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Case Series

A case series of sweet syndrome like erythema nodosum leprosum at tertiary care centre in Western India

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ABSTRACT

Leprosy is a chronic disease caused by Mycobacterium Leprae, mainly affecting skin and nerves. Chronic course of leprosy may be interrupted by acute inflammatory conditions called lepra reactions. Type 2 reaction (Erythema Nododsum Leprosum/ENL) classically presents as crops of multiple tender, evanescent nodules. Several pleomorphic variants of ENL has been described in the literature such as erythema necroticans, sweet syndrome–like, erythema multiforme like, livedoreticularis like and bullous ENL. Identification of unusual cutaneous features of ENL are of paramount importance ,which poses a diagnostic challenge. The study aimed at identifying the sweet syndrome like ENL, their clinical and histopathological feautures. This is a retrospective study done at a tertiary care centre of western India. There were eight cases of sweet syndrome like ENL. Out of 8 patients, 6 had lepromatous leprosy, 1 each of borderline lepromatous leprosy and histoid leprosy. All patients had a sudden onset of painful erythematous oedematous plaques and nodules with pseudovesiculation. The study emphasizes the importance of early diagnosis and prompt treatment of atypical ENL reactions. WHO Global Leprosy strategy 2030 also emphasizes on early detection to prevent deformities and disabilities, and thereby improving the quality of life of the patients living with the leprosy.

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1. Introduction

Leprosy is a chronic, granulomatous disease caused by Mycobacterium lepra. In the course of leprosy, a patient could obtain an acute inflammatory episode called lepra reaction. This can occur before, during, or after the treatment of multiple drug therapy (MDT). There are three main types of lepra reactions (Suryawati & Saputra 2018). The Type 1 lepra reaction is a delayed type of hypersensitivity reaction type- 4 (Coombs and Gell classification) and usually observed in borderline spectrum of the disease. The Type 2 reactions, also called as erythema nodosum leprosum (ENL), are hypersensitivity reaction type-3(Coombs and Gell classification) which is mediated by immune complexes. Usually it occurs in multi-bacillary patients and is characterized by diverse clinical manifestations.The Type 3 reactions, also called Lucio phenomenon, is a phenomenon which is usually observed in untreated cases of leprosy.Sweet's syndrome (SS)-Like ENL is characterized by acute onset of erythematous, evanescent, tender papules or plaques with pseudovesiculation with constitutional symptoms such as fever, malaise, arthralgia, as well as systemic complications (Suryawati & Saputra 2018, Heng & Chiam 2011).[1,2]There are reports of other atypical and rare clinical manifestations such as Pustular (Ghorpade A et al 2014),[3] Bullous (Vashisht & Das AL 2013),[4] Livedoreticularis (Naveen & Athanikar 2014),[5] Ulcerative, (Yogeesh & Chankramath 2012),[6] erythema multiforme (EM)-like

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reaction (Sgambatti & Andrade 2010)[7] and Necrotic ENL (Sirka & Panda 2017).[8] Here we report eight cases of sweet syndrome like ENL reaction.

2. Case Series

All cases of the sweet syndrome like lepra reactions including outpatients as well as indoor patients attending department of Dermatology, Venereology and Leprosy at tertiary care hospital from March, 2022 to September, 2023 of all age groups were included in study. Detailed history taking, thorough clinical examination were done in all the cases to diagnose them as atypical sweet syndrome like lepra reaction and which was further confirmed by histopathology, Zeihl- neelsen stain and Fite-Faraco stain.

3. Results

Total 8 patients were included in case series. Seven were males, one was female. Mean age at diagnosis in our study is 37 (Range 24-50) years. Out of total 8 cases, 6(75%) had lepromatous leprosy, 1 (12.5%) had histoid leprosy and 1 (12.5%) had borderline lepromatous leprosy (figure 1). At the time of presentation, 4 patients (50%) were on MDT-MB packet, 2 patients (25%) had interrupted the anti-leprosy treatment while 2 (25%) had completed MDT-MB packet. All cases were characterised by abrupt onset of painful erythematous papules, plaques and nodules with pseudo vesiculation. Fever (>38 degree Celsius) was seen in all cases along with neutrophillic leucocytosis. Mean leukocyte count is 18800 ± 3466.62/ cmm. ESR was raised > 20 mm/hr in all patients. Pedal edema was present in 6 cases, while facial edema was present in 1 case. New onset of neuritis was noted in 2 cases. All the cases were subjected to the slit skin smear (for AFB) and six cases were subjected to biopsy. The Zeihl- Neelsen Stain for acid fast bacilli was positive in 6 cases; Bacillary index in 4 cases was ≥+4, 2 cases had ≥+3 and rest 2 cases had negative Slit skin smear. The Fite-Faraco stain was positive in 6 patients. In our study three patients had identifiable trigger factor. Two patients had upper respiratory tract infection and one had urinary tract infection. All patients had sensory impairment in form of glove and stocking anaesthesia. Grade 2 eformity was observed in one patient in form of bilateral partial claw hands, As per World Health Organization disability grading system (Brandsma &Van Brakel et al 2003).[9] Three patients were having recurrent ENL.

Histopathological examination revealed edema in upper dermis in 4 cases. Superimposed Infiltration of neutrophils over pre-existing macrophages throughout the dermis was seen in 6 cases. Six cases showed features of vasculitis; characterized by perivascular infiltration of intact and fragmented neutrophils and extravasation of red blood cells. Periappendageal as well as diffuse infiltration of neutrophils, lymphocytes were seen in dermis in 6 cases. All patients were categorized as sever ENL according to modified ENLIST ENL severity scale (Walker and Sales 2017).[10] All of them were admitted to the dermatology ward and were treated with systemic steroids initially and shifted to oral corticosteroids on discharge. Three patients with recurrent ENL were put on cap thalidomide.

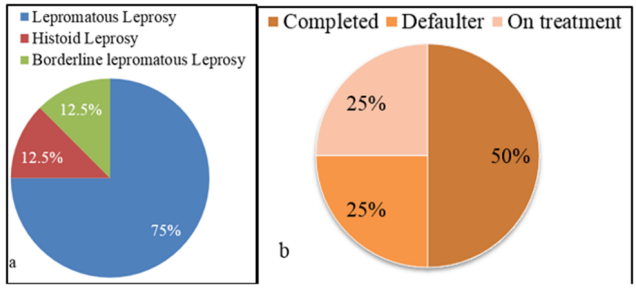

Figure 1: a: Spectrum of leprosy; **b:** Treatment status.

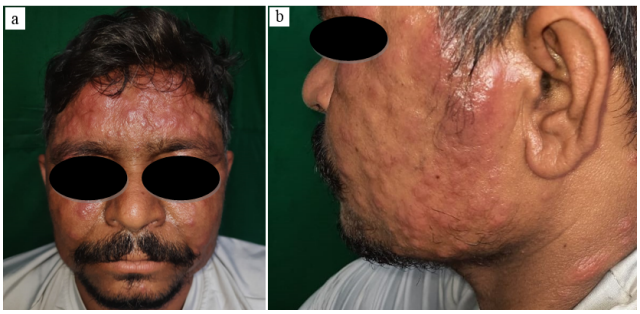

Figure 2: a: Multiple erythematous plaques over face with pseudo-vesiculation; **b:** Multiple erythematous plaques with pseudo-vesiculation

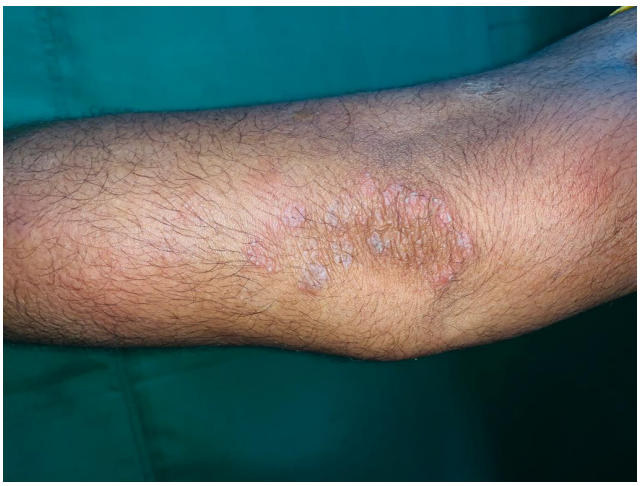

Figure 3: Multiple erythematous plaques with pseudo-vesiculation

Table 1: Clinical and histopathological details

S.No.	Age (in years) /sex	Diagnosis	Prior history of treatment taken	BI	Fite-Faraco stain	Histopathology	Laboratory parameters
1	33/M	Lepromatous leprosy	11 MDT-MB taken	4+	Positive	Epidermis- Irregular acanthosis Dermis-Edema in papillary dermis and diffuse perivascular, periappendageal neutrophilic and lymphocytic infiltration in dermis, macrophages in dermis	HB-10.5 gm/dl TC-17,300cells /cumm DLC-91(N)/07(L)/01(E)/ 01(M), ESR-114mm/hr CRP-Positive
2	30/M	Lepromatous leprosy	6 MDT-MB taken before 12 months (defaulter)	4+	Positive	Epidermis- Normal Dermis- Edema in papillary dermis, Foamy macrophages and diffuse neutrophilic, lymphocytic infiltration perivascular, periappendageal and perineural	HB-9.6 gm/dl TC-19,900cells /cumm DLC-80(N)/11(L)/01(E)/ 08(M), ESR-90mm/hr PS-neutrophilia CRP- Positive
3	42/M	Lepromatous leprosy	10 MDT-MB taken before 9 months (defaulter)	4+	Positive	Epidermis- Normal Dermis- Grenz zone, edema in papillary dermis, Foamy macrophages, perivascular, periappendageal and perineural neutrophilic & lymphocytic infiltration infiltration in papillary and reticular dermis	HB-7.5 gm/dl TC-17,200cells /cumm DLC-91(N)/06(L)/01(E)/ 02(M), ESR-108mm/hr CRP-Positive
4	24/M	Borderline lepromatous leprosy	3 MDT-MB taken	3+	Positive	Epidermis- Mild acanthosis Dermis-Diffuse infiltration with foamy macrophages, perivascular, periappendageal Neutrophilic and lymphocytic infiltration.	HB-11 gm/dl TC-15,300cells /cumm DLC-87(N)/11(L)/01(E)/ 01(M), ESR-93mm/hr CRP-Positive
5	27/M	Lepromatous leprosy	3 MDT-MB taken	3+	Positive	Epidermis- Atrophy Dermis – Diffuse, perivascular, periappendageal neutrophilic and lymphocytic infiltratre, macrophage in dermis	HB-9.8 gm/dl TC-22,000cells /cumm DLC-82(N)/15(L)/01(E)/ 02(M), ESR-20mm/hr CRP-Positive
6	42/M	Histoid leprosy	6 MDT-MB taken	4+	Positive	Epidermis- Irregular acanthosis Dermis – Edema in papillary dermis, Foamy macrophages, diffuse neutrophilic and lymphocytic infiltrate in dermis	HB-10.2 gm/dl TC-13,600cells /cumm DLC-90(N)/07(L)/01(E)/ 02(M), ESR-114mm/hr PS-neutrophilia CRP- Positive
7	50/ F	Lepromatous leprosy	RFT case of leprosy	Negative	Negative	*	HB-9.9 gm/dl TC-24,800cells /cumm DLC-86(N)/08(L)/03(E)/ 03(M), ESR-59mm/hr CRP-Positive
8	48/M	Lepromatous leprosy	RFT case of leprosy	Negative	Negative	*	HB-11.6 gm/dl TC-21,200cells /cumm DLC-87(N)/09(L)/02(E)/ 02(M), ESR-80mm/hr ASO-positive CRP- Positive

*Negative consent for biopsy

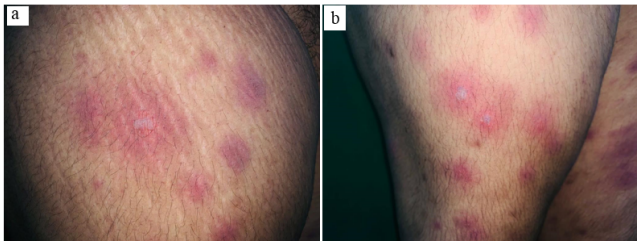

Figure 4: a,b: Pseudovesiculation over erythematous plaque, on evolution

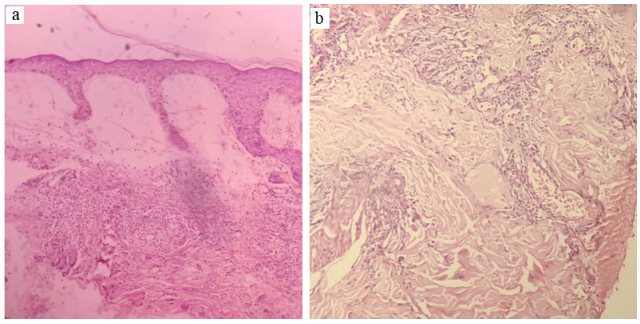

Figure 5: a: Histopathology shows irregular acanthosis in epidermis, edema in papillary dermis and diffuse neutrophilic infiltration; **b:** Histopathology shows Perivascular infiltration of intact and fragmented neutrophils with extravasation of RBCs and Foamy macrophages

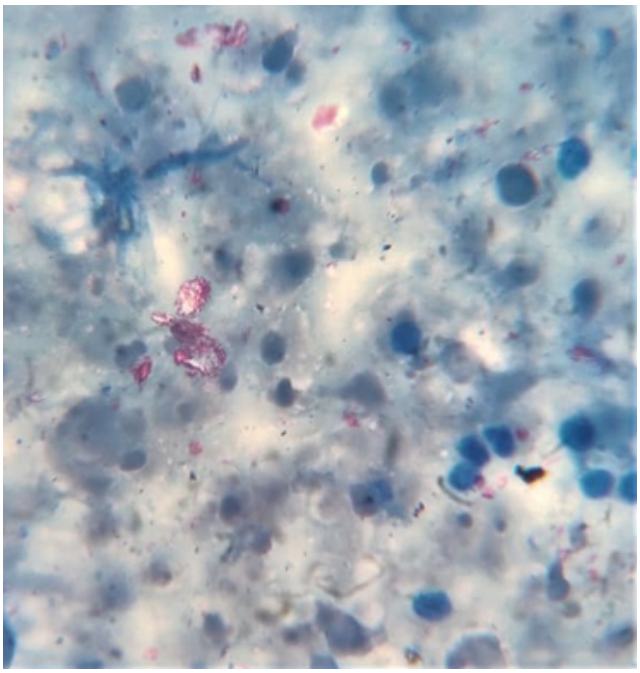

Figure 6: Positive Fite-Faraco stain showing acid fast bacilli

4. Discussion

Lepra reactions are immunologically mediated episodes of acute or subacute inflammation which interrupt, the relatively uneventful chronic course of disease affecting the skin, nerves and other organs. Erythema nodosum leprosum is classified as Type 3 hypersensitivity reaction under Coombs and Gell division. Antigens produced from degenerating bacilli react with antibodies to form antigen-antibody complexes. These immune complexes activate complementary pathway which causes acute inflammation of skin, tissue and nerves (Kar & Gupta 2017).[11] It is most commonly seen in lepromatous leprosy and sometimes in borderline lepromatous leprosy. Patients with higher bacterial index posses higher chances of getting ENL (Bala & Sen 2014).[12] ENL mostly presents within 6 months of starting multi drug therapy (MDT), though it can occur before starting or after completing the MDT (Jopling & McDougall).[13] Risk factors for ENL include intercurrent bacterial, viral or parasitic infection, vaccination, physical and mental stress, surgical intervention, pregnancy.

ENL presenting as Sweet's syndrome first reported in 1987 by Kuo and Chan (Kou & Chan 1987).[14] Kuo and chan et alreported a case clinically suggestive of Sweet's syndrome with histopathological features of lepromatous leprosy. The Sweet syndrome like ENL is classically characterised by sudden appearance of evanescent crops of erythematous, tender nodules or plaques with constitutional symptoms like fever, malaise, headache, myalgia, joint pain, bone pain, etc. Other manifestations of Type-2 reactions include neuritis, iridocyclitis, iritis, orchitis, glomerulonephritis, arthritis and lymphadenopathy (Vinitha & Thankappan 2019, Prakruthi & Rajesh 2015).[15,16] These plaques may contain pseudo-vesicles due to severe oedema of the papillary dermis; as the lesion progress, they may exhibit a central clearing, leading to target- like appearance similar to erythema multiforme. (Chiaratti & Daxbacher et al 2016).[17] The occurrence of a Sweet syndrome-like lepra reaction is infrequently reported. The parts most frequently impacted are the face, neck, chest and upper extremities (Chiaratti & Daxbacher et al 2016). It is usually more common in the BL patients, due to the immunologic instability of the borderline group (Aires & Refkalefsky 2009).[18]

Histopathology of sweet syndrome like ENL shows edema in papillary dermis, superimposed infiltration of intact as well as fragmented neutrophils over pre existing macrophage in dermis. HP shows features of vasculitis with Perivascular neutrophilic infiltration and extravasation of red blood cells. Periappendageal, perineural infiltration of neutrophils, lymphocytes and histiocytes can also be seen in SS like ENL (Mahajan & Abhina C 2014, Wankhade et al 2019).[19,20] Sweet syndrome is characterised by tender erythematous skin lesions such as papules, nodules and plaques with systemic symptoms such as fever or malaise.

These plaques may contain pseudo-vesicles (Cohen PR et al 2017).[21] Sweet syndrome is diagnosed by A modified diagnosing criterion as proposed by von den Driesch (1994) is given below (von den Driesch P et al 1994).[22]

It is imperative to diagnose individuals who have not been diagnosed with leprosy previously and to start anti leprosy treatment (Multi Drug Therapy). The identification of Mycobacterium leprae though positive Fite-Faraco stain and slit skin smear as well as sensory and motor impairment provides valuable diagnostic insights for leprosy. It is crucial to recommence multi drug therapy in patients who have not successfully completed their treatment. Short courses of oral corticosteroids are used in treatment of lepra reactions (Vijendran & Verma 2014).[23]

Systemic review of literature of online available case reports and case series of Type-2 lepra reaction resembling sweet syndrome till 2019 (Chavez-Alvarez et al 2020)[24] include 21 cases (67% Males and 33% females). In our study a male preponderance was noted (87.5%) similar to A case control study (Nayak et al 2022)[25] on risk factors for erythema nodosum leprosum which revealed a male predominance of 81.44%; the study attributed this trend to conventional social norms and gender specific health-seeking behaviour. Mean age at diagnosis in our study is 37 (Range 24-450) years as compared to Chavez-Alvarez et al (2020), in which mean age was 45 years (Range 27-61). In our study, majority of patients (75%) had lepromatous leprosy as compared to Aires et al, in which all seven cases had borderline lepromatous leprosy. All of our patients were treated with systemic corticosteroids, While three (37.5%) were concurrently administered thalidomide in conjunction with systemic corticosteroid. Sweet's syndrome-like leprosy reaction can be easily recognized in patients with leprosy already diagnosed than in those without previous diagnosis of the baseline disease.

5. Conclusion

Timely diagnosis and prompt treatment of atypical erythema nodosum leprosum (ENL) reactions are of utmost importance to prevent adverse consequences such as deformities and disabilities. While the prevention of long-term physical impairments is a critical goal, it is equally vital to address the immediate need to minimize morbidity and ensure the patient's comfort. Prioritizing early intervention not only mitigates the risk of lasting deformities but also focuses on swiftly reducing morbidity, enhancing overall patient well-being, and fostering a more effective healthcare approach in managing atypical ENL reactions. It is crucial to go through clinical and laboratory evaluation to diagnose leprosy in a suspicious case presented with sweet syndrome like ENL. This remains the one of the pillars towards achieving the Zero disability and Zero leprosy under WHO GLOBAL LEPROSY STRATEGY 2030.

6. Abbreviations

ENL- Erythema nodosum leprosum; EM- Erythema multiforme; SS- Sweet syndrome; MDT- MB- Multi bacillary Multi drug therapy; T1R- Type 1 reaction; T2R- Type 2 reaction; AFB- Acid fast bacilli; ZN stain- Ziehl-neelsen stain; FF- Fite-Faraco; LL- Lepromatous leprosy; BL- Borderline leprosy; BI- Bacteriological index; RFT- Released from treatment; WHO- World Health Organization; SSS- Slit skin smear.

7. Conflict of Interest

None.

8. Source of Funding

None.

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