Leprosy Presenting as Orofacial Pain: Case Report

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This article reports an unusual case of neuropathic orofacial pain secondary to leprosy. To the authors' knowledge, it is the first case of leprosy reported in the Western literature that was initially thought to be dental pain, then mistaken as a temporomandibular disorder before the correct diagnosis was made. The patient had migrated to Australia from India 24 years previously and was otherwise healthy without any overt features suggestive of infection. A review of the literature revealed that the trigeminal nerve is frequently involved in leprosy, usually associated with sensory loss rather than neuropathic pain. Even in Western countries, patients originally from countries where leprosy is endemic may develop symptoms of the disease many years later. The possibility of leprosy should be considered in the diagnosis of neuropathic orofacial pain in such patients. J ORO-FAC PAIN 2012;26:142–147

Key words: leprosy, neuropathic pain, orofacial pain

Leprosy (Hansen disease) is a chronic infectious disease caused by the bacteria acid-fast bacillus *Mycobacterium leprae*. Leprosy is primarily a granulomatous disease of the peripheral nerves and mucosa of the upper respiratory tract.[1,2] Skin lesions are common, with cooler, exposed areas the most frequently affected. Leprosy is considered the most common cause of treatable peripheral neuropathy in the world causing sensory loss, which leads to susceptibility to trauma and the deformity seen in affected areas.[3,4] Left untreated, leprosy can be progressive, causing permanent damage to the skin, nerves, limbs, and eyes.

The disease is probably transmitted via close contact and nasal droplets and has a variable incubation period of up to 30 years.[1,2] At highest risk are those living in endemic areas (such as India, Brazil, Nepal, Egypt, Somalia, and Northern Australia) with poor conditions, such as contaminated water, as well as factors that compromise immune function, such as malnutrition.[1,2] Diagnosis in Western countries is often delayed because health care providers are unaware of leprosy and its symptoms. Early diagnosis and treatment prevents nerve involvement, the hallmark of leprosy, and the disability it causes.[2]

The following describes an unusual case of a patient who had migrated to Australia from India some 24 years previously and initially presented to her dentist with orofacial pain. After the patient initially underwent unhelpful dental treatment, a temporomandibular disorder and then trigeminal neuralgia were considered as possibilities until the definitive diagnosis was made.

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Case History

A 51-year-old woman who had migrated from India to Australia some 24 years previously presented with a 3-month history of numbness and tingling with intermittent pain and a sensation of swelling that affected the right maxillary region. The patient also described a burning sensation, such that she constantly felt the need to rub the area. The patient had initially developed severe pain in her face, ear, and jaw during the landing of a plane flight. As a mandibular right second molar had recently fractured, she consulted a dentist who diagnosed a dental pulpal problem requiring prescription of antibiotics and endodontic treatment. Due to ongoing pain, the tooth was extracted at the patient's request, but the symptoms persisted. Indeed, the right side of the face had become more generally tender such that she was unable to lie on her right side. The pain had spread to involve her right temporomandibular joint (TMJ), ear, and temple regions and was aggravated if she opened her mouth fully. The patient's family physician was concerned about the possibility of osteomyelitis and prescribed further antibiotics: penicillin and metronidazole. A computed tomography (CT) scan was arranged, which failed to reveal any evidence of bone infection or regional lymphadenitis. The family physician prescribed carbamazepine and prednisolone and, suspecting a temporomandibular disorder, referred the patient to one of the authors. As the carbamazepine had little effect and was poorly tolerated, in the meantime, the patient had sought advice from a second family physician who had prescribed gabapentin.

The patient considered herself in generally good health. She was married with two sons. The medical history was considered noncontributory but was positive for stress/anxiety, paronychia, resection of a ganglion cyst from the left hand, and perimenopausal symptoms. The patient did not report any widespread aches or pains, any history of migraine or other primary headache, nor symptoms suggestive of neurologic disease such as polyneuropathy. Her father had died at 60 years having suffered cardiovascular disease and mature onset diabetes. Her mother was described as healthy.

Examination Findings

The extraoral examination was unremarkable without obvious skin rash or other cutaneous findings in the region of the complaint or evident facial swelling. The cranial nerve screening examination was unremarkable apart from revealing a slight loss of sensation to both light touch and pin prick in the right infraorbital nerve distribution. The same area was noted to be slightly hyperalgesic to palpation. The cervical spinal and jaw functional examinations were considered normal. No myofascial trigger point referral patterns were elicited into the region of the chief complaint from the masticatory, cervical, and shoulder girdle musculature. The intraoral examination revealed dental attrition and some large restorations. The right maxillary teeth were slightly tender to palpation, but pulp-tested normally. There was no evidence of any active dental or periodontal infection or oral mucosal disease. The extraction wound in the right mandibular second molar site appeared to be healing normally.

Imaging

A cone beam CT failed to reveal any significant orodental, TMJ, or maxillary sinus pathology. What appeared to be a small buccal cortical bone fenestration at the apex of the buccal root of the upper right first premolar was demonstrated (Fig 1). The right TMJ had evidence of early degenerative joint disease.

Initial Diagnostic Impressions

Based upon the history and clinical findings, the authors suspected the patient was likely suffering orofacial neuropathic pain, possibly a prodromal form of trigeminal neuralgia. The possibility of a dental pulpal problem affecting the maxillary right first premolar was in the differential diagnosis because of the large dental restorations and cone beam CT suggestion of a periapical lesion. Therefore, the patient was referred back to her general dentist for further investigation of all the teeth on the right side. The patient was advised that it was unlikely that her symptoms were due to a temporomandibular disorder or to stress-related bruxism.

Further Investigations

The patient was also referred to an otorhinolaryngologist whose clinical examination was unremarkable for ear, nose, oropharyngeal, or parotid pathology. Due to the complaint of numbness, pre- and postcontrast magnetic resonance imaging (MRI) of the maxilla, brain, and skull base was arranged.

The MRI revealed pathologic signal hyperintensity and enhancement of right infraorbital nerve, extending from the subcutaneous tissue of the anterior

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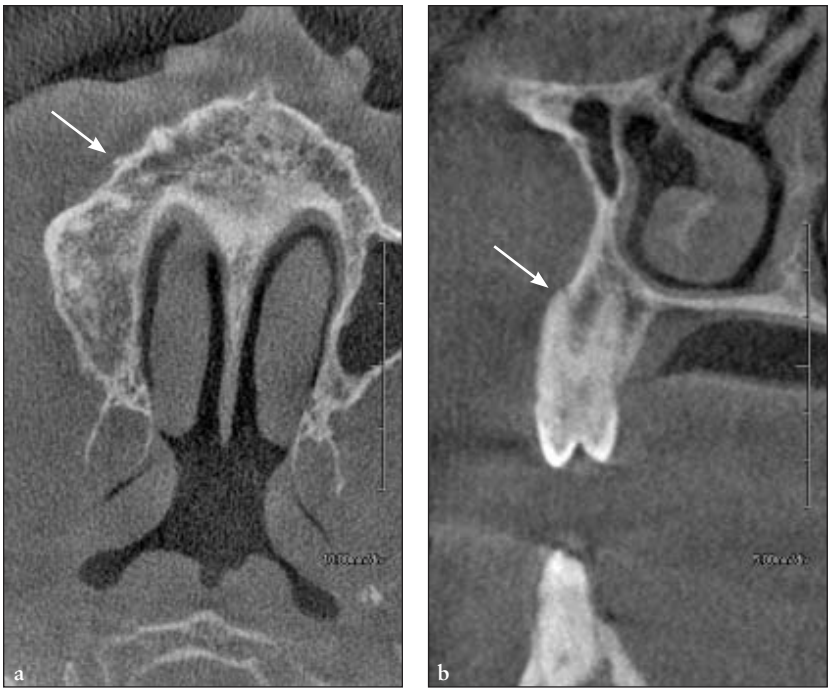

Fig 1a Axial reformatted cone beam images demonstrate a focal buccal cortical fenestration over the buccal root apex of the birooted maxillary right first premolar.

Fig 1b Coronal reformatted cone beam images demonstrate a focal buccal cortical fenestration over the buccal root apex of the maxillary right first premolar.

cheek, along the infraorbital canal to the main trunk of maxillary nerve within the foramen rotundum and cavernous sinus (Fig 2). Additionally, there was abnormal hyperintensity and enhancement of the proximal right mandibular nerve within the foramen ovale. The possibility of perineural spread, typically seen with skin melanoma, squamous cell carcinoma, or minor salivary gland malignancy such as adenoid cystic carcinoma, was raised.

To rule out malignancy, a whole body positron emission tomography (PET)-CT was arranged and was clear, with no finding of any primary source of malignancy in the head, chest, abdomen, or pelvis. Fine needle aspiration biopsy of a small lesion found in the right parotid gland revealed a reactive lymph node, without evidence of metastatic malignancy or lymphoma.

A biopsy of the right infraorbital nerve was arranged which revealed evidence of a chronic perineurial and endoneurial inflammatory neuropathy. A mixed cell infiltrate of the affected nerve included lymphocytes, macrophages, and rare eosiniphils. No acid-fast bacillus (AFB) was identified with special Wade Fite or Ziehl-Neelsen stains, but polymerase chain reaction (PCR) testing detected *Mycobacterium leprae* DNA.

At this stage, the patient was referred to an infectious disease specialist who noted hyperpigmented lesions on the arms, with normal sensation to light touch over the whole body except for slightly impaired pin prick and cold perception affecting a small area of skin over the right cheek, extending to the upper lip. The malar region itself was of normal appearance, but on palpation was slightly indurated and tender. In agreement with the authors' findings, the cranial nerve examination was otherwise normal, including cranial nerve VII. The visual acuity, funduscopic, and corneal reflex examinations were also normal.

Further investigations included slit skin smears from eyebrows and cheek skin as well as nasal smears. Blood tests including G6PD, HIV, and Hepatitis serology were normal. Quantiferon and chest x-ray were normal, eliminating tuberculosis from the differential diagnosis. The patient was diagnosed with leprous leprosy and prescribed the WHO Mycobacterium (MB) leprosy pack, which includes dapsone, clofazimine, and rifampicin. The patient was advised that she would be required to take the medications for 12 to 24 months to reliably cure the infection. Additionally, the patient was prescribed gabapentin 2,400 mg for the neuropathic pain.

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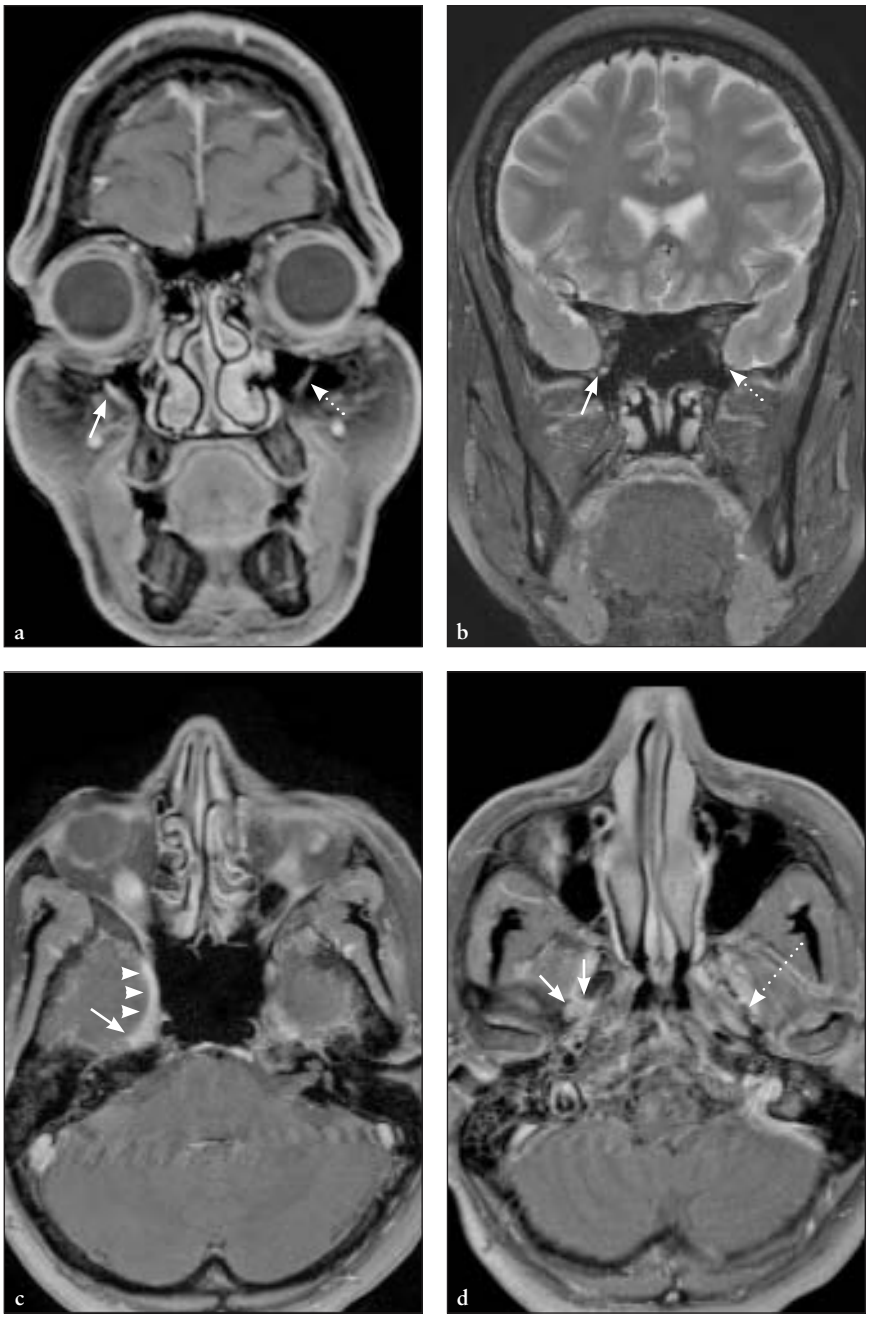

Fig 2a Coronal postcontrast T1-weighted fat-saturated MRI image at the level of the anterior face, showing an abnormally enhanced, mildly thickened right infraorbital nerve *(arrow)* within the infraorbital canal. Compare with the normal left nerve *(dotted arrow)*.

Fig 2b Coronal T2-weighted fat-saturated MRI image at the level of the sphenoid sinuses, showing the abnormally thickened hyperintense maxillary division of the right trigeminal nerve (V2) within the right foramen rotundum *(arrow)*. Normal left V2 in left foramen rotundum is shown for comparison *(dotted arrow)*.

Fig 2c Axial postcontrast T1-weighted fat-saturated MRI image at the level of Meckel's caves, showing the thickened, enhanced V2 traversing the right foramen rotundum and the inferior cavernous sinus *(arrowheads)* to the level of the trigeminal ganglion in Meckel's cave *(arrow)*.

Fig 2d Axial postcontrast T1-weighted fat-saturated MRI image 12 mm inferior to Fig 2c, showing an abnormal, thickened, and hyperintense right mandibular division (V3) *(arrows)* exiting the skull base via the foramen ovale. Note normal left V3 in left foramen ovale *(dotted arrow)*.

Discussion

The historical focus on leprosy as an infectious disease process of the skin has shifted toward it being considered a disease of the peripheral nervous system. Indeed, leprosy can be considered the most common cause of treatable peripheral neuropathy in the world.[3] There are a number of different clinical presentations of leprosy that probably reflect the individual patient's cellular immune response to *M leprae*.[1] Patients with good T-cell immunity (Th1 type) towards *M leprae* exhibit tuberculoid (TT) leprosy, also known as paucibacillary leprosy, which is a milder form of the disease and is characterized by skin discoloration. At the other end of the spectrum, those with poor T-cell immunity towards

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M leprae often exhibit lepromatous (LL) leprosy or multibacillary leprosy, which is associated with symmetric skin lesions, nodules, plaques, thickened dermis, and frequent involvement of the nasal mucosa that may result in congestion and nose bleeds. In between these two polar forms of leprosy are the variously termed borderline forms.[1]

Leprous neuropathy is characterized by the involvement of superficial peripheral nerve trunks in cooler body regions such as ulnar, median, radial, common peroneal, supraorbital, and great auricular nerves. Leprous neuropathy can take any of three forms: mononeuropathy, mononeuritis multiplex, or symmetric polyneuropathy.[4] Cutaneous nerves are universally affected in leprosy, even where the skin is apparently normal. Damage to peripheral nerves is a key component of leprosy and, together with the typical skin lesions, accounts for its major clinical features, including disability. The sensory and motor nerve loss that accompanies nerve damage is the basis for many of the classic features of the disease on exposed areas such as skin wounds, clawed hands, plantar ulcers, etc. Sensory nerve damage is associated with an early loss of sensation, but pain was until recently not considered a remarkable aspect of leprosy.[4] However, recent studies have demonstrated that neuropathic pain is in fact far more widely prevalent than previously believed, with one Brazilian study reporting an overall prevalence of neuropathic pain in 56% of leprosy patients.[5]

Cranial nerve involvement is also commonly seen in patients with leprosy.[6–11] The facial nerve is most commonly involved, but the trigeminal nerve may also become involved and, in one study, hypoesthesia and anesthesia were most often observed in the maxillary divisions of the trigeminal nerve.[12] Another case study, in which an initial erroneous diagnosis of facial cellulitis was made, highlighted the need for clinicians in countries with diverse immigrant populations to be aware of leprosy.[13] One study found about 18% of new leprosy patients seen over an 8-year period in India had evidence of involvement of either the trigeminal or facial nerves.[14]

The mechanism by which the mycobacterium invades the neural cells and elicits an immune response may involve a glycoprotein that attaches to both the surface of the mycobacterium and a molecule on the surface of Schwann cells.[4,5] With time, the immune response can provoke so-called "leprosy reactions," which are associated with inflammation and acute peripheral nerve damage. Although the molecular mechanisms that trigger nerve damage and inflammation in leprosy are unknown, it is likely that neuropathic pain is due to an ongoing neuritis with resultant axonal damage, spontaneous nociceptor discharge, lowered activation thresholds, etc, as is seen following nerve damage from other causes.[5] Leprosy-related nerve damage is immune-mediated and may start before diagnosis, during antimicrobial treatment, or even after completion of treatment.[3] Of course, host genetic factors control the different patterns of the immune response to *M leprae*, but the immunological markers that could predict disease susceptibility and progression have yet to be identified.[3]

Intraorally, the nodular and ulcerative manifestations of leprosy are well known, particularly to oral medicine specialists in the countries where leprosy is endemic. Oral manifestations usually appear in lepromatous leprosy where the premaxilla, hard and soft palate, tongue, and uvula are most commonly affected. Leprosy patients tend to have poor dental and periodontal status.[15,16] In general, oral mucosal involvement occurs only after the nasal cavity has been affected.[17–19]

This case report highlights a relatively poorly considered infectious cause, at least in Western countries, of orofacial neuropathic pain and trigeminal sensory loss. Interestingly, leprosy is resistant to, and does not usually respond to, the antibiotics used to treat the common orofacial infections. It is for this reason that the WHO Leprosy Pack combines three agents (dapsone, clofazimine, and rifampicin) to be taken for at least 1 year. In the presented case report, the patient failed to respond to antibiotics and her symptoms actually progressed. Failure of a patient to respond to antibiotic treatment, with worsening of symptoms, should alert the clinician to reevaluate the diagnosis and consider further testing, including antibiotic sensitivity. The case also highlights that any report of numbness in the orofacial region should always be taken seriously, and therefore warrants appropriate investigations including sensory testing and imaging. As well as the possibility of neoplastic disease affecting the oropharyngeal and intracranial structures, the possibility of other secondary causes of neuropathic pain, including infection, must also be considered. Moreover, whenever a clinician encounters patients originally from areas where leprosy is endemic, this highly prevalent disease should be considered in the differential diagnosis of orofacial pain.

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