor. It is important to note both that the MRI appearance of lepromatous nerves can vary depending on the severity of the neuritis and that the resolution of changes may cor-
respond with successful treatment, so that a lack of enhancement does not preclude the diagnosis of leprosy. Ultrasound has also been used to evaluate lepromatous nerves and may demonstrate diffuse thickening as well as endoneural color flow signals that correspond to symptomatic neural involvement and may resolve with successful treatment. Computerized tomography may also demonstrate nerve thickening as well as calcifications. Some cases of leprosy will present with an intraneural abscess and may be mistaken for an isolated nerve sheath tumor or sarcoma. 

Fascicular Biopsy

Given the patient’s travel history, a clinical presentation suggestive of multiple nerve involvement, and the lack of clear cutaneous manifestation, we believed that surgical exploration and biopsy were warranted. Fascicular biopsy is thought to be contraindicated in the diagnosis of leprosy given the risk of damaging the parent nerve. In our experience, fascicular biopsy of some proximal nerves such as the sciatic nerve is well tolerated, and based on the established practice of ulnar nerve fascicular transfer for brachial plexus reconstruction, we believed that the need for tissue diagnosis in this case outweighed the risk especially since the delayed treatment of ulnar nerve lesions is known to lead to permanent atrophy and contractures.

Medical Treatment

Multidrug therapy and a course of steroids are the primary treatment strategy in patients with leprosy. The treatment varies based on whether the patient is categorized in the paucibacillary or multibacillary end of the disease spectrum and continues for 12 to 24 months, respectively. Despite adequate treatment, patients may have a progressive decline in neurological function during treatment. Notably, even after M. leprae has been killed by antimycobacterial treatment, the dead bacilli and their antigens can remain in tissues for several years, offering continuing stimuli for injury. The exact cause of this is not clear, but it has been noted that apoptosis in in vitro studies of various cell types can be triggered by the ingestion of dead but not live M. leprae. Host immune response to infected Schwann cells and perineural fibrosis may also play a role and provide the rationale for using steroids acutely. A delayed decline in neurological function can also occur following successful treatment, again for unclear reasons. Overall, recovery primarily depends on the severity and duration of neural deficit prior to treatment, so delaying diagnosis with serial imaging can be detrimental in these cases. For those practicing in the United States, the National Hansen’s Disease Clinical Center in Baton Rouge, Louisiana, can be a valuable resource. It offers free consultations, free pathological review of skin biopsies, free antibiotics for leprosy treatment, and free educational materials. The WHO also offers multidrug therapy free of cost to those suffering from leprosy.

Surgical Decompression of Lepromatous Nerves

Pertinent to neurosurgeons is the fact that decompressive surgery as an adjunctive treatment in leprosy has a long and controversial history. As previously noted, leprosy typically involves major nerves at and above areas associated with compressive neuropathy. Relative compression of the nerves in their fibro-osseous tunnels can be demonstrated by imaging studies and at surgery. When explored, the nerves, as in our case, have a dense fibrotic consistency. The fibrotic epineurium and external compression are thought to create relative venous obstruction, capillary stasis, edema, and ischemia. External decompression and epineurotomy have been used in an effort to improve overall outcomes in patients with leprosy. We decompressed the ulnar nerve at the time of biopsy in our case to alleviate any contribution of compression to his deficit, to prevent potential worsening compression in the face of swelling related to the biopsy, and to theoretically maximize his neural regeneration. We believed that the small added morbidity in this case was justified given the typically poor prognosis seen with severe ulnar palsy at the arm level. Had we been able to make the diagnosis of leprosy in this case without the biopsy, however, we would have recommended initial treatment with multidrug therapy and steroids and would not necessarily have intervened surgically unless his pain had not improved.

Numerous reports suggest various benefits of surgical decompression, including improved neurological status, less deformity, and alleviated pain, but the nature of these studies has called into question the true effectiveness of surgery. The literature relating to this issue has been summarized in a Cochrane review last updated in...
2012, 2013, 2014, 2015. No clear statistical benefit from surgical decompression could be demonstrated based on the existing literature, and recommendations have been made for careful randomized controlled trials. As per Husain and Mishra, we disagree with this recommendation given that the number of uncontrollable variables precludes an ability to get adequately comparable groups. The variable nature of the host response, occasional spontaneous recovery without treatment, clinical worsening during and even months after successful treatment, variable number of nerves and extent of their involvement, variable ability of individual nerves to recover from injury, inability to blind surgical trials, and inability to obtain meaningful outcome measures in the field setting where most care is given make the likelihood of obtaining a legitimate answer regarding surgical decompression in a randomized multicenter trial essentially nil. Large clinical registries and/or experimental studies in armadillos may help provide some insight in the future, but for now the decision about decompression will need to be made on a case-by-case basis. In our patient, biopsy was critical in making the diagnosis and initiating definitive medical treatment. As his ulnar nerve function was only moderately improved after 8 months of treatment, it is not clear if our decompression added any benefit.

Conclusions

In summary, leprosy is a cause of significant neurological morbidity worldwide, and because it involves nerves near regions of entrapment such as the ulnar nerve at the elbow, neurosurgeons may be involved in the care of patients with this disease. Diagnosis may be difficult in nonendemic areas since electrodagnostic and imaging studies are not specific to leprosy. In cases of pure neuritic leprosy with no significant cutaneous manifestations, diagnosis can be particularly challenging and may necessitate fascicular biopsy. Surgical decompression in individual cases with no response to therapy or with clinical worsening may be appropriate but remains controversial. Although the bacteria can be eradicated with multidrug therapy, a delay in diagnosis can lead to permanent neurological morbidity, so leprosy needs to be considered in the differential diagnosis of neuropathy even in nonendemic areas of the world.

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Author Contributions

Conception and design: Payne, Baccon, Dossett, Scollard, Harbaugh. Acquisition of data: all authors. Analysis and interpretation of data: Scollard, Harbaugh. Drafting the article: Payne, Baccon, Dossett, Scollard, Harbaugh. Critically revising the article: Payne, Baccon, Harbaugh. Reviewed submitted version of manuscript: Payne, Dossett, Scollard, Byler, Patel, Harbaugh. Approved the final version of the manuscript on behalf of all authors: Payne. Study supervision: Harbaugh.

Supplemental Information

Previous Presentation

Portions of this work were presented in poster form at the 82nd AANS Annual Scientific Meeting held in San Francisco, California, on April 5–9, 2014.

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