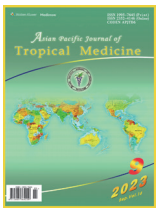

Case Report

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/1995-7645.386077

Impact Factor: 3.1

Type 2 reaction associated sensorineural hearing loss in a drug resistant lepromatous leprosy patient: A case report

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ABSTRACT

Rationale: Leprosy, a chronic granulomatous disease often present clinically as erythema nodosum leprosum, a type 2 reaction. The involvement of cochlear part of audiovestibular system is a rarity.

Patient concerns: A 26-year-old male patient with lepromatous leprosy developed bilateral sensorineural hearing loss (SNHL) during type 2 reactional episode.

Diagnosis: Recurrent erythema nodosum leprosum in rifampicin-resistant lepromatous leprosy.

Interventions: Corticosteroids and second-line multidrug therapy.

Outcomes: The patient improved significantly and was further referred for management of psychosocial impact due to sensorineural hearing loss.

Lessons: The hearing impairment is a rare complication of type 2 reaction. Any patient with suspected cranial nerve involvement should essentially be screened by tuning fork tests for early detection of hearing impairment and offer timely intervention as required. All high bacteriological index cases should be investigated for antimicrobial resistance in high endemic areas.

KEYWORDS: Leprosy reactions; Erythema nodosum leprosum; Sensorineural hearing loss; Drug resistant leprosy

1. Introduction

The reactions in leprosy are classified into type 1 reaction (reversal reaction), type 2 reaction or erythema nodosum leprosum (ENL)[1]. The highly diverse skin lesions and immunological reactions in leprosy often mimics other more common conditions and might be misdiagnosed under low clinical-suspicion settings with delayed treatment, which results in increased impairments and nerve involvement[2,3].

The rare involvement of cochlear part of audiovestibular system was found associated with recurrent ENL in this case report of rifampicin resistance in a leprosy patient being treated with standard multidrug therapy (MDT). The second line drugs ofloxacin and minocycline were started along with higher doses of clofazimine in the intensive phase[4]. The reactional episode was managed by thalidomide and prednisolone successfully. The drug resistance to standard MDT regimen is an important reason behind nonresponsive patients with high bacteriological index (BI) and WHO recommends testing of drug resistance determining regions containing folP1, rpoB, and gyrA for antimicrobial resistance (AMR) surveillance[5]. AMR in neglected tropical diseases can be the challenge for public health management struggle as being reported in the present case. This report offers a unique opportunity to understand the significance of timely diagnosis and AMR surveillance in cases with high bacteriological index.

2. Case report

A 26-year-old male patient, known case of lepromatous leprosy presented in the outpatient department of our hospital with

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How to cite this article: Pawar HS, Singh I, Sagar HK. Type 2 reaction associated sensorineural hearing loss in a drug resistant lepromatous leprosy patient: A case report. Asian Pac J Trop Med 2023; 16(9): 425-427.

Article history: Received 11 April 2023 Revision 13 September 2023
Accepted 21 September 2023 Available online 29 September 2023

complaints of painful, erythematous eruptions from the past 10 days with moderate grade fever and edema over bilateral hands from the past 15 days (Supplementary Figure 1A). The patient had severe hearing impairment with distress due to poor psychosocial adjustment and was accompanied by a family member for detailed clinical history.

The patient had a history of treatment from multiple local practitioners for similar complaints for around 18 months. After 6 months of treatment without any improvement, he was referred to a tertiary care hospital and was investigated for inflammatory polyarthritis. The clinico-pathological evaluation under indoor settings revealed lepromatous leprosy with type 2 reaction. His average BI from four sites on slit skin smear was 1+ and on biopsy was 6+. After multi drug therapy with corticosteroids, the patient was improved and discharged. The two months following discharge remained uneventful. The patient reported again to the hospital with severe type 2 reaction and bilateral hearing loss. There was no history of chills, rigor, hemoptysis, burning micturition, loss of weight. No history of hypertension, nasal mass, head and neck trauma, ear discharge, ear pain or fullness and vertigo. There is no documented history of any ototoxic drug, neurological or autoimmune disorder. There was no significant past or personal history. The patient was admitted for management of type 2 reaction. Unmasked air and bone conduction testing in pure tone audiometry (PTA) revealed severe to profound sensory neural hearing loss (Figure 1) and intratympanic dexamethasone was also started. The type 2 reactional episode was managed with oral prednisolone and the patient was discharged with MDT continued. Another PTA after 2 months didn't show any improvement and aided PTA was conducted. The patient completed the one year of MDT with recurrent ENL episodes managed by steroids, anti-inflammatory drugs and thalidomide. The BI in slit skin smear at the tertiary care center was 2+ at the end of one year and a morphological index of 10.52%.

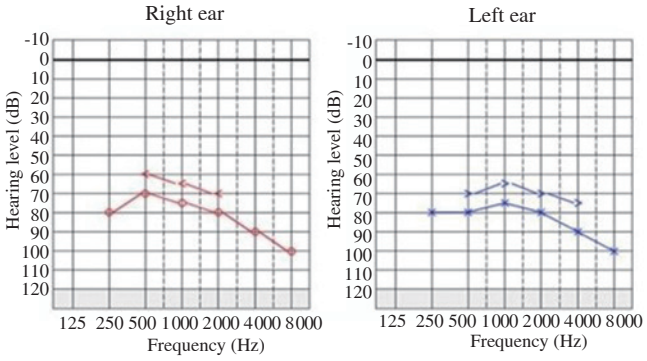

Figure 1. Severe sensorineural hearing loss in a 26-year-old male patient with lepromatous leprosy developed bilateral sensorineural hearing loss during type 2 reactional episode.

After 3 months, the patient was reported with erythema nodosum leprosum and was taking thalidomide 300 mg per day in divided doses and prednisolone 10 mg per day. The nodular eruptions were erythematous which were warm and painful, associated with moderate fever, joint pain, swollen inguinal lymph nodes and focal ulcerations. Pitting bilateral hand edema was not associated with cardiac, renal or hepatic manifestations. On physical examination, his bilateral ulnar and radial cutaneous nerves are thickened with grade 2 tenderness. The card test and book tests were positive. On otoscopy, tympanic membrane was intact. There was no canal edema or erythema. The hearing examination by tuning fork's tests suggested sensorineural hearing loss. A slit skin smear from the same four sites as earlier showed average BI of 4+. Taking into account the non-decline of BI and recurrent ENL reaction, drug resistance was tested by PCR amplification targeting *rpoB*, *folP* and *gyrA* genes according to guidelines of WHO 2017 followed by sequencing. Sequence data were analysed using MEGA software and the patient was found rifampicin resistant. We detected mutation in *rpoB* gene at codon position 439 (Phe-Leu) which is responsible for rifampicin resistance[6,7] (Supplementary Figure 1B). The treatment regimen was changed for rifampicin resistance along with management of reactional episode and patient improved significantly. The patient was referred to psychiatry department for assessment and management of psychosocial impact.

3. Discussion

The sensorineural hearing loss due to ENL in a lepromatous leprosy patient is a rarity unlike other complications like uveitis, neuritis, polyarthritis, lymphadenopathy, orchitis and renal complications[8]. The present case also shows a difference in bacteriological index in slit skin smear and biopsy on diagnosis signifies the importance of proper site for sample collection and technical expertise of manpower involved which is becoming a challenge with declaration of leprosy elimination in India. It is also to be emphasized that delay in diagnosis increases the bacillary load and often the propensity towards type 2 reactional episodes in anergic patients. An earlier study by Gopinath *et al.* found facial nerve to be most commonly involved cranial nerve in leprosy and the involvement was significantly associated with lepra reactions[9]. Another study on evaluation of hearing impairment in leprosy, a more prominent effect on cochlear system was noticed than vestibular system with over 13% (cochlear systems) showing moderate or severe sensory neural hearing loss, however, the study didn't mention the any association with reactional states[10]. Another study of 100 leprosy patients has also reported the association of sensorineural hearing loss with lepra reaction in lepromatous leprosy. No ototoxic effect of MDT has been reported on long term follow-up of the patients[11]. The hearing impairment is a rare

complication of type 2 reaction with high psychosocial impact. The hearing loss results in low self-esteem, poor quality of life and higher likelihood of depression in already stigmatized leprosy patient[12]. Any leprosy associated visual impairment issues are reported timely to the clinicians as it affects the activities of daily living like eating, dressing *etc*. and such ocular complications are frequently addressed[13]. However, any patient with suspected cranial nerve involvement should essentially be screened by tuning fork tests for early detection of hearing impairment and offer timely intervention as required.

In this study, we detected mutation in *rpoB* gene at codon position F439L by PCR followed by Sanger sequencing, in line with the WHO recommendation of AMR surveillance in patients who are non-responding to the anti-leprotic treatment[14]. All high BI cases should be investigated for AMR in high endemic areas. Early identification of AMR with prompt treatment modifications will improve bacillary clearance ensuing less frequent complications.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

The study procedures followed were in accordance with the ethical standards of the Institute Human Ethics Committee and with the Helsinki Declaration of 1975, as revised in 2000. The written informed consent was obtained and the confidentiality of participant was maintained.

Funding

The authors received no extramural funding for the study.

Authors' contributions

HSP performed conceptualization, data acquisition, literature search and manuscript preparation. IS performed data acquisition and data analysis. HKS contributed to the manuscript preparation, manuscript editing and review and is designated as 'guarantor'.

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