

Full Length Research Paper

Langerhans cell histiocytosis (LCH) associated with *Helicobacter pylori* infection

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Langerhans cell histiocytosis (LCH) is defined as a clonal proliferation of Langerhans phenotypic-like cells. Letterer-Siwe disease is the most common and serious of these entities, affecting mainly infants up to two years of age. We report an interesting, previously misdiagnosed and relapsing case of adult skin limited to LCH in a 25 years old female patient presented with well defined erythematous, dry scaly plaques in the face, trunk and extremities for 10 years duration, and then remains stable over the time. The case is diagnosed and confirmed histopathologically, considered to be the second case of LCH and first case as adult Letterer Siwe been reported in Sudan.

Key words: Immunology, Langerhans cell histiocytosis, lymphoid, *Helicobacter pylori*.

INTRODUCTION

In 1868, Paul Langerhans discovered the epidermal dendritic cells that now bear his name. The ultrastructural hallmark of the LC, the Birbeck granule, was described a century later. The term Langerhans cell histiocytosis (LCH) is generally preferred to the older term, Histiocytosis X. This new name emphasizes the histogenesis of the condition by specifying the type of lesional cell and removes the connotation of the unknown (X) because its cellular basis has now been clarified (Cotran et al., 2005).

LCH is a clonal proliferative disease of Langerhans cells that express an immunophenotype positive for S100 and CD1a, and which contain cytoplasmic Birbeck granules. LCH occurs worldwide and most commonly develops in children aged 1 to 3 years, although disease can develop at any age. An annual incidence of at least 5 per million children has been reported for LCH, with the adult incidence suspected to be less than one-third that of children. LCH is more common in boys, with a male: female ratio of nearly 2:1. In adults, there may be a slight female predominance (Gerlach et al., 1998). Histiocytosis X includes three components: Eosinophilic granuloma,

Hand-Schüller-Christian disease and Letterer-Siwe syndrome (Peric et al., 1993). Letterer-Siwe disease is an acute fulminant, disseminated disease on one end of the clinical spectrum, on the other end, solitary or few, indolent and chronic, lesions of bone or other organs called eosinophilic granulomas (Komp et al., 1980).

LCH is defined as a clonal proliferation of Langerhans phenotypic-like cells. Letterer-Siwe disease is the most common and serious of these entities, affecting mainly infants up to two years of age (Ferreira et al., 2009). One neonatal patient with letterer-Siwe disease has been documented (Sun et al., 2003). LCH most frequently involves bone, but also involves the skin in 40% of cases; in 10% of patients it is limited to the skin. Cutaneous findings of skin-limited LCH include scaly papules, vesicles, and nodules, tumors with erosion, ulceration, crusting or purpura (Chang et al., 2002). Nail involvement in LCH is rare, but findings include paronychia, nail-fold destruction, onycholysis, and subungual expansion with nail plate loss (de Berker et al., 1994). Adult LCH is much rarer than infant or childhood LCH; the most commonly involved sites are the skin, lung and bone (Goodman and Terry, 2003). Adult LCH is also more difficult to treat. Disseminated multisystem adult LCH has a more benign chronic course; it has a slowly progressive or undulating course in contrast with the childhood type (Gerlach et al.,

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1998).

Dhillon and Sawyer (1989) reported three cases of granulomatous gastritis associated with *Helicobacter pylori* infection. An et al. (2001) reported focal or diffuse mucosal nodularity was found in seven cases of 22 patients with low-grade mucosa associated lymphoid tissue (MALT) lymphoma, and multiplicity of lesions in MALT lymphoma was closely associated with *H. pylori* infection. Gastric MALT lymphoma is the major consideration in the differential diagnosis of a nodular antral mucosa in patients with *H. pylori* gastritis. However, in practice, these suggested differentiating radiological signs have a limited role because of the lack of specificity of the imaging findings, and the rarity of gastric LCH.

THE CASE

A female patient, single, 25 years old, teacher, descent from second degree relative parents, resident in Kalakla, Gaalei tribe (Mixed Arab race). The condition started since the patient was 10 years old with insidious onset and progressive course, with low grade fever, malaise, loss of appetite and loss of weight, where seen at Khartoum Skin Teaching Hospital 2002 and put on Prednisolone oral therapy with good response and severe relapse after cessation of treatment. A year ago 2009 patient suffered from massive nasal bleeding, admitted to ENT Khartoum Teaching Hospital where a biopsy is taken from a polyp to show LCH, put again on Prednisolone with good response, then relapsed again to the recent condition of report as the condition started at face and extremities as raised red and hot lesions, non itchy and mildly painful, variable in size, with high grade fever, loss of appetite and lassitude. The patient was without any family history for LCH.

General examination

The patient general condition was ill, buffy face, not icteric, as well a palpable spleen 13 cm, and liver 13.7 cm. No palpable lymph nodes. No ascites or bone involvement.

Dermatological examination

Widespread symmetrically, well defined, erythematous dry scaly plaques, variable in size 2 to 10 cm in diameter, involving convex of face, upper back and along costal margins, flexor aspects of forearms and legs of 10 years duration. Few crusted nodules were noticed at face, no erosions and ulcers seen. The lesions were firm on palpation.

Palms and soles: No purpuric rashes at both soles and palms.

Nails: No nails dystrophy has been detected.

Ears: No persistent aural discharge or deafness.

Hair: No abnormality detected.

Oral cavity: No periodontal involvement or fleeting teeth.

Face: No palpable tender masses over calvarium or mandible bone.

Investigations done

Skin biopsy

Sections show perivascular and peridnexial cellular infiltrate composed of cells with foamy cytoplasm, lymphocytes and few eosinophils and mast cells. The cells are positive for S- 100 protein pattern and in the H&E sections appearance suggest Xanthogranuloma, however cell of Xanthogranuloma are negative for S- 100 protein. The mere likely diagnosis is LCH. It is known that some are from the Letterer Siwe is associated with foamy cells. It is uncommon in adults but described (Figures 1 and 2).

Complete blood count

TWBs 3.200/ μ l

Lymphocytes 36.1%

Neutrophils 54.5%

Hb 10.7 g/dl

MCT 30.8 fl MCV 85.6 MCH 29.7 pg MCHC 34.7 g/dl

Platelets 185000/ μ l

Abdominal U/S: Normal U/S scans.

Helicobacter pylori serum ICT test: Reactive.

Chest radiographs (posteroanterior (PA) and lateral)

(i) No bullae were noted on both lung fields, with sparing of the costophrenic angles.

(ii) No basal pleural effusion.

(iii) No hilar mass.

(iv) Normal heart size.

Skeletal radiograph survey-Skull

(i) No unifocal LCH presents as a single osteolytic lesion, affecting long or flat bones (the calvaria).

(ii) No multifocal LCH show osteolytic lesions involving the calvaria, the sella turcica, and the mandible.

DISCUSSION

This case is distinguished for involvement limited to skin, acute fulminant, disseminated, the histopathology pattern is associated with foamy cells positive for S- 100 protein, as well as the age of the patient, adult of 25 years. Letterer Siwe adult cutaneous LCH is an extremely rare syndrome (Gerlach et al., 1998). This is an uncommon

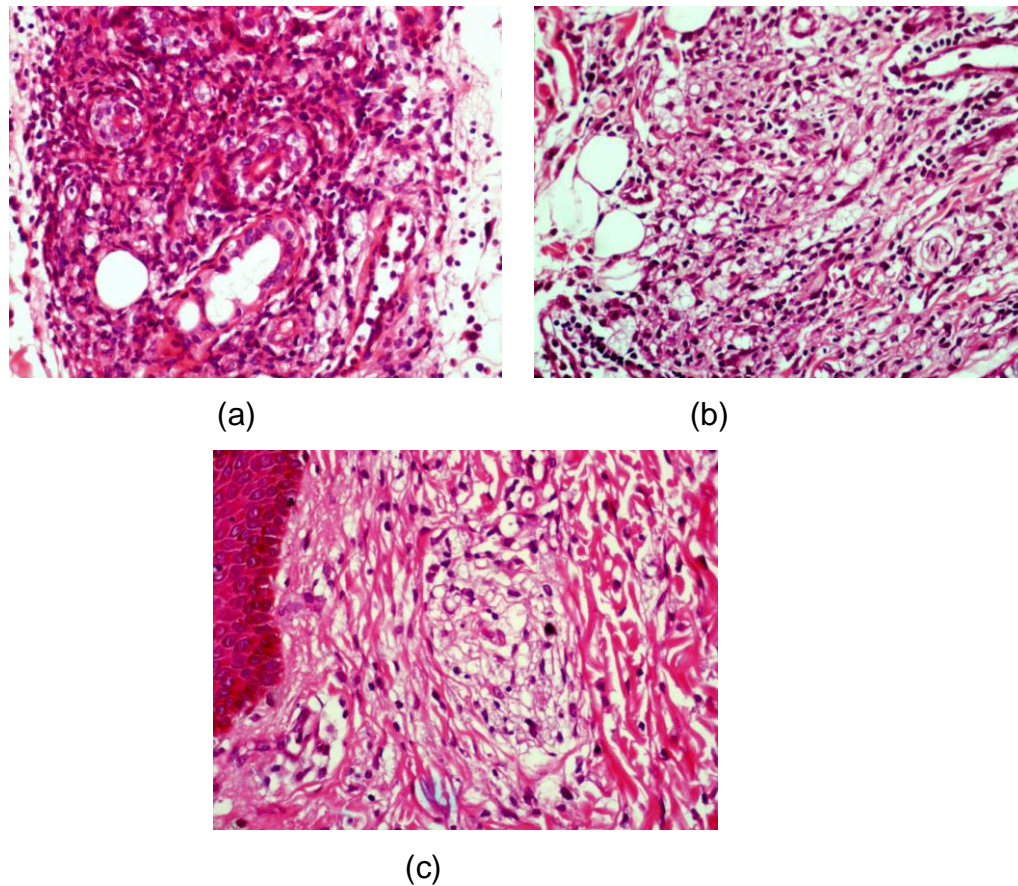


Figure 1. H&E staining. (a) A dense cellular infiltrate composed of lymphocytes, plasma cells, eosinophils, some neutrophils and foamy cells (H&Ex40), (b) An infiltrate in the mid dermis composed of lymphocytes, plasma cells, eosinophils and foamy cells. The arrow points to a large foamy cell (H&Ex40), (c) A focus composed largely of foamy cells (H&Ex40).

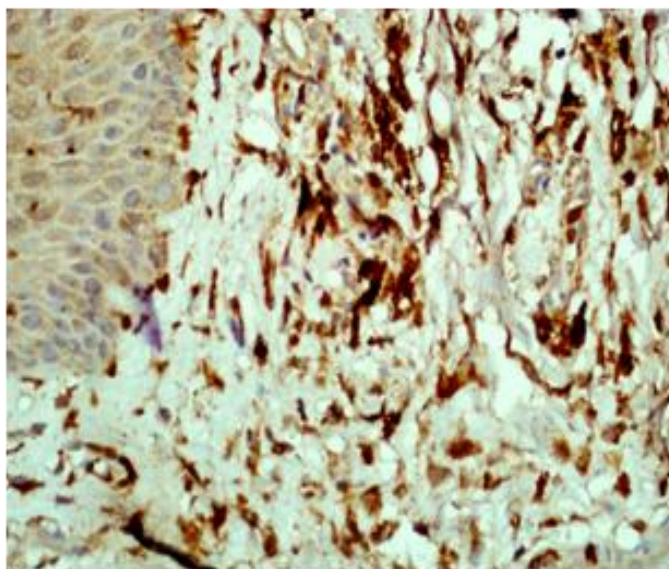


Figure 2. S-100 protein pattern. Many cells in the dermis are positive for S-100 protein. (Immunoperoxidase stain x40). The epidermis is on the left side of the figure. It shows dendrites of normal Langerhans cell.

form of LCH associated histopathologically with foamy cells where it is known to be rare. Detection of *H. pylori* antibodies with dyspeptic manifestations in this case could be related to possible underlying cause as has been observed in the study of Dhillon et al. (1989) and in the first case for the same author of disseminated cutaneous LCH with nail involvement. The case is dramatically responded to triple therapy first line, as Doxycyclin 100 mg bid for 8 days, Cefixime 400 mg bid for 5 days and Rabeprazole as proton pump inhibitor (PPI) 20 mg bid for 28 days, the *H. Pylori* – stool Ag test has been done to show antigen is not detected. Patient was observed for 8 months with no relapse.

Our case had an adult onset of presentation, clinical features and histopathology are typical, it is uncommon in adults and females, but described, to be considered as the 2nd adult case of cutaneous LCH reported for the same author, and first case of Letterer Siwe been reported in Sudan as extra digestive *H. pylori* skin manifestation (EdHpSm) where responded dramatically to triple therapy with no relapse for 8 months (Figures 3, 4, 5, 6 and 7).



Figure 3. Shows face erythematous greasy (A) scaly plaques (B) Closer view (C) Closer view (before triple therapy).

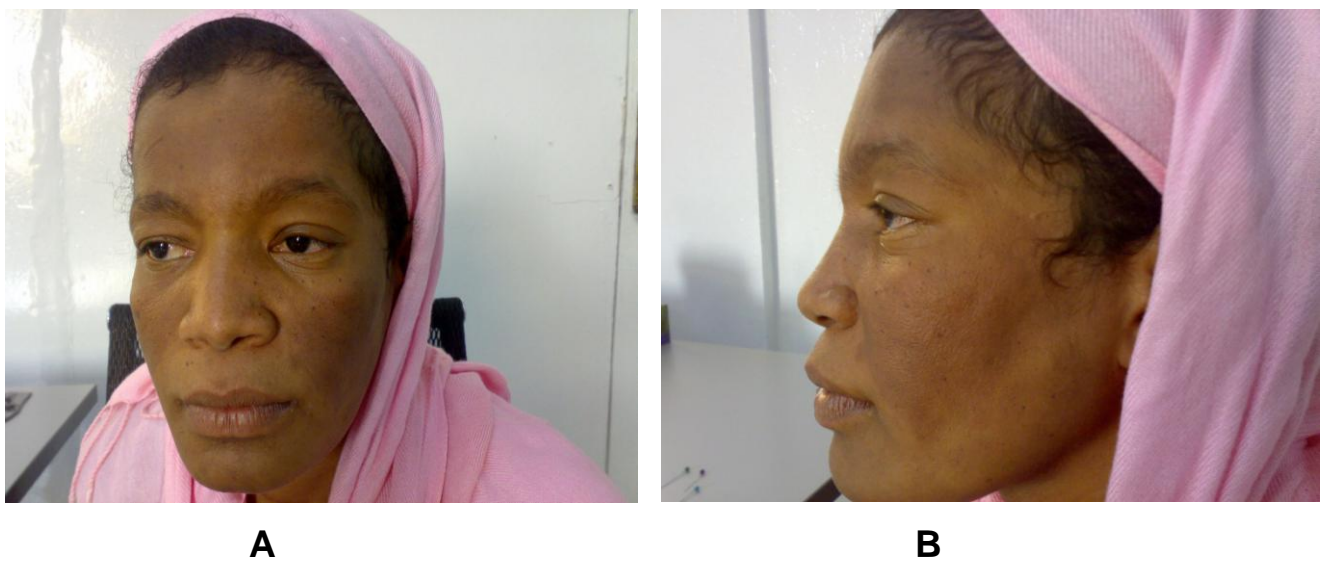


Figure 4. Shows same patient face (A) after receiving (B) profile after receiving triple therapy- 2 months.

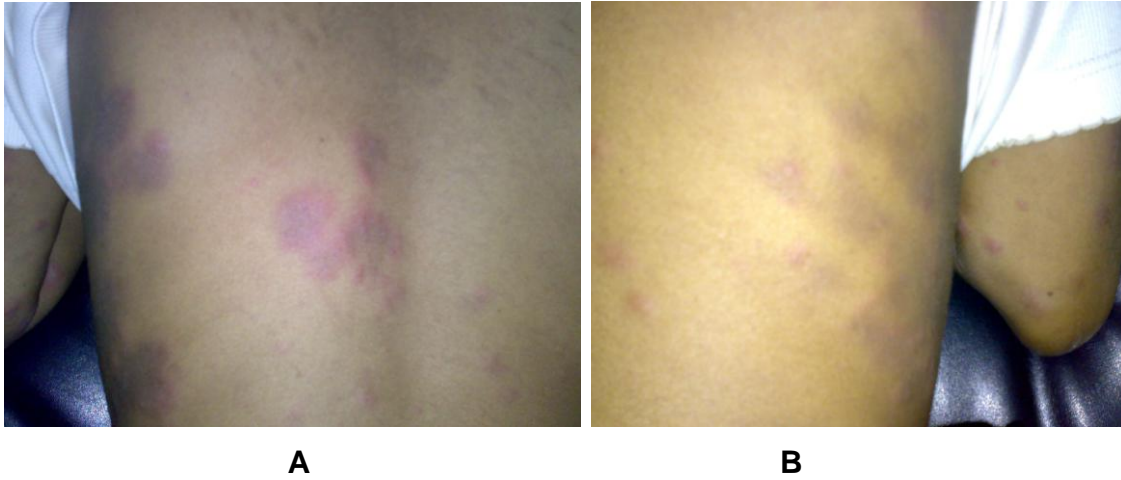


Figure 5. Shows upper back erythematous greasy scaly plaques (before triple therapy).



Figure 6. Shows forearm erythematous greasy scaly plaques (before triple therapy).



Figure 7. Shows forearm erythematous greasy scaly plaques after receiving triple therapy- 2 months.

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