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ORIGINAL ARTICLE

Neurosurgical treatment of leprosy neuropathy in a low-incidence, European country

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Abstract

Introduction Leprosy is nowaday increasingly encountered in non-endemic countries. Nerve involvement is common. Swelling of the nerves may lead to entrapment neuropathy causing pain and neurological deficits. Delay in diagnosis and treatment may lead to loss of chance of improvement. Surgical decompression in conjunction with medical therapy allows relief of symptoms.

Methods We present a retrospective series of 21 patients surgically treated in our center for leprosy entrapment neuropathy. We report presentation, treatment, and outcome at follow-up including a brief literature review.

Results Twenty-one patients were treated for nerve entrapments in four different anatomical districts. We reported good clinical outcomes mainly in motor deficits but also in improvement of sensitive deficits and pain symptoms. We did not experience surgical complications.

Discussion Although there is a lack of high-quality prospective studies comparing medical and surgical treatment of leprosy neuropathy, benefits of surgery are widely reported in series and case reports from endemic countries. There is scant literature from low-incidence countries even if leprosy incidence is nowaday increasing in these countries and will likelihood further increase in the future. Our results are in line with the literature presenting good outcomes after surgery.

Conclusion We believe that a precise knowledge of the pathology and its management is crucial also for physicians who work in low-incidence countries to maximize healing chances with timely diagnosis and treatment.

Keywords Leprosy · Entrapment neuropathy · Epineurotomy · Surgical decompression · Neurolysis endoneural abscess

Introduction

Leprosy (Hansen disease) is a chronic granulomatous infectious disease, caused by *Mycobacterium leprae*, an obligate intra-cellular bacillus, which mainly involves skin and peripheral nerves [1]. *Mycobacterium leprae* shows a marked neurotropism and virtually all patients with leprosy present some degree of nerve involvement at the time of diagnosis [2].

In fact, leprosy is characterized by hypoesthetic lesions, thickened peripheral nerves, and a positive skin-smear examination for lepra bacilli. Moreover, even if rarely encountered, it is described as a pure neuritic form of leprosy, presenting with peripheral neuropathy with negative skin-smear examination and without detectable skin lesions [3]. The pure neuritic form may be under-reported due to the difficulty of diagnose until the skin involvement is present.

Leprosy nerve lesions consist in chronic damage that can be worsened by acute immunological reactions classified as type 1 or reversal reaction and type 2 or *erythema nodosum leprosum* and neuritis [2].

Neurosurgical treatment plays an important role in treatment of Hansen's neuropathy allowing relief of symptoms [4]. Decompressive surgery is indicated after failure of corticosteroid therapy, and it should not be performed alone but in addition to medical therapy [5].

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Leprosy is an important global health concern; early diagnosis and proper treatment are critical for preventing lifelong neuropathy and disability; however, even if the World Health Organization (WHO) set the ambitious goal of eliminating the disease, leprosy is still a major issue around the world [6].

Worldwide, epidemiological data suggest 3.2 new cases every 100,000 people per year [7].

India accounts for 60% of all leprosy cases, Brazil for 13%, and Indonesia for 8%, while 11 countries from the Africa region and South East Asia region account for 14% of global cases. While diagnosis and treatment of leprosy in these high-incidence countries has been widely discussed [8–10], few reports are from low-incidence countries, like Italy one of the 92 countries that account for the remaining 5% of cases [7].

In fact, leprosy in low-incidence countries is usually diagnosed in migrants from endemic countries or less frequently in travelers who have been staying in those areas. Small series [11] and case reports [12, 13] tend to show a delay in diagnosis often due to a lack of specific knowledge by physicians of possible leprosy presentations. Neurological symptoms tend to be misdiagnosed especially in cases where no skin lesions are present [11]. Diagnosis and management of the disease in a non-endemic region may be more challenging than in endemic countries.

One of the possible complications of leprosy neuropathy is entrapment neuropathy, namely compression of a nerve by narrow, inextensible tunnels, or canals. The latter is likely to occur in leprosy neuropathy because the affected nerve often is swollen, thus it increases its volume and is more prone to entrapment [14].

Treatment of entrapment neuropathy includes steroid treatment and surgical decompression. Lacking high-quality evidence showing which treatment is better and in what cases, surgical nerve decompression has been widely used to treat entrapment neuropathy in leprosy leading to better functional outcomes due to improvement of motor function and sensory function thus preventing development of deformities [8]. Surgical treatment is indicated in entrapment neuropathy caused by compression of swollen edematous nerves passing through rigid tunnel-like structures [15]. External neurolysis and epineurotomy are considered treatments of choice, especially after the failure of corticosteroid therapy in these patients. Moreover, surgery is indicated when nerve abscesses are present, surgical decompression by drainage of the abscess being indicated in this type of neuropathy [3]. The aim of our study was to report a retrospective case-series of 21 patients treated with neural decompression procedures in a large teaching hospital in a low-incidence country.

Methods

We retrospectively analyzed all patients operated for leprosy-caused entrapment neuropathy in the last 10 years at the Unit of Neurosurgery of the Policlinico San Martino Hospital, Ligurian region, Italy. We reviewed demographic parameters, clinical data, radiological exams, pathology records, and follow-up documentation.

All patients underwent preoperative neurological examination, electroneurography, and ecography. Postoperative follow-up for patients treated with external neurolysis consisted in electroneurography (ENG) performed at 6 months and repeated at 36 months. Unfortunately, postoperative ecography was available for the majority of patients but not for all. It was repeated at 6 months and at 36 months after surgery.

Finally, a literature review was performed to find all reported cases of neurosurgical treatment of leprosy neuropathy in low-incidence countries. The latter was performed using an online database search (Medline/Pubmed) applying the following keywords: “abscess leprosy,” “entrapment leprosy,” “leprosy neuropathy treatment,” “decompression nerve leprosy,” and “surgery leprosy.” We included only papers in English language.

Results

We surgically treated 21 patients for leprosy neuropathy caused by neural entrapment, 12 males (57%) and 9 females (43%). Some patients were treated in more than one anatomical district, a total of 50 procedures were made, in four different anatomical districts (Table 1). Right side was affected in 57% of cases and left side in 43%. Of the 50 neurolysis performed, 24 were release procedures of ulnar nerve at cubital tunnel, 13 of median nerve at carpal tunnel, 12 of tibial nerve at tarsal tunnel, and 1 of ulnar nerve at Guyon’s canal. The latter patient was included in the cubital canal release group for data analysis. We here report pre- and postoperative clinical and electrophysiological status for each procedure. There were no postoperative complications.

Of the patients treated for ulnar nerve release at cubital tunnel and Guyon’s canal, motor deficit was present in 10 patients (41.7%), sensitive deficit in 11 (45.9%), paresthesia in 12 (50%), and pain in 22 (91.7%). At 6 months follow-up after decompression motor deficits improved in 90% of cases, sensitive deficits in 91%, paresthesia in 92% and pain in 82%. Three patients (13%) had normal ENG findings in spite of clinically symptomatic deficits in the territory of ulnar nerve, 21 (87%) had impaired ENG preoperatively. Of these, at 6 months, 16 patients (76%) had normal ENG findings, 3 cases (16%) still had impaired but improved ENG and all of these 3 patients were found normal at 36 months. Nineteen patients underwent ecography follow-up, in 2 patients (10%) the nerve was of physiologic dimensions in spite of altered ENG findings. In 17 patients (89%) at 6 months, the nerve appeared increased in volume, this was found to be stable at

Table 1 Summary and clinical outcomes of nerve entrapment release procedures

	Preoperative (*n*)	Postoperative (*n*)	
Ulnar nerve decompression (*n* = 25)			
Motor deficit			
Yes	11 (44%)	1	*P* = 0.0019
No	14	24	
Sensitive deficit			
Yes	12 (48%)	1	*P* = 0.0008
No	13	24	
Paresthesia			
Yes	12 (48%)	1	*P* = 0.0008
No	13	24	
Pain			
Yes	23 (92%)	4	*P* = 0.00001
No	2	21	
Median nerve decompression (*n* = 13)			
Motor deficit			
Yes	5 (38.5%)	0	*P* = 0.0502
No	20	25	
Sensitive deficit			
Yes	7 (53.8%)	2	*P* = 0.1383
No	18	23	
Paresthesia			
Yes	6 (46.1%)	3	*P* = 0.4635
No	19	22	
Pain			
Yes	9 (91.7%)	1	*P* = 0.0106
No	16	24	
Tibial nerve decompression (*n* = 12)			
Motor deficit			
Yes	4 (33%)	0	*P* = 0.1099
No	21	25	
Sensitive deficit			
Yes	5 (42%)	1	*P* = 0.1895
No	20	24	
Paresthesia			
Yes	6 (50%)	2	*P* = 0.2467
No	19	23	
Pain			
Yes	8 (67%)	1	*P* = 0.0232
No	17	24	

P values are for Fisher's exact test

6 months in 8 patients (47%) and decreased to physiologic size in the remaining 9 patients (53%).

In the group of patients treated for median nerve release at carpal tunnel, preoperatively motor deficits were found in five cases (38.5%), sensitive deficits in seven (53.8%), paresthesia in six (46.1%), and pain in nine (91.7%). At the 6 month follow-up, all the motor deficits were improved, sensitive deficits improved in 71.4% of patients, paresthesia in 50%, and pain in 88.9%. All of the patients in this group had impaired preoperative ENG. Postoperative follow-up ENG at 36 months was found to be normal in six cases (42%), of these, one patient still had impaired ENG at 6 months but it resolved subsequently. The other 8 patients (58%) still presented impaired ENG at 36 months but improved compared with preoperative status. Of 12 patients, postoperative ecography was available, in 10 cases (83%) was reported enlargement of the nerve at 6 months, at 36 months was resolved in only 2 cases, and persisted enlarged in the remaining 8. In two cases, nerve volume was normal in spite of impaired ENG.

In the tibial nerve release at tarsal tunnel procedures, group motor deficits were found preoperatively in four cases (33%), sensitive deficits in five (42%), paresthesia in six (50%), and pain in eight (67%). All of the motor deficits were improved at 6 months follow-up, sensitive deficits were improved in 80% of cases, paresthesia in 67%, and pain in 87.5%. Eleven of these 12 patients presented preoperative impairment of ENG findings, 1 had normal ENG even with symptomatic deficits of the tibial nerve. ENG follow-up was normal in three cases, improved but still impaired in 7 patients. It is of note that the remaining 2 patients had normal ENG at 6 months but impaired at 36 months. Eight of 12 patients had ecographic follow-up, all had nerve enlargement at 6 months, resolved at 36 months in five cases, and maintained stable in the others.

Discussion

Despite many published series of surgical treatment of leprous neuropathy reported the benefits of surgery [4, 8–10, 16, 17], there is a lack of a high-level evidence in favor of nerve decompression versus medical therapy. A recent Cochrane review [5] found only two randomized control trials (RCTs) that were of too low quality to permit strong conclusions on the efficacy of surgical nerve decompression in leprous neuropathy. We join the authors and others [5, 18] in the call for new high-quality RCTs that compare surgical and medical treatment in leprous neuropathy to provide high level of evidences.

Our patients were all treated concomitantly to corticosteroid therapy. We reported favorable outcomes with improvement in 95.2% of motor deficits, 84% of sensitive deficits, in 75% of cases of paresthesias and 85.4% of pain symptoms. Due to the limited number of patients of our series, our results were statistically significant almost only for ulnar nerve decompression procedures, which was the most represented group. Even with the limitation of the relatively small number of patients, we did not report complications related to the surgical procedure accounting for the safety of this treatment. Our results are in line with other studies in the literature [4, 8–10, 16, 17].

Surgical management of lepromatous neuropathy has been widely reported to have benefited by many authors from high-volume centers in endemic areas. Husain et al. [8] in 2013 reported a large series from New Delhi (India) of nerve entrapment syndromes in leprosy patients showing that surgical decompression after failure of 12 weeks steroid therapy along with basic care of hands and feet allowed recovering of symptoms which would not have been possible with medical therapy alone. Kumar [9] and Salafia [10] reported series of peripheral lepromatous nerve abscesses surgically treated concluding that when a nerve abscess is recognized it has to be surgically opened and drained being aware of not damaging intact nerve fibers. This procedure anyway must be performed concomitantly with medical therapy either steroid or antibiotic depending on which subtype of leprosy and on the history of the pathology. These studies showed the importance of a correct diagnosis of nerve abscess because the surgical treatment is different than in swollen nerve entrapment.

Despite management of leprosy neuropathy is nowaday well established in literature from endemic countries, but only few papers report treatment of leprosy neuropathy in low-incidence areas [15, 19]. In our literature review, we have found only two neurosurgical reports of treatment of lepromatous neuropathy in centers from non-endemic countries. Gennaro [15] described a case of a supraorbital nerve entrapment at supraorbital foramen causing left migraine-like headache in a patient with a previous diagnosis of leprosy. Surgical opening of the supraorbital foramen was performed to decompress the nerve. The reported headache completely disappeared after surgery. Payne [19] reported a case of pure neuritic leprosy treated with ulnar nerve release surgery. The patient referred to medical care for a long-standing slowly progressive right ulnar palsy associated with paresthesias and numbness and abnormal non-specific MRI findings. Given the absence of skin lesions, diagnosis was not clear so they decided to perform a decompressive nerve surgery and biopsy that led to leprosy diagnosis. The patient was then treated with guidelines-based antibiotic and steroid therapy. At 8 months postoperatively, both sensitive and strength deficits were satisfactorily improved.

In time of large human migration from endemic countries to low-incidence countries, awareness and precise knowledge of the pathology presentation and treatment strategies will be important to avoid delay in diagnosis leading to loss of chance of neurological improvement. In Genoa (Italy), there is one of the three "National Hansen Disease centers" and the only Italian third level diagnostic laboratory for Hansen disease. We report the largest series of leprosy patients surgically treated for entrapment neuropathy in a non-endemic region.

Making prompt diagnosis and timely treatment of lepromatous neuropathy is critical to avoid long-term disabilities [11]. Even though in low-incidence countries, physicians and health-care workers usually have little or no experience in diagnosis and treatment of Hansen disease, it is important to stress that leprosy has to be considered in all patients with neurological symptoms and associated skin lesions. This is particularly important if the patient is original from an endemic area or has a history of travels in endemic areas even if the exposure happened many years before [11]. In non-endemic regions, travel history or skin lesions may not be noticed unless actively sought.

Despite leprosy is a slowly progressive disease, leprosy reactions are common and may result in rapid progression of neurological deficits and permanent disability. "Preventive neurolysis" has been suggested in patients who are immunologically unsteady which is the case of borderline subtype forms according to the classical Ridley-Jopling classification [20]. These patients frequently suffer from reversal reactions (type 1). Preventive opening up of the tunnels of nerves at higher risk of involvement prevents future acute inflammatory reactions from causing possibly irreversible damage [21].

Conclusion

Leprosy entrapment neuropathy may lead to permanent neurological deficits or permanent deformities if not properly and timely treated. Even if we do not have high levels of evidence from high-quality prospective studies, surgical nerve decompression is widely reported to have benefit in conjunction with medical therapy.

As an effect of large human migrations from leprosy endemic areas, leprosy is nowaday increasingly encountered in countries that used to account for a very limited number of cases.

We believe that a precise knowledge of the pathology and its management is crucial also for physicians who work in low-incidence countries to maximize healing chances with timely diagnosis and treatment.

Limitations

Our work has the limitation of being a retrospective study. It does not compare surgical and medical treatment, the aim of our study was to report presentation, neurosurgical treatment, and outcome of leprosy neuropathy in a low-incidence country. Although to the authors' knowledge, this is the largest series of neurosurgical treatments of leprosy neuropathy from a non-endemic country, it has the limitation of a limited number of patients.

Compliance with ethical standards

All procedures were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments.

Conflict of interest The authors declare that they have no conflict of interest.

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