

Case Study

ERYTHEMA NODOSUM LEPROSUM: CONDITION DEVELOPED BY NON-ADHERENCE

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Received: 20 Jun 2024, Revised and Accepted: 11 Jul 2024

ABSTRACT

Erythema Nodosum Leprosum (ENL) is a rare immune-mediated complication of leprosy, characterized by painful nodules and fever, and can lead to anemia and leucocytosis. A 19 y old male with a history of non-adherence to 12 adult multi-bacillary multi-drug therapy packs for leprosy presented with a 15 d complaint of fever and aggravated painful, raised, red skin lesions over two y. Laboratory findings showed neutrophilia, thrombocytosis, microcytic anemia, and traces of blood and ketones in the urine. Acid-fast bacilli with a grade of 1+ were observed in Ziel-Neelson-stained smears, confirming the diagnosis. The patient received systemic Dexamethasone, the standard treatment for Erythema Nodosum Leprosum, and resumed leprosy treatment. Symptomatic care was given, and the patient was discharged. This case highlights the importance of early detection, efficient monitoring, and adherence to therapy to reduce ENL-related morbidity and mortality. The study emphasizes that a regular watch should be kept on leprosy patients to ensure early intervention and prevention of complications.

Keywords: Hansen's disease, Immune-mediated, Type II reaction, Ziel-Neelson stain, Nodules

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INTRODUCTION

Leprosy, or Hansen's Disease (HD), is a chronic granulomatous skin condition caused by the Mycobacterium Lepra Complex, which affects both the skin and peripheral nervous system [1]. Erythema Nodosum Leprosum (ENL) is a rare but severe immune-mediated reaction of HD, impacting half of lepromatous leprosy and 10% of borderline leprosy. While ENL is a well-documented condition, its incidence is relatively rare, ranging from 0.2% to an average of 1.2% in India [2]. It results from tissue damage due to chemokine production. Clinical manifestations include tender erythematous nodules, fever, and malaise. Lesions frequently occur on both extremities and may fade as brawny induration [3]. Despite its rarity, ENL poses substantial challenges in the management of leprosy, particularly due to its potential complications such as uveitis, neuritis, and anemia [4]. The Erythema Nodosum Leprosum International Study (ENLIST) Severity Scale uses a 10-item scale to assess the severity of ENL, with a score of ≤ 8 categorized as mild ENL [5]. Histopathological examination through the Ziehl-Neelsen (ZN) stain reveals neutrophils within granulomas [6]. WHO Guidelines recommend corticosteroids as the main treatment (40–60 mg/day for 1-2 w). High-dose clofazimine (300 mg/night) acts as a steroid-sparing agent [7]. This case report presents a patient with ENL, caused by non-adherence to leprosy treatment. While non-adherence to leprosy treatment is known to exacerbate disease progression, its direct link to ENL development is less commonly documented. This study contributes novel insights by correlating non-adherence with the onset of ENL, supported by

comprehensive clinical and laboratory findings, thereby contributing to better patient outcomes and public health strategies in managing HD.

CASE REPORT

A 19 y old male patient presented with a fever for 15 d and an aggravated, red-raised, painful skin lesion all over the body for the last 2 y. The patient has had a history of leprosy for 2 y with an episode of epistaxis. The patient had completed 12 adult Multi-Bacillary Multi-Drug Therapy (MB-MDT) packs but was non-adherent to the therapy.

On examination, pedal edema and joint pain were seen with multiple, tender erythematous and hyperpigmented plaques over the face, neck, chest, abdomen, back, buttocks, and both extremities (fig. 1).



Fig. 1: Hyperpigmented plaques over right arm

Cutaneous examination showed well-defined erosions over the left arm and lower abdomen, as well as a tender radio-cutaneous nodule on the ulnar region (fig. 2). The ENLIST severity scale was 16 (table 1) [8].

Table 1: Enlist score of patient on admission and on discharge

S. No.	Scale Item	Patient result on admission	Score on admission	Score on discharge
1	Visual Analogue Scale – Pain	40 mm	2	1
2	Fever (°C)	History of fever for 15 d	1	0
3	Number of ENL skin lesions	≥ 21	3	1
4	Inflammation of ENL skin lesions	Red-raised, painful	2	1
5	Extent of ENL skin lesions	Face, neck, chest, abdomen, back, buttocks and both extremities	3	1
6	Peripheral edema	Pedal edema	1	1
7	Bone pain	Bone pain on examination	1	0
8	Inflammation of joints and/or digits due to ENL	Joint pain and inflammation	1	0
9	Lymphadenopathy due to ENL	None	0	0
10	Nerve tenderness due to ENL	Present	2	1
Total Score			16	06

ENLIST: A Severity scale of Erythema Nodosum Leprosum, ENL: Erythema Nodosum Leprosum, Laboratory investigations are elaborated on in table 2. ZN stain confirmed Acid-Fast Bacilli (AFB) have a grade of 1+(1–10 AFB/100 OIF).

Table 2: Abnormal laboratory parameters of the patient

Parameter	Patient's value	Normal range
On the day of admission		
Hemoglobin	10.7 (Low)	13-17g/dl
Neutrophils	94 (High)	30-70%
White Blood Corpuscle Count	33990 (High)	4000 - 10000/mm ³
Hematocrit	31.9 (Low)	37-47%
mean Cell Volume	66.4 (Low)	76-90fl
G6PD Level	18.40 (High)	4.6-13.5U/g Hb
On 6 th day of hospitalization		
Hemoglobin	11 (Low)	13-17g/dl
Platelet	603000 (High)	150000-450000/ μ L
Hematocrit	34.1 (Low)	37-47%
mean Cell Volume	67.4 (Low)	76-90fl
White Blood Corpuscle Count	15890 (High)	4000-10000/cmm

G6PD: Glucose-6-phosphate dehydrogenase

During hospitalization, the patient received dexamethasone (1.5 cc IV once), multivitamin (500 ml IV once), ceftriaxone (1 g IV twice), pheniramine (22.7 mg IV twice), paracetamol (150 mg IV once), fusidic acid cream for crust (twice), aloe vera (10.0 w/w), and vitamin E (0.5% w/w) lotion (twice) every day. Ferrous fumarate, folic acid, zinc sulfate (PO once), and pheniramine IV Stat were given on the second day. From day 3 onwards, the first adult MB-MDT pack was started. All medications continued until day ten. On discharge, the patient was prescribed prednisolone (30 mg PO once), cefadroxil (500 mg PO twice), levocetirizine (10 mg PO once), multivitamin (PO once), ferrous fumarate-folic acid-zinc sulfate (PO once) every day for 15 d, and rabeprazole-domperidone (20 mg+30 mg PO twice daily) for 30 d. The first adult MB-MDT pack was advised to be continued. Fusidic acid cream over the crust area (twice daily) and aloe vera-tocopherol lotion (2-3 times daily) were prescribed. The hyperpigmented plaques started to reduce, and the patient was discharged. On discharge, the ENLIST score was 6.

DISCUSSION

Leprosy reactions are inflammatory reactions caused by *Mycobacterium leprae* bacilli, further exacerbating the disease. It is divided primarily into two types of reactions: type-1 and type-2 reactions [9, 10].

Type-1 reactions occur commonly in patients with immunocompromised status or those with borderline leprosy. It is a main cause of leprosy-induced disability and deformity as it induces nerve damage [11].

ENL, a type-2 lepra reaction, is characterized by painful skin nodules. The condition is rare but can significantly affect patients with leprosy. The prevalence of ENL in India is 49.4% [12]. ENL can be triggered by drug defaulting and in patients with immunocompromised states. Matthew *et al.* mentioned that antecedent influenza vaccination and upper respiratory tract infection can also be factors in causing ENL [13]. Liran *et al.* opened a new perspective by discussing the occurrence of ENL post-COVID-19 vaccination [14]. This study emphasizes non-adherence as a risk factor for developing ENL.

The factors at risk for the development of ENL include lepromatous leprosy and an elevated bacillary index [15]. It occurs due to the tissue damage caused by the immune response of the T-cells as a result of lepra invasion (fig. 3). The onset of ENL is typically in the first year of using MDT. Patients with leprosy may develop ENL if they show non-adherence to anti-leprotic therapy due to increased CD64 levels following MDT initiation.

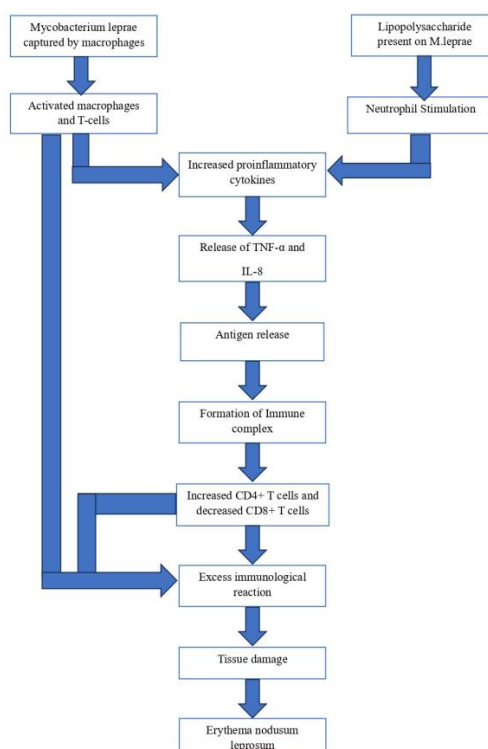


Fig. 3: Pathophysiology of Erythema nodosum leprosum. This fig. was created by the author of this article. Credit goes to Evangeline for making this fig. for the article

Treatment involves analgesics for acute ENL and corticosteroids and immunosuppressants for chronic ENL (fig. 4). A study conducted by Mishra SR *et al.* to compare the efficacy of thalidomide and clofazimine as adjuvants to steroid therapy showed these drugs to be effective in treating recurrent ENL [16].

The study showed patients with classic complaints of ENL, including multiple painful skin lesions, fever, and a history of epistaxis. The patient had leprosy for 2 y but was not taking 12 MB-MDT packs regularly. A cutaneous examination revealed various parts of the body affected by tender erythematous and hyperpigmented plaques, which are characteristic of ENL. Along with neutrophilia and microcytic anemia, thrombocytosis also becomes an indicator of bacterial infection and resulting inflammation [17]. The ZN stain for AFB showed the presence of *Mycobacterium leprae*, confirming ENL. The management strategies included the patient receiving intravenous dexamethasone, the standard treatment for ENL.

Symptomatic treatment involved intravenous fluids, antihistamines, antipyretics, and antibiotics. A topical agent such as fusidic acid cream was prescribed to be applied over crusting. Upon discharge, the patient was prescribed a prednisolone tablet for 15 d. Symptomatic treatment was given, and the patient's condition improved. The patient was advised to continue the first adult MB-MDT pack and be adherent to treat the underlying infection. On subsequent follow-up, the patient had gotten into remission. Comprehensive monitoring of the patient's response is necessary to prevent relapse. Moreover, the pedal edema was not treated on admission but was mildly reduced on follow-up.

The strength of the study is that it emphasizes the importance of patient adherence in order to prevent ENL. Further research is required to understand the impact of adherence on the development of ENL.

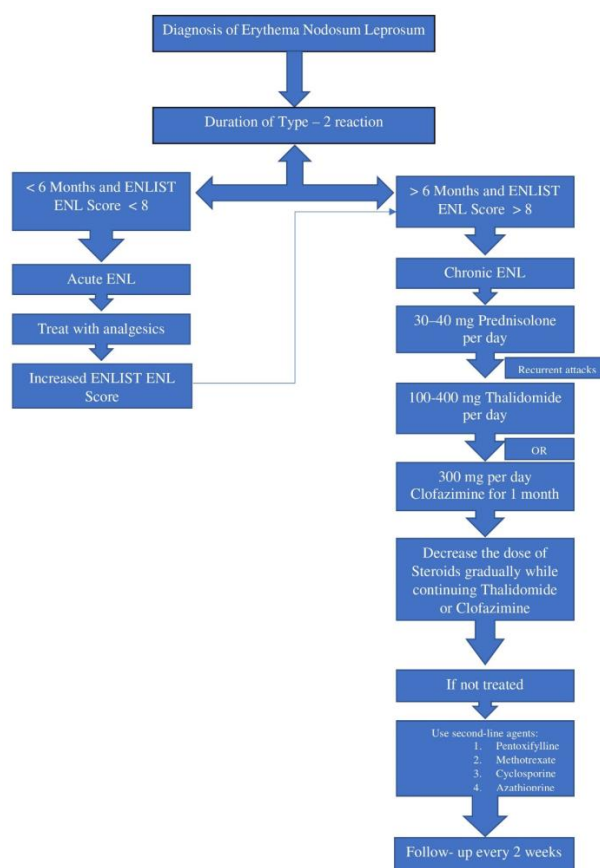


Fig. 4: Treatment of Erythema nodosum leprosum. This fig. was created by the author of this article. Credit goes to evangeline for making this fig. for the article

CONCLUSION

ENL demands immediate attention and thorough care as a severe leprosy complication. This case shows timely recognition, appropriate treatment, and efficient monitoring and follow-up to reduce ENL-related morbidity and mortality. Awareness about the importance of compliance with anti-leprotic measures must be emphasized to prevent the occurrence of ENL.

ABBREVIATIONS

HD-Hansen's disease, ENL-Erythema Nodosum Leprosum, ENLIST-Erythema Nodosum Leprosum International Study, ZN-Ziehl-Neelsen, MB-MDT-Multi-bacillary multi-drug therapy

AUTHORS CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Evangeline Gladwin and Mudra Patel. The first draft of the manuscript

was written by Evangeline Gladwin and all authors commented on previous versions of the manuscript. Dr. Mansi Mistry critically revised the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

Declared none

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