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Case Report

Necrotic Erythema Nodosum Leprosum in a Lepromatous Patient Diagnosed as Disseminated Phaeohyphomycosis – A Case Report

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A forty-six year female diagnosed as rheumatoid arthritis was started on systemic steroids, azathioprine and hydroxychloroquine. The patient then developed fever and cystic swellings on right elbow and right ankle joint. A biopsy from the cystic lesions on the elbow and ankle joint showed an inflammatory cystic lesion with pigmented branching septate fungal hyphae. Fungal culture demonstrated dematiaceous fungi, phaeohyphomycosis and she was put on anti-fungal therapy with regression of cystic lesions. Later the patient developed high grade fever and multiple painful necrotic ulcers on the trunk and limbs, but not responding to antifungal therapy and was referred to us with a diagnosis of disseminated phaeohyphomycosis. On examination the patient had multiple discrete painful necrotic ulcers on the trunk and limbs, saddle nose deformity, papules on the face and infiltration of the forehead. There was bilateral complete claw hand and foot drop. Ear lobe and smear from the facial papules were positive for AFB. Biopsy of the ulcers was suggestive of necrotic ENL, but negative for fungus. The patient was diagnosed as lepromatous leprosy and started on MB-MDT, ofloxacin and prednisolone. We are reporting a case of missed diagnosis of necrotic ENL in a LL patient on immunosuppression, who had developed subcutaneous phaeohyphomycosis.

Key Words : Necrotic ENL, Phaeohyphomycosis, Immunosuppression, Lepromatous Leprosy

Introduction

Necrotic erythema nodosum leprosum (ENL) occurs as a severe variant of Type 2 lepra reaction presenting with erosions and ulcers on the limbs and trunk (Barman et al 2021). They most commonly occur in lepromatous leprosy (LL) and sometimes in borderline lepromatous leprosy (BL). They initially present as bulla and pustules which later ruptures to form erosions and ulcers with severe constitutional symptoms. The patient may also have other features of Type 2 lepra reaction. This presentation may mimic ecthyma gangrenosum, pyoderma gangrenosum and extensive pyoderma. Necrotic ENL if not diagnosed may eventually lead to septicemia and may contribute to mortality. Herein we are reporting a case of LL with necrotic ENL diagnosed as disseminated phaeohyphomycosis by the rheumatologist and the infectious disease department as the patient initially had a cystic swelling of phaeohyphomycosis due to immunosuppressive therapy for rheumatoid arthritis.

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Case Report

A forty-six year female with recurrent and chronic early morning joint stiffness and pain of the small joints of the hand was diagnosed as rheumatoid arthritis by the rheumatologist and started on systemic steroids, azathioprine and hydroxychloroquine. The pain subsided with the aforementioned drugs and the steroids were gradually tapered. The patient then developed fever and cystic swellings on right elbow and right ankle joint (Fig. 1a). These cysts were soft and slightly tender. A fine needle aspiration cytology (FNAC) from the cystic lesion on the elbow demonstrated dematiaceous fungi. A biopsy from the cystic lesions on the elbow and ankle joint showed an inflammatory cystic lesion with pigmented branching septate fungal hyphae. A fungal culture from the biopsy specimen on SDA fungal medium at 22°C and 37°C demonstrated dematiaceous fungi at day 6 with greyish black downy colonies with black reverse and lactophenol cotton blue stain of the growth showed multiple branching septate hyphae suggestive of phaeohyphomycosis (Fig. 1b,c). However, MALDI-TOF (Matrix assisted laser desorption ionization -Time of flight) for species identification was inconclusive. A diagnosis of subcutaneous phaeohyphomycosis was made and the patient was started on liposomal amphotericin B, 5 mg/Kg body weight for one and a half months by the Infectious Disease department. The cystic lesions subsided and the patient was continued on itraconazole (100 mg b.d.). At the time of discharge the patient was put on posoconazole 300 mg once daily. Later the patient developed high grade fever, asthenia and multiple painful erosions and necrotic ulcers on the trunk and limbs, but not responding to posoconazole. Due to this she was referred to the Dermatologist with a diagnosis of disseminated phaeohyphomycosis.

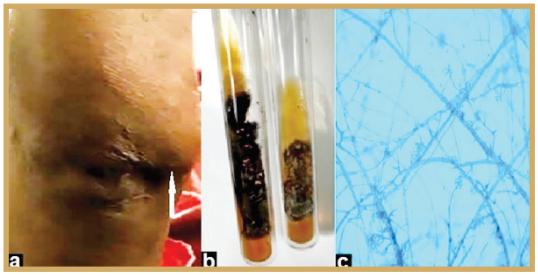

Fig. 1: a. Cystic swelling on right elbow, b. Fungal culture showing grey colonies and black reverse, c. Dematiaceous fungi with branching septate hyphae, Lactophenol cotton blue x400.

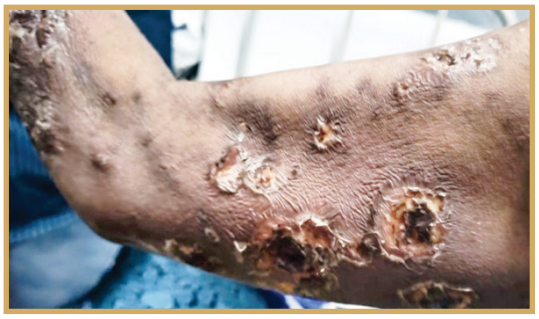

Fig. 2 : Multiple necrotic ulcers on the elbow.

When we examined the patient was sick looking, febrile and had multiple discrete painful necrotic ulcers and erosions on the trunk and extensor aspects of the upper limbs and thighs. On taking a detailed history the patient said that the ulcers first started as painful blisters and pustules which later ruptured to form the present ulcers. The ulcers were ill defined with sloping edges and the floor showing granulation tissue, necrosis and slough (Fig. 2). On further history taking the patient gave history of difficulty in walking, paraesthesia of lower legs and palms and frequent blistering of both palms and slipping of chappals. On examination there was saddle nose deformity and multiple discrete papules on the face and infiltration of the forehead (Fig.

Fig. 3 : a. Infiltration of forehead, facial papules, b. Thenar and hypothenar wasting with ulcers and complete claw hand.

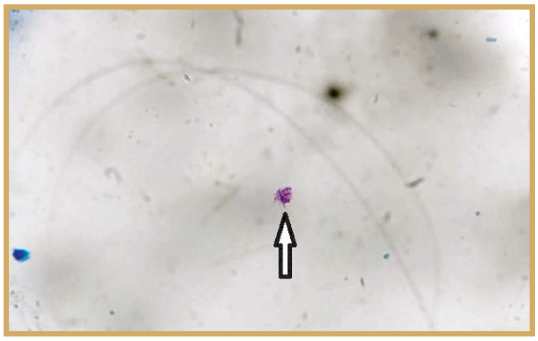

Fig. 4 : Earlobe smear showing AFB and globi (arrow), Zeihl Neelson stain x1000.

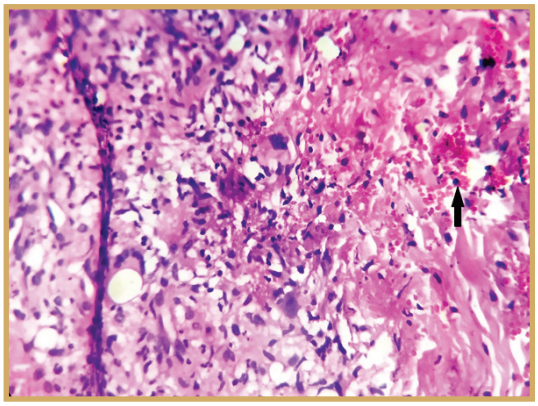

Fig. 5 : Skin biopsy showing dilated blood vessels with extravasated RBC's, thrombus formation (arrow) and neutrophil infiltration, H & E 400x.

3a). Both palms showed wasting of the thenar and hypothenar muscles with ill defined erosions and ulcers on fingers and thumb (Fig. 3b). CNS examination showed normal higher functions and normal cranial nerves. There was loss of all modalities of sensation on both hands below the wrist. There was patchy loss of all modalities of sensation of both feet extending to just above the ankle joint. The sensations over the erosions and ulcers on the trunk and limbs and over the papules on the face were intact. The peripheral nervous system examination showed thickened (Grade 2) left infraorbital, left median nerve, left radial cutaneous nerve, left common peroneal nerve and bilateral sural, superficial peroneal and ulnar nerve. The ulnar nerve showed nodular thickening (Grade 3). The card test, book test and pen test were positive in both hands and there was bilateral foot drop. The musculo-skeletal system showed fixed flexion deformity of both elbows (Rheumatoid arthritis). There was complete claw hand and shortening of the toes.

The patient's hemogram showed anemia, neutrophilia and high ESR. Liver function test and renal function tests were normal. Chest X-ray was normal. Viral markers for HIV, HBsAg and HCV were negative. Pus culture from the erosions and ulcers did not grow any organisms. Ear lobe smear showed Bacteriological index (BI) 6+ with globi and Morphological index (MI) of 10% (Fig. 4). Slit skin smear from papule on face showed BI of 2+ and MI 10%, while smear from normal skin was negative for AFB. A skin biopsy from the ulcer showed the dermis with multiple blood vessels with extravasated RBC's, thrombus formation and neutrophil infiltration into the vessel walls and dermis suggestive of necrotic ENL (Fig. 5). Fungal stain was negative. We made a final diagnosis of lepromatous leprosy with necrotic ENL and Grade 2 disability. The patient was put on Multi-bacillary MDT along

with 400 mg ofloxacin, 60 mg prednisolone and prophylactic posoconazole 300 mg. The necrotic ulcers healed within a period of 2-4 weeks leaving behind post inflammatory hyperpigmentation and post inflammatory scarring. In the last follow up the patient was on tapering dose of 10 mg prednisolone. The patient is also undergoing regular physical medicine exercises for the claw hand and foot drop.

Discussion

Our patient first presented with early morning joint stiffness and pain. The rheumatologist diagnosed it as rheumatoid arthritis and she was put on long term immunosuppressive therapy. Following this the patient's joint pain subsided. However, later the patient developed cystic swellings on the elbow and ankle which FNAC, biopsy and fungal culture demonstrated dematiaceous fungi, phaeohyphomycosis and she was diagnosed as subcutaneous phaeohyphomycosis. Consequently the patient was put on antifungal therapy and showed initial improvement. But later the patient developed multiple discrete ulcers and erosions on the trunk and limbs which was attributed to disseminated phaeohyphomycosis and she was put on posoconazole. When there was lack of response she was referred to the dermatologist. When we examined the patient had saddle nose deformity, infiltration of forehead, multiple discrete papules on the face, bilateral wasting of the thenar and hypothenar muscles with erosions, crusting and necrotic ulcers on both palms, sensory loss to all modalities of sensation on the hands and feet suggestive of glove and stocking type of anaesthesia, generalized, but asymmetrical nerve thickening, positive smear from earlobe and skin papule. These were all suggestive of lepromatous leprosy. The patient also presented with multiple necrotic ulcers of the trunk and limbs, the skin biopsy from the ulcers were consistent with necrotic ENL and negative for fungus, thus ruling out disseminated phaeohyphomycosis for which she was referred to us. There was prompt response to MB-MDT and prednisolone. Therefore, we made a final diagnosis of lepromatous leprosy with necrotic ENL, with focal subcutaneous pheohyphomycois, which regressd with systemic antifungal therapy. The localised infiltrated papules and nodules rather than generalized and the asymmetrical nerve thickening are are not the usual features of LL, but this can be explained by the fact that the patient could have downgraded from an initial spectrum of BL to LL subpolar. LL subpolar may not present with symmetry of skin lesions or symmetrical nerve thickening as in classical LL. The patient might have downgraded from BL to LL in the natural course of the disease and it is possible that the immunosuppressive therapy for rheumatoid arthritis could have also contributed to this downgrading and the development of subcutaneous pheophyphomycosis.

The most important message in this case report is that while the patient initially presented with few cystic swellings of phaeohyphomycosis, the diagnosis of underlying lepromatous leprosy was missed and the patient was considered only as a case of disseminated phaeohyphomycosis. The wasting of the hand muscles with erosions and ulcers, saddle nose deformity and infiltration of the forehead were pointers to the presence of leprosy. Necrotic ENL is often misdiagnosed it may mimic ecthyma gangrenosum, pyoderma gangrenosum, nodular vasculitis and extensive pyoderma (Thomas et al 2013).

Necrotic ENL is a severe form of Type 2 lepra reaction where the patient presents with bulla, pustules which later ruptures to form erosions and ulcers in contrast to ENL which presents with tender subcutaneous nodules (Agarwal et al 2013). Classical ENL following a severe

Type 2 lepra reaction can also later rupture into ulcers leading to necrotic ENL. Erythema multiforme like presentation has also been reported in ENL (Verma & Pandhi 1993). The skin biopsy of necrotic ENL and classical ENL are the same with the epidermis showing ulcer in the case of the former. There is endothelial swelling, extravasation of RBC's, infiltration of the vessel walls and dermis with neutrophils in both, but neutrophil infiltration is more severe in necrotic ENL and sometimes microabscesses and thrombus formation (as in our case) may be seen in the leprous granuloma which contributes to the ulceration (Saritha et al 2013). Karryohexis and necrotizing vascultis may be seen in cases of severe necrotic ENL. In ENL Wade-Fite stain of biopsy specimen may show no or a few granular forms, while in necrotic ENL solid forms can be demonstrated. However, true vasculitis is not seen in both (Sehgal 2005). Eventhough it is a question of semantics some authors denote necrotic ENL and Lucio phenomenon as "Lazarine leprosy" (Bhattachargee et al 2020, Vargas-Ocampo 2007). Necrotic ENL if not diagnosed early may lead to septicemia and may contribute to mortality in leprosy. Systemic steroids are the drug of choice for necrotic ENL, while continuing MB-MDT. A combination of steroids and clofazimine is also effective and may aid as a steroid sparing agent once steroids are tapered. Some workers advocate combination of steroids with thalidomide (Walkers et al 2007). There are also reports of TNF-α inhibitors like etanercept, infliximab being beneficial and of late apremilast is also found to be useful. We are reporting a case of necrotic ENL in a LL case misdiagnosed as disseminated phaeophyphomycosis to highlight the need to consider necrotic ENL in the differential diagnosis of any patient from Indian subcontinent presenting with widespread necrotic ulcers.

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