Unmasking the mimic: Leprosy neuropathy misdiagnosed as chronic inflammatory demyelinating polyneuropathy: A case report from Saudi Arabia

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ABSTRACT

الجذام هو حالة تؤثر بشكل رئيسي على الجلد والأعصاب المحيطية، وعادة ما يتم تشخيصها من خلال فحص الآفات الجلدية ووجود العصيات الحمضية في عينة من خزعة الجلد. يتم تأكيد اعتلال الأعصاب المزيل للميالين الالتهابي المزمن (CIDP) غالبًا عن طريق دراسة توصيل الأعصاب وخزعة العصب السوري، وهي الطرق الأكثر موثوقية ودقة. تساعد نتائج هذه الاختبارات في التمييز بين الجذام واعتلالات الأعصاب المزيلة للميالين مثل CIDP. نقدم هنا حالة لاعتلال الأعصاب الجذامي الذي تم تشخيصه خطأً على أنه CIDP بعد إجراء دراسة توصيل الأعصاب وخزعة العصب. تعتبر هذه الحالة غير عادية وجديرة بالملاحظة نظرًا لندرة الحالات المماثلة المسجلة عالميًا. يسلط هذا التقرير الضوء على أهمية النظر في الجذام عند تشخيص اعتلالات الأعصاب، حتى في المناطق غير الموبوءة، وضرورة إجراء تقييم شامل للمرضى الذين يعانون من أعراض عصبية غير نمطية.

Leprosy neuropathy can mimic chronic inflammatory demyelinating polyneuropathy (CIDP), especially in non-endemic areas. We report a 72-year-old Saudi woman initially misdiagnosed with CIDP based on nerve conduction studies. The patient presented with widespread pruritus, erythematous cutaneous lesions, and progressive sensorimotor symptoms. Despite treatment with intravenous immunoglobulin, her condition worsened. Subsequent sural nerve and skin biopsies revealed acid-fast bacilli, confirming leprosy. This case highlights the importance of considering leprosy in the differential diagnosis of neuropathies, even in regions where it is rare. Nerve ultrasound, a valuable diagnostic tool in differentiating leprosy from CIDP, should be incorporated into the diagnostic workup of atypical neuropathies.

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There are approximately 208,619 new leprosy cases each year.[1] Leprosy is diagnosed by the presence of at least one of 3 primary indicators: (i) Red skin patches with reduced sensation and numbness. Mycobacterium leprae is an internal pathogen that gives rise to leprosy, and the clinical characteristics impact the severity of skin lesions and their dispersal tendencies. The World Health Organization (WHO) has formally labelled leprosy a neglected tropical ailment; (ii) an enlarged peripheral nerve with accompanying loss of sensation and/or weakness of the muscles supplied by that nerve; or (iii) the detection of acid-fast bacilli in a slit-skin smear.[2] In Saudi Arabia, leprosy is considered a rare disease. According to recent data, the incidence of leprosy in the country has significantly decreased, with only a few new cases reported annually. This rarity in a non-endemic area poses a diagnostic challenge for clinicians, potentially leading to misdiagnosis and delayed treatment. The preferred investigative method to verify neurological dysfunction in leprosy patients is nerve conduction studies (NCSs), as the initial presentation commonly involves nerve function impairment (NFI), which occurs at a considerable rate. NCS findings indicative of leprosy align with either a mononeuropathy or polyneuropathy pattern. Chronic inflammatory demyelination polyneuropathy presents as distal symmetrical sensorimotor polyneuropathy, causing both proximal and distal limb weakness, sensory deficits, and loss of reflexes.

In regions such as Saudi Arabia, where leprosy is not prevalent, subacute peripheral nerve lesions are unlikely to be attributed to leprosy. We report a case of leprosy neuropathy that was initially misdiagnosed as chronic inflammatory demyelination polyneuropathy (CIDP).

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Case Report. *Patient information and clinical findings.* This is a 72-year-old Saudi woman whose clinical history began approximately two years ago with a complaint of widespread pruritus, along with erythaematous cutaneous lesions and articulatory inflammation that predominantly affected her lower extremities and persisted for several months (**Figure 1**). Afterwards, she complained of discomfort marked by paresthesia, tingling, and numbness in the same areas of her body. Notably, she also had red patches on her back and lower limbs. Furthermore, weakness in the distal extremities became apparent.

After a comprehensive evaluation, the patient displayed reduced sensory reactions in the L3, L4, and L5 dermatomes, as well as a lack of vibration and proprioception (joint position sensory testing) in both lower limbs. The patient's reflexes were absent, and there was a bilateral strength rating of -4/5 in the lower limbs and 4/5 in the upper limbs.

Diagnostic assessment. All tests related to rheumatology, metabolism, and infection were conducted on the patient, yielding no notable abnormalities except for immunoglobulin G levels exceeding 49.2 g/L (much higher than the usual range of 7.51-15.6 g/L). Concurrently, CSF analysis did not reveal any notable abnormalities. Moreover, the findings derived from electrodiagnostic nerve conduction studies (NCSs), as outlined in **Tables 1**, demonstrated patterns suggestive of a combination of demyelinating and axonal sensory-motor polyneuropathy without prolonged F-wave latencies. A diagnosis of chronic inflammatory demyelinating polyneuropathy was made based on nerve conduction study findings, leading to the initiation of treatment with intravenous immunoglobulin (IVIG).

Therapeutic intervention, follow-up and outcomes. The patient received five consecutive IVIG doses, followed by a sixth treatment one month later. Surprisingly, this sixth dose was associated with a significant decrease in the patient's condition.

After a few months following these evaluations, microscopic examination (**Figure 2a-c**) of the sural nerve biopsy revealed lymph histiocytic infiltration involving the epineurium, perineurium, and endoneurium with perivascular aggregation; however, there was no evidence of fibrinoid necrosis or other forms of vascular wall damage. A non-necrotizing granuloma was observed. Ziehl–Neelsen and Fite's acid fast staining highlighted the presence of numerous acid-fast bacilli throughout the nerve fascicles, including the granuloma. Congo red staining was negative for amyloid deposition. Immunohistochemical staining revealed that the inflammatory infiltrates were mostly CD3-positive T lymphocytes and CD68-positive histiocytes.

A dermatologist examined the patient and recommended a skin biopsy of the erythaematous cutaneous lesions. Microscopic examination of the skin biopsy specimen revealed mixed dermal inflammation with non-necrotizing granuloma formation. Ziehl–Neelsen staining results showed numerous acid-fast bacilli within the dermal histiocytes. Tests for fungal infection using Grocott methenamine silver (GMS) and periodic acid Schiff (PAS) stains were negative. Currently, the antibiotics prescribed for the patient's illness seem to be effective, as there are obvious signs that the patient's health is improving.

Discussion. As a nonendemic location, leprosy (sometimes known as Hansen's disease) is noteworthy in Saudi Arabia even though it has been officially proclaimed to be eradicated. The incidence of leprosy has decreased by more than 90% worldwide within the last 20 years. However, a small number of new leprosy cases are still reported each year. Accordingly, the difficulty of accurately diagnosing leprosy has increased. This circumstance has reduced the number

Table 1 - Clinical and histopathological features of leprosy neuropathy in our patient.

Nerve conduction studies	Prior treatment history	Histopathology	Endoneurial fibrosis	Acid-fast bacilli	Treatment/follow-up
Initial NCS findings indicate the presence of a combination of demyelinating and axonal sensory-motor polyneuropathy. Follow up NCS Showing signs of a mixed sensorimotor with secondary axonal loss polyneuropathy, compared to her last study there is no substantial change, and the picture is within expected time frame.	Developed symptoms of neuropathy before and during the treatment	Lepromatous leprosy	Not present	Positive	Treatment still on-going

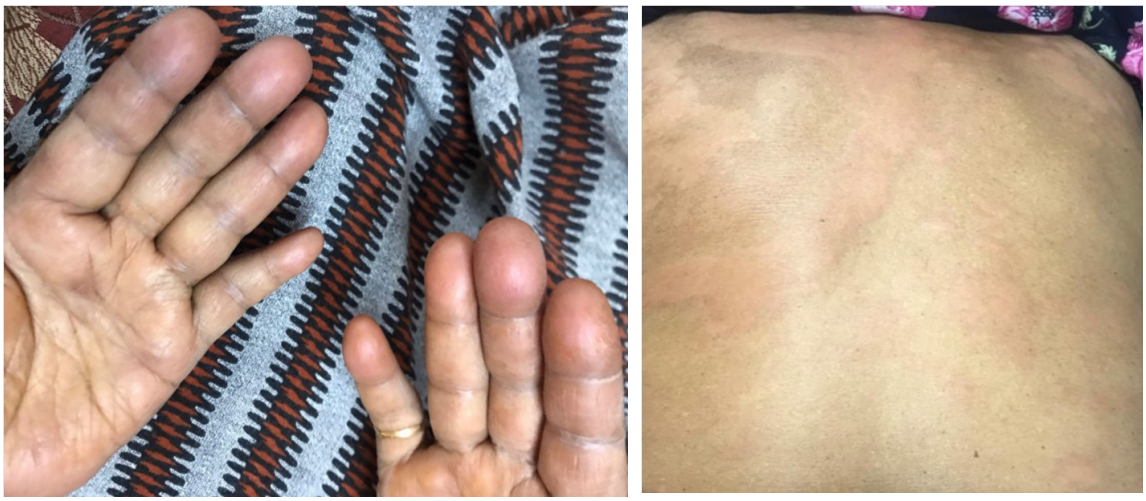
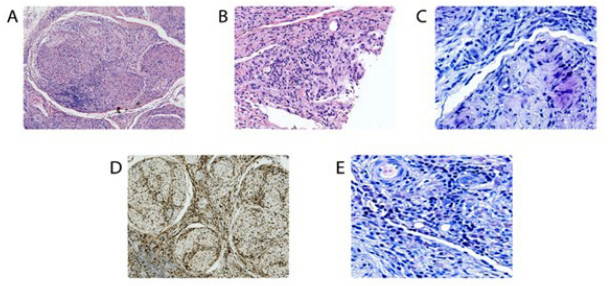


Figure 1 - Multiple erythematous cutaneous lesions and joint swelling in her limbs.



A H&E-stained section (10X) showing cross section of the sural nerve with lympho-histiocytic infiltrate involving epineurium, perineurium and endoneurium.

B H&E-stained section (20X) showing longitudinal section of the sural nerve with aggregation of histiocytes, forming ill-defined granuloma.

C Ziehl-Neelsen special stain highlights acid-fast bacilli in the nerve biopsy.

D Immunohistochemical staining for CD68 highlights the histiocytic infiltrate of the nerve.

E -Fite special stain highlights numerous acid-fast bacilli in the nerve biopsy.

Figure 2 - Histopathologic findings of nerve biopsy.

of practitioners who are knowledgeable about leprosy.

Further complicating the accurate diagnosis of leprosy by medical practitioners is its broad clinical spectrum, which is impacted by unique immunization statuses, different latency durations, and various environmental factors. The clinical symptoms of leprosy exhibit considerable variation and are strongly influenced by the host immune response to M. leprosy. The manifestations are categorized as tuberculoid, borderline, or lepromatous. Leprosy reactions occur due to the T-cell response to mycobacterial antigens, leading to spontaneous changes in clinical manifestations. The uncommon characteristics of this disease typically result in initial misdiagnosis and delayed care, frequently leading to advanced-stage diagnoses and considerable collateral damage. The complex nature of leprosy symptoms can occasionally coincide with that of rheumatic disorders, leading to confusion and incorrect diagnosis.[3,4] A study by Vengadakrishnan et al[5] revealed that 61.4% of individuals diagnosed with leprosy exhibited symptoms such as rheumatic disorders, including conditions affecting the nerves and muscles, such as arthritis, soft tissue infection, and enthesitis. Patients with autoimmune illnesses may exhibit similar dermatological symptoms and serological test results.[6] Nevertheless, our patient stands out because she showed no signs of rheumatism and had negative serological test results.

Nerve ultrasound has emerged as a valuable tool in differentiating leprosy from CIDP. Our study is a recent investigation demonstrating that ultrasound can provide crucial information in distinguishing these conditions. In CIDP, ultrasound typically reveals diffuse nerve enlargement with increased cross-sectional area, while leprosy often shows more focal enlargements and increased echogenicity.[1] Additionally, ultrasound can detect nerve abscesses, which are characteristic of leprosy but not seen in CIDP.[2] Had nerve ultrasound been performed in our patient, it might have raised suspicion for leprosy earlier in the diagnostic process.
Chronic inflammatory demyelinating polyneuropathy is a rare condition in which the immune system attacks

Table 2 - Timeline of patient's case.

Dates	Relevant past medical history and interventions		
2 years prior to presentation	Onset of widespread pruritus and erythematous cutaneous lesions, primarily affecting lower extremities		
Dates	**Summaries from initial and follow-up visits**	**Diagnostic testing**	**Interventions**
Month 0	Initial presentation with widespread pruritus, erythematous cutaneous lesions, and articulatory inflammation	- Rheumatology, metabolism, and infection tests: No notable abnormalities - Immunoglobulin G levels: 49.2 g/L (elevated) - CSF analysis: No notable abnormalities	
Month 6	Development of paresthesia, tingling, and numbness		
Month 8	Initial medical evaluation: - Reduced sensory reactions in L3, L4, L5 dermatomes - Lack of vibration and proprioception in lower limbs - Absent reflexes - Bilateral strength rating: -4/5 in lower limbs, 4/5 in upper limbs	Nerve conduction studies: Suggestive of combined demyelinating and axonal sensory-motor polyneuropathy	
Month 9	Diagnosis of CIDP based on nerve conduction studies		
Month 10-11			Five consecutive IVIG treatments
Month 12	Significant decline in condition		Sixth IVIG treatment
Month 14		Sural nerve biopsy: Revealed lymph histiocytic infiltration and acid-fast bacilli Skin biopsy: Showed mixed dermal inflammation with non-necrotizing granuloma and acid-fast bacilli	
Month 15	Diagnosis of leprosy confirmed		
Current	Signs of improvement		Ongoing antibiotic treatment

the peripheral nerves, damaging the protective covering of the nerves. This condition is characterized by periods of nerve demyelination and the gradual development of symmetrical sensory-motor impairments and areflexia over a 2-month period. The results of a nerve conduction study and cerebrospinal fluid analysis, which showed albumin-cytological dissociation contributed to the diagnosis of CIDP in our patient. The exact cause of CIDP is still unknown, although CIDP is considered an autoimmune disease caused by T and B cells that attack the body's tissues. The CIDP has been linked to autoimmune disorders such as diabetes mellitus and Sjogren's syndrome, as well as neoplastic conditions, including melanoma and lymphoma, and infections caused by human immunodeficiency virus and hepatitis C virus.[5] Andrade et al[7] described a patient who developed chronic CIDP twelve years after completing therapy for mid-borderline leprosy. Kim et al[8] reported a case of leprosy neuropathy in which the initial diagnosis of chronic inflammatory demyelinating polyneuropathy was incorrect based on the results of a nerve conduction study and a histopathological examination of a sural nerve biopsy specimen. The biopsy revealed the presence of dispersed mononuclear inflammatory cells and mild fibrosis.[9] A conclusive diagnosis of leprosy was established when acid-fast bacilli were identified using Ziehl–Neelsen staining of histopathology samples.

The purpose of this case report was to highlight how leprotic neuropathy might be mistakenly diagnosed for various peripheral neuropathies, especially in nonendemic areas.

Patient perspective. The patient expressed relief at finally receiving a correct diagnosis after months of worsening symptoms despite treatment. She emphasized the importance of thorough diagnostic procedures in cases of atypical neuropathy.

In conclusion, in areas where leprosy is not common, leprotic neuropathy can occasionally be mistaken for a distinct kind of peripheral neuropathy. This case highlights the importance of clinical markers for leprosy diagnosis beyond the use of biopsy specimens for diagnosis, particularly in the presence of demyelination features and scattered inflammatory cells.
tumor.

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