Cytological Diagnosis of Erythema Nodosum Leprosum in Clinically Unsuspected Cases: A Report of Two Cases

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Abstract

Leprosy is a chronic infectious disease caused by Mycobacterium leprae. The manifestations of this disease vary across the spectrum of tuberculoid (TT) to lepromatous (LL) leprosy. The course of this indolent disease is interrupted by acute exacerbations in the form of lepra reactions. Erythema nodosum leprosum (ENL), a type 2 lepra reaction, occurs in lepromatous or borderline lepromatous cases, usually in response to multidrug therapy. Early detection and timely management of these patients is important to reduce the associated morbidity. We report two clinically unusual cases of ENL on fine-needle aspiration cytology. In one case, antileprosy treatment was completed 10 years back, whereas in the other case, ENL was the presenting feature of the disease. Cytological examination of swelling in both the cases showed neutrophils, lymphoid cells, clusters of foamy macrophages, histiocytes, and giant cells. Fite stain was positive, which confirmed the cytological diagnosis of ENL.

Keywords: Erythema nodosum leprosum, fite, foamy macrophages, leprosy

Introduction

Leprosy, a chronic inflammatory granulomatous disease, chiefly involves the skin and peripheral nerves. According to The Ridley and Jopling’s (1966) classification, leprosy is classified as tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL) and lepromatous (LL).[1] The acute or subacute clinical manifestations of leprosy are often attributed to lepra reactions. These reactions are divided into type 1 reaction (or reversal reaction, RR), and type 2 reaction (or erythema nodosum leprosum, ENL).[2,3] We report two clinically unusual cases of ENL, which were diagnosed primarily on fine-needle aspiration cytology (FNAC), thus, highlighting the utility of this simple diagnostic tool in diagnosing ENL.

Case History

Case 1

A 60-year-old male presented with complaints of tenderness and swelling in the left inguinal region. The patient was a known case of lepromatous leprosy, and completed the multidrug treatment therapy 10 years back. On clinical examination, a tender diffuse swelling measuring 3 × 1.5 cm the in left inguinal region was palpated. Skin over the swelling was warm. FNAC was performed and both air-dried and alcohol-fixed smears were prepared. The Wright–Giemsa (WG) stained smears showed lymphoid cells along with degenerated and intact neutrophils, clusters of foamy macrophages, histiocytes, and giant cells in a hemorrhagic background. Occasional shadows of negative images of bacilli were seen. In view of clinical and cytological findings, Fite stain for lepra bacilli was performed, which showed numerous intracellular and extracellular lepra bacilli [Figure 1].

Case 2

A 70-year-old male presented with complaint of swelling over right forearm. There was a history of weakness in the right forearm 4 years back. On examination, there were multiple tiny nodular swellings on the right forearm largest...
measuring 0.8 × 0.6 cm. FNA was performed which yielded granular aspirate. The WG stained smears showed dense mixed inflammatory cell infiltrate comprising polymorphs, foamy macrophages, eosinophils, and lymphoid cells. Few of the macrophages were present in clusters and showed epithelioid transformation forming ill-formed granulomas. Fite stain for lepra bacilli was positive [Figure 2].

In both the cases, Gram's stain and bacterial culture were performed which came out as negative.

**DISCUSSION**

Leprosy is a slowly progressive infection caused by *Mycobacterium leprae*. Nerves and skin are the primarily affected organs, however, lymph nodes, spleen, liver, bone marrow, eyes, and testes may also be affected. Lymph node involvement can either be because of ENL or because of visceral involvement in leprosy. ENL is a type III hypersensitivity reaction with acute inflammation in leprosy patients due to excessive immunological response of the host to *M. leprae* or its breakdown products. It generally occurs in LL cases and rarely in BL cases. Young patients, patients with high bacillary index, and those with skin infiltration are more prone for development of ENL reactions.

ENL lesion presents as tender, inflamed subcutaneous nodules lasting for a duration of 1 to 2 weeks. Severe reactions may be associated with low grade fever and arthralgia. Other lesions that have been described in the literature are enlargement of the liver and spleen, epididymo orchitis, arthritis, periostitis, myositis, glomerulonephritis, peritonitis, and oral destruction.

Case 1 was unusual as the reaction occurred after 10 years of completion of multidrug therapy because most ENL reactions are reported to occur within the first 2 years of successful completion of multidrug therapy. Other common causes of lymphadenopathy such as tuberculosis needs to be excluded in such cases, as any other tropical infection or connective tissue disorder can coexist with leprosy. Various authors have reported cases of ENL where lymphadenopathy was clinically and morphologically misinterpreted as either tuberculosis or lymphoma. The past history of leprosy, presence of suppurative inflammation, and negative images of bacilli inside the macrophages prompted us to evaluate the patient for leprosy. Occasionally, ENL can be the presenting feature of LL. ENL-like reaction takes place in clinically unsuspected patients when they receive antimicrobial therapy for some other diseases. Case 2 presented with multiple tiny nodular swellings over the right forearm and had never received leprosy treatment in the past. The patient received multiple drugs from various physicians before he reached our hospital. Apart from these lesions and weakness in the right forearm, he did not have any other significant complaints. The aspirates suggested the presence of suppurative inflammation along with vague granuloma formation.

Ziehl–Neelsen stain and Periodic acid Schiff's stain were performed to exclude the possibility of tubercular or fungal infection, however, these stains were found to be negative. Fite stain was performed as a part of a routine diagnostic work-up for nontubercular granulomatous inflammation. It was found to be positive, and the patient was subsequently started on multidrug therapy for leprosy. Steroids were prescribed for the type II reaction. Cytology has been successfully used to determine the bacillary index by slit skin smear examination in leprosy patients. Few authors have described the cytomorphology of nerve involvement in leprosy. Our paper highlights the role of FNAC in diagnosing two clinically unsuspected cases of ENL, while most authors have described cytological findings of ENL in clinically suspected cases of reactionary leprosy. Because ENL can involve unusual sites and can occasionally be the presenting feature of the disease, this possibility should be excluded in smears showing suppurative inflammation with macrophages and granuloma formation.

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**Figure 1:** (a) Photomicrograph showing lymphoid cells, degenerated and intact neutrophils, foamy macrophages, histiocytes, giant cells and occasional shadows of negative images (Wright Giemsa stain, x200). (b) Fite stain positive for lepra bacilli

**Figure 2:** (a) Photomicrograph showing polymorphs, foamy macrophages, eosinophils and lymphoid cells. (Wright Giemsa stain, x100); (b) Fite stain positive for lepra bacilli

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CONCLUSION
The cytological features of ENL is similar to its histomorphological counterpart and includes the presence of acute inflammatory infiltrate, focal necrosis, foamy macrophages, and high acid fast bacilli positivity. In order to achieve the goal of leprosy eradication, the need for early detection of such cases by minimally invasive diagnostic procedures such as FNAC cannot be overemphasized. A high degree of suspicion combined with the cytological features characterizing ENL, as described above, can help in arriving at a conclusive diagnosis.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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