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Case Report

Letterer–Siwe Disease (LSD): A Case Report

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Abstract

Background: Letterer–Siwe Disease (LSD) is one of the variants of Langerhans cell histiocytosis (LCH), which is considered as a rare disease that affects many systems in the body; it is characterized by monoclonal migration and proliferation of specific dendritic cells. The disease affects the bones and skin primarily, but can involve other organs as well, or appear as a multi-system disease leading to different clinical manifestations and eventually death. **Summary:** The authors present a case report of LSD in a two-year-old child from western Sudan, Messeria tribe, who is presented with one and a half-month history of fever, cutaneous ulcers, purprae, scaly crusted scalp, and pallor. His full blood count showed very low Hb with marked reduction of platelets. TWBC was normal. US showed hepatosplenomegaly with lymphadenopathy. A suspicion of sickle cell anemia and leukemia was suggested. He received treatment in his area in the form of antibiotics, skin care, blood transfusion and platelets aggregate without improvement. Patient was referred to Khartoum for further investigations and management. On presentation, a diagnosis of histiocytosis x was suggested depending on the clinical presentation of a general ill health in a child with purpurae, skin ulcers, and a scaly crusted scalp. A skin biopsy, bone marrow aspirate, and a skull x-ray were requested. Bone marrow aspiration showed hyper cellular BM with marked hemophagocytosis. Patient was admitted in a pediatric ward for further general investigations and blood transfusion, but he passed few days later before starting chemotherapy. Usually this is the prognosis of this rare and fatal aggressive form of histiocytosis x. **Conclusion:** A sick child with fever, anemia, hepatosplenomegaly, scaly scalp, and skin lesions should be investigated for LSD.

Keywords: Langerhans cell histoctosis (LCH), Letterer–Siwe Disease (LSD), seborrheic dermatitis

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1. Introduction

Letterer–Siwe Disease (LSD) is one of the variants of Langerhans cell histiocytosis (LCH), which is considered as a rare disease, prevalence is estimated as 1:500,000. The disease almost exclusively occurs in children less than three years old. It affects many systems in the body characterized by monoclonal migration and proliferation of specific dendritic cells. It affects the bones and skin primarily, but also involves other organs as well or appears as a multi-system disease leading to different clinical manifestations [1, 9, 13]. LCH includes three main classes, including dendritic cell disorders, disorders of macrophages, and histocytes malignant disorders [2]. LSD is caused by clonal proliferation of Langerhans cells that are functionally immature dendritic cells associated with other cells like lymphocytes, eosinophils, and macrophages, but multi-nuclear giant cells can also be affected [3]. Langerhans cells in LCH lesions accounts for less than 10% of cells [4, 5]. There is a significant difference morphologically, phenotypically, and in gene expression between epidermis Langerhans cells and those that are in LCH lesions [6, 7].Clinical classification of LCH includes three groups, the localized single-system disease, multifocal single-system disease and multisystem disease. Langerhans cells histiocytosis includes diseases previously designated as histiocytosis X, namely LSD, Hand-Schüller-Christian syndrome, and eosinophilic granuloma. They all share similar clinical morphology [10]. The involvement location has prognostic importance, so that the involvement of liver, spleen, and bone marrow are considered as involvement of high-risk organs, and the involvement of skin, bone, lung, lymph nodes, gastrointestinal ducts, pituitary gland, and central nervous system are considered as low risk organs [2, 8]. LSD is an idiopathic invariably fatal illness of infants; it has no apparent hereditary or familial tendency with an age incidence from two months to two years [11]. Death can occur during intrauterine life or within a few weeks of birth. A three-days-old infant's death was reported due to diffuse infiltration mainly of lungs with Langerhans histolytic cells [12]. Onset is indefinite with no specific symptomatology, but with a febrile course lasting for a few weeks or a few months to death. A hemorrhagic tendency commonly producing a purpuric or ecchymotic skin rash is most marked shortly before death [11]. Hematological picture shows hypochromic anemia, sometimes severe, while radiological imaging shows destructive lesions in bones, commonly in the skull, rarely, if ever, in the bones of the hands and feet, but often occurring elsewhere in the skeleton, for example, in the ribs, pelvis, humerus, or femur. Bony lesions may be clinically silent or associated with pain and tenderness with or without overlying soft tissue swelling. Lungs show

mottling of the lung fields on X-ray examination; less commonly, secondary bacterial infection such as otitis media or angina of the throat and leukocytosis can occur. The characteristic pathological feature is excessive hyperplasia of the reticuloendothelial tissue throughout the body, particularly in the spleen, lymph nodes, and skin [11].

Leonardo Mello et al. reported two cases of LSD from Brazil; the first was a 14-month female who was presented with one-month history of abdominal distension, palpable mass on the left inguinal area, jaundice, and skin lesions. Patient was admitted to a pediatric ward, and empirical antibiotics were started with no improvement, a dermatologic consultation was then requested and LSD was suspected. The diagnosis of LSD was confirmed by investigations and histopathology. Early treatment with systemic chemotherapy and prednisolone was started, patient discharged in a good condition with a plan of taking the proposed subsequent doses of chemotherapy.

The second case was an eight-month male patient who was presented with a two-month history of lower limb edema, seborrheic dermatitis-like lesions over the scalp, dry cough, dyspnea, fever, oliguria, and general ill health. Lab investigations showed severe hepatic failure, thrombocytopenia, and anemia. Apediatric diagnostic hypothesis included sepsis, severe malnutrition, fulminating hepatitis, kalazar, leucosis, and many other conditions. Antibiotic was started with no improvement. Dermatologic consultation was ordered and a suspicion of LSD was put. Patient died with multi-organ failure before confirmation of diagnosis. Autopsy showed organ infiltration with Langerhans cells.

The two cases herein were diagnosed after dermatologic examinations, in spite of the knowledge and diagnostic hypothesis of the specialized service. The authors have concluded that LSD is a rare condition, but, due to its severity, dermatologists should be able to recognize its typical dermatological signs, which may be decisive to define the treatment and prognosis of patients affected (14). Anderi et al. reported clinical and histopathological pictures in a neonate from Belarus with unrecognized congenital LSD who died due to diffuse infiltration of lungs with histiocytic cells; authors concluded that LSD should be suspected in neonates with vesiculated crusted skin lesions in patients not responding to antibiotic therapy [15].

2. Presentation

A two-year-old male child from western Sudan, Messeria tribe, was presented to an outpatient clinic in his area with a three-days history of fever, refusal of eating, skin and scalp lesions, and general ill health. He was seen first by a GP, who admitted him to

hospital with a diagnosis of sickle cell anemia, investigations showed severe anemia, thrombocytopenia, severe UTI, and negative sickling test. Patient was then followed by a pediatrician who gave him three pints of blood, injectable antibiotics, metronidazole infusion, skin wash solution, and topical antibiotic creams. Investigation for malaria and enteric fever were negative. His condition was deteriorating, and then he was referred one and a half month later to Khartoum for further investigations and management.

On presentation, patient was ill, irritable, pale, and febrile. Mother claimed that he had low appetite, disturbance of sleeping, and general fatigue. His past medical history before this attack was unremarkable with no previous hospital admission or blood transfusion. No family history of similar condition or blood disorder. Socially, family is of low socioeconomic status; father is a farmer and mother is a house wife.

Physical examination: He was irritable, pale with generalized lymphadenopathy and hepatosplenomegaly.

Skin: Generalized purpuric rash, ulcers especially over the hands and feet with hemorrhagic crustations, and scaly crusted scalp.

He was Admitted in a pediatric ward for blood transfusion and further investigations and follow-up. A punch biopsy from skin lesions for histopathology was taken; he was seen by a senior pediatric consultant who assessed the patient and his diagnosis was leukemia. In the ward, he received blood, platelet aggregate, antibiotics, and skin-care treatment. Close monitoring of the patient with follow-up chart for temperature, blood pressure, respiratory rate in addition to fluid input and output was performed. Investigations showed uncountable pus cells in urine.

CBC showed:

WBC 6.4x 1000/L

RBC 1.2 million/L

HB 3.5 gm/dl

HCT 12%

MCV 99.2 fl

MCH 28.9 Pg

MCHC 29.2%

Platelets 21,000/mm3

ESR 59 mm/hr

Film report revealed nucleated RBCs with dimorphic population. WBCs normal.

Platelets showed severe thrombocytopenia.

Bone marrow aspirate showed hyper cellular bone marrow with marked haemophagocytosis, marked erythroid hyperplasia, granulopoiesis is active with normal maturation, megakaryocytes are adequate, consistent with a hemophagocytic syndrome. No leukemic cells were identified in the bone marrow aspirate.

The patient passed on the third day of admission, the cause of death was stated as multi-organ infiltration and cardiac failure.

Contact of his relatives was missed for submitting the histopathology result of the skin.

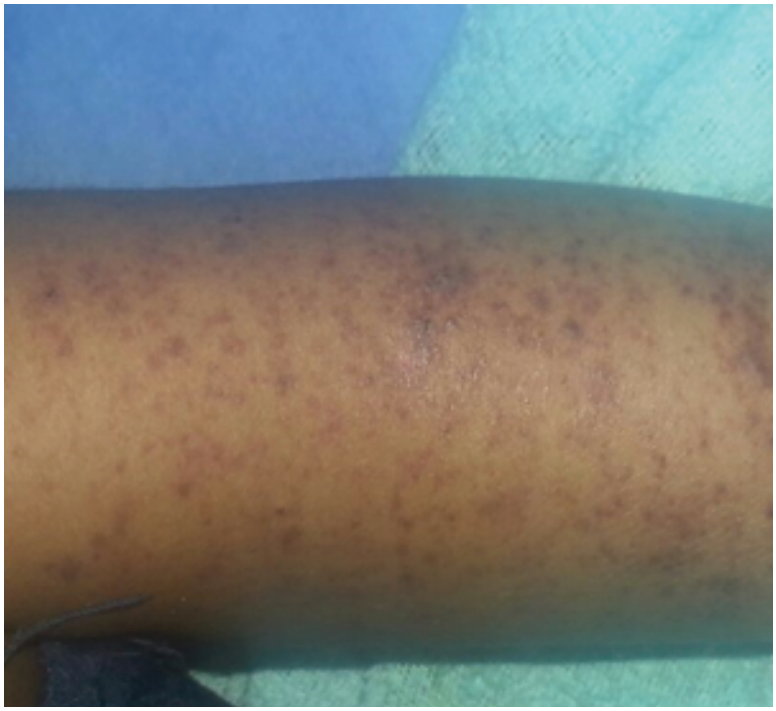


Figure 1: Extensive purpurae.

3. Discussions

LSD is a rare and fatal variant of histiocytosis [1, 9]. It can easily be missed for other conditions causing anemia, thrombocytopenia, and hepatosplenomegaly. Suspicion of this condition is raised from the presence of scalp lesions of scaling and crustations that greatly mimic seborrheic dermatitis. Examination findings in patients with LSD can be found in any patient due to organ infiltration by dendritic cells, namely, skin and bones. Other organ infiltration can cause hepatosplenomegaly, lymphadenopathy, and skin rash, as well as lung involvement [11]. This case was misdiagnosed on first presentation as sickle cell anemia because of the severe anemia and hepatosplenomegaly in a child from Messeria tribe, which is known to have high incidence of sickle cell anemia.

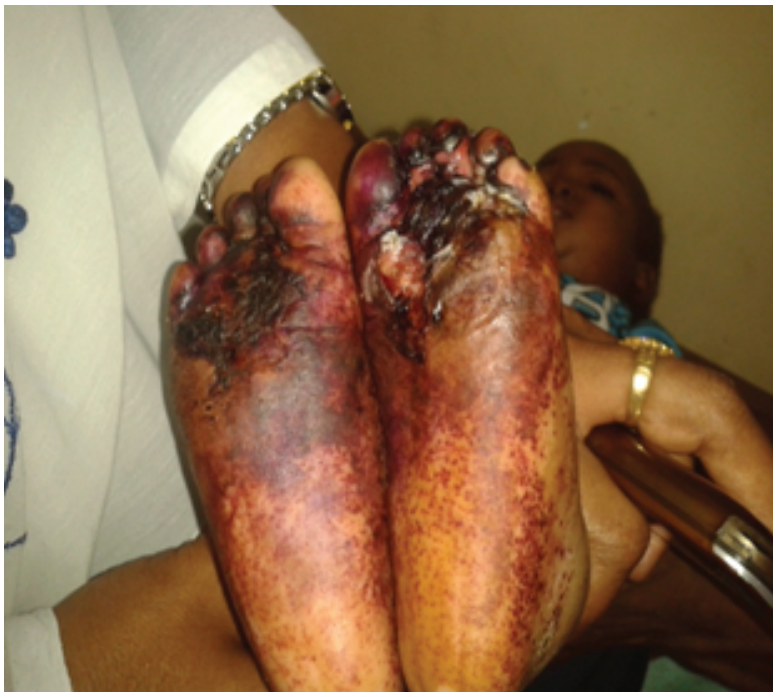


Figure 2: Hemorrhagic crust and purpura.

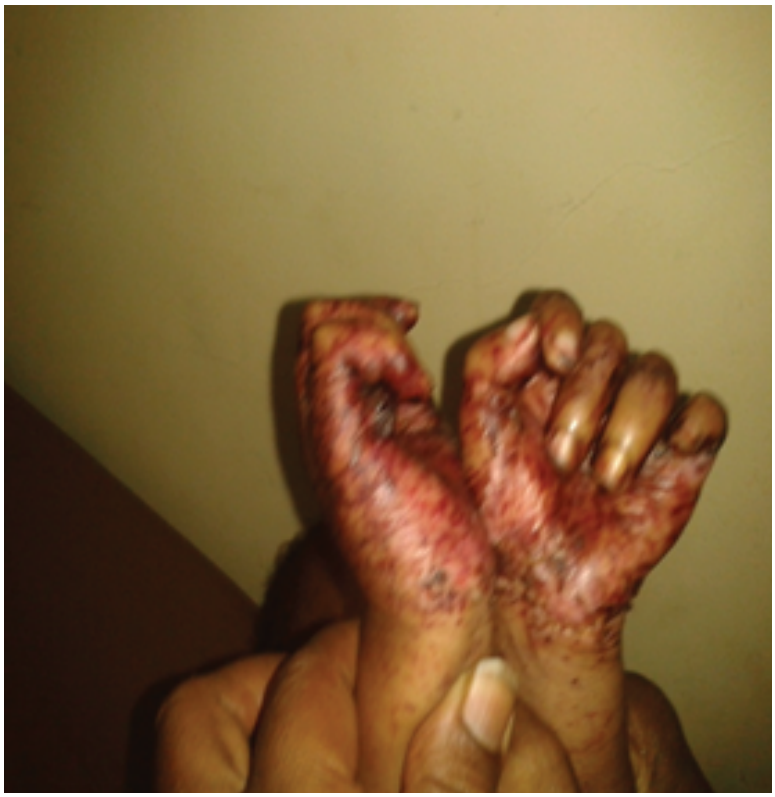


Figure 3: Hands purpura and crusts.

Then was also seen by a pediatrician who suspected leukemia again by the similar presentation of the general ill health, anemia, and thrombocytopenia, but absence

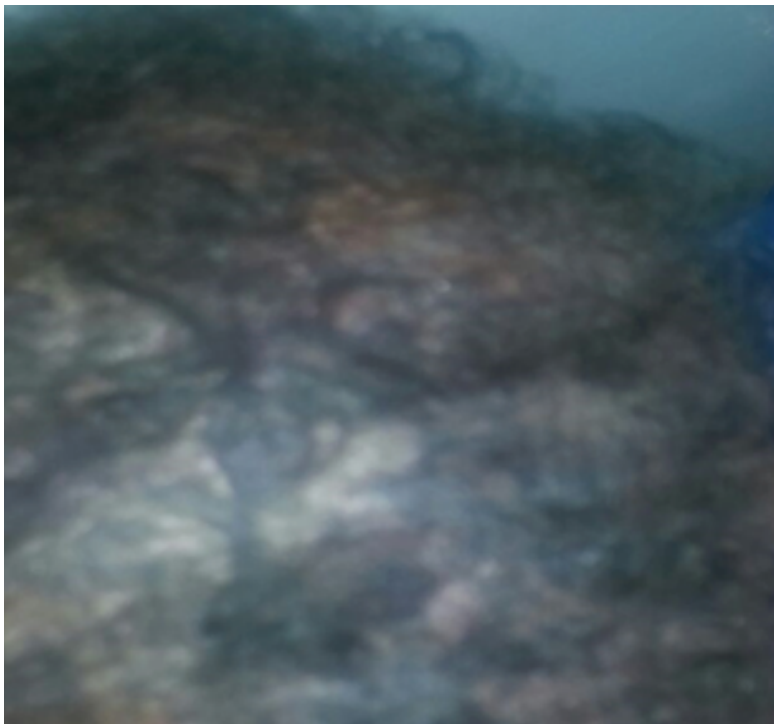


Figure 4: Scaly scalp.

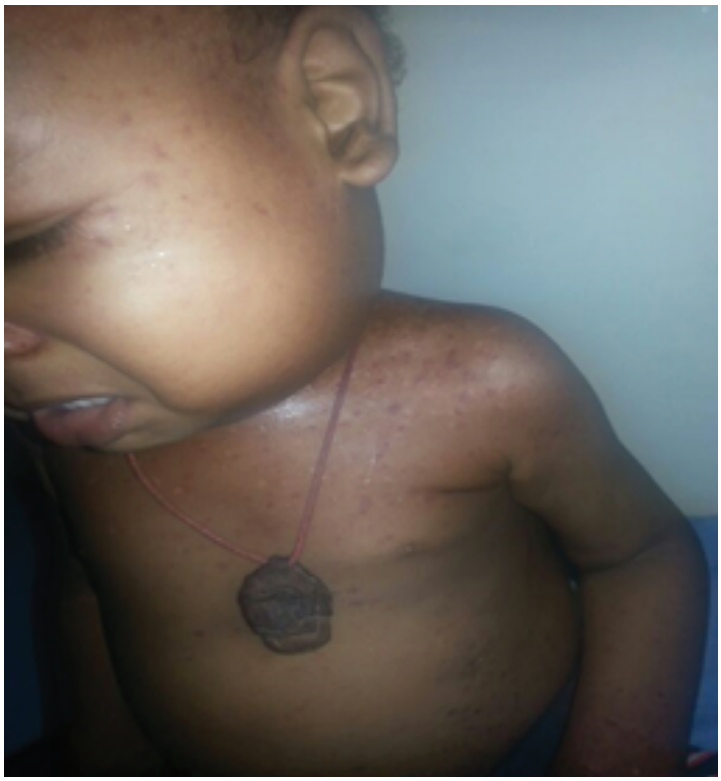


Figure 5: Facial edema and purpura of the face and chest.

of leukemic cells in bone marrow ruled out this suspicion. The patient passed before starting chemotherapy, this is the prognosis of the aggressive forms of LCH involving

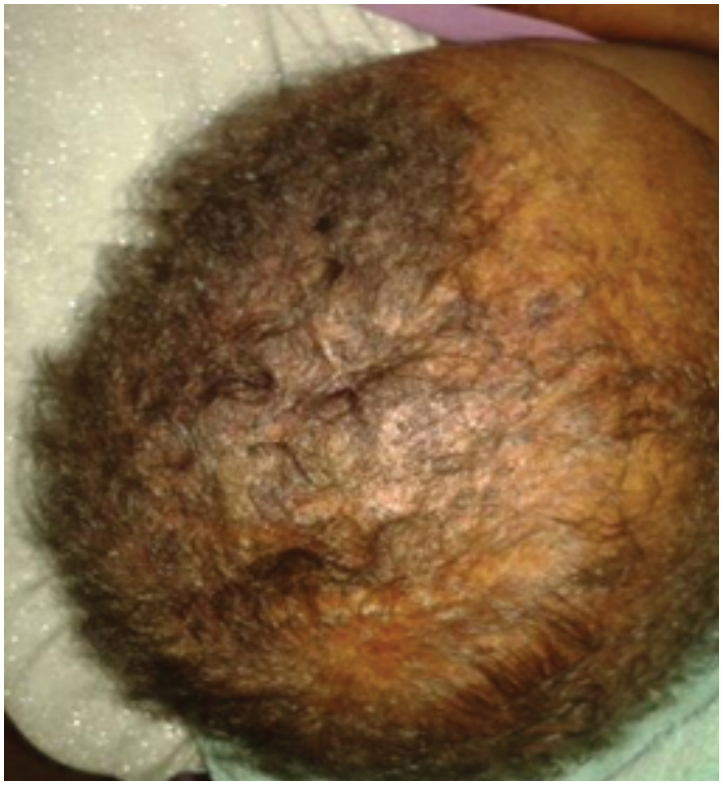


Figure 6: Scales and cru station of the scalp.

high-risk organs. The cause of death was stated as mufti organ infiltrations and cardiac failure.

Death of this patient and the aggressive outcome is justified by the early involvement of high-risk organs like liver, spleen, and bone marrow [2, 8].In the reported cases from the literature and also this case, the suspicion of the diagnosis was considered after dermatological consultation, so in the presence of any dermatologic signs an opinion of a dermatologist should always be considered even before antibiotic prescription because of the importance of early decision of starting therapy [14].

4. Conclusion

LSD is a rare aggressive form of LC histiocytosis that should be suspected in any sick febrile child with scaly scalp, purpurae, ulcers, crustations, anemia, hepatosplenomegaly, and other symptoms of organ infiltrations, especially those failed to respond to antibiotics. Awareness of dermatologists with LSD is important for early diagnosis and treatment, which can be life saving for patients with this fatal disease.

Consultation of a dermatologist is always important in cases with skin involvement.

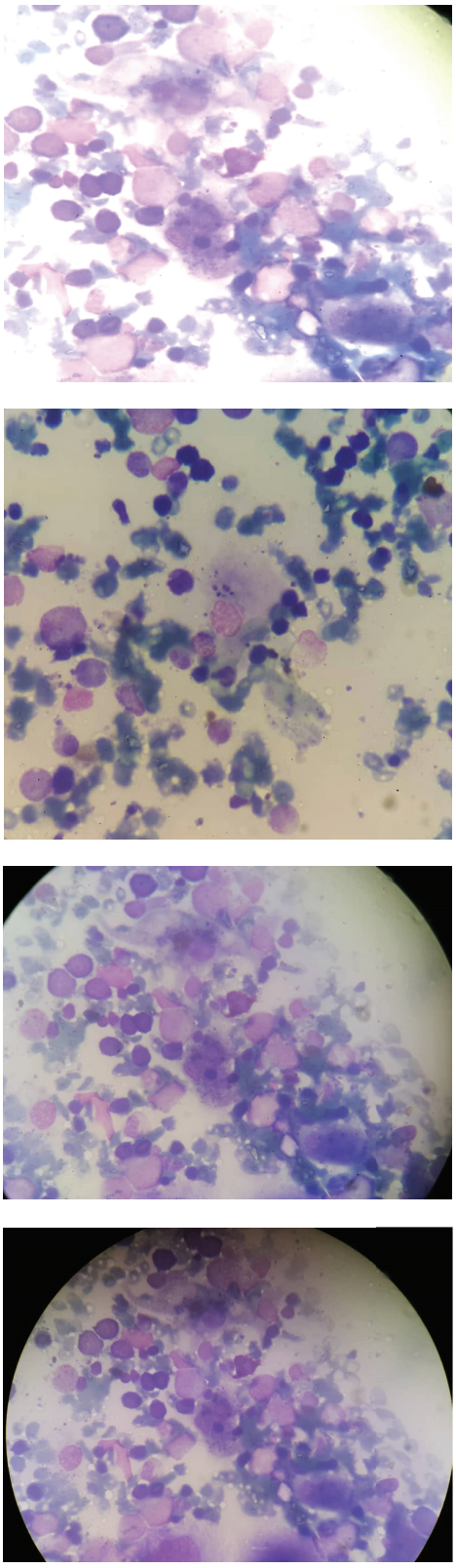
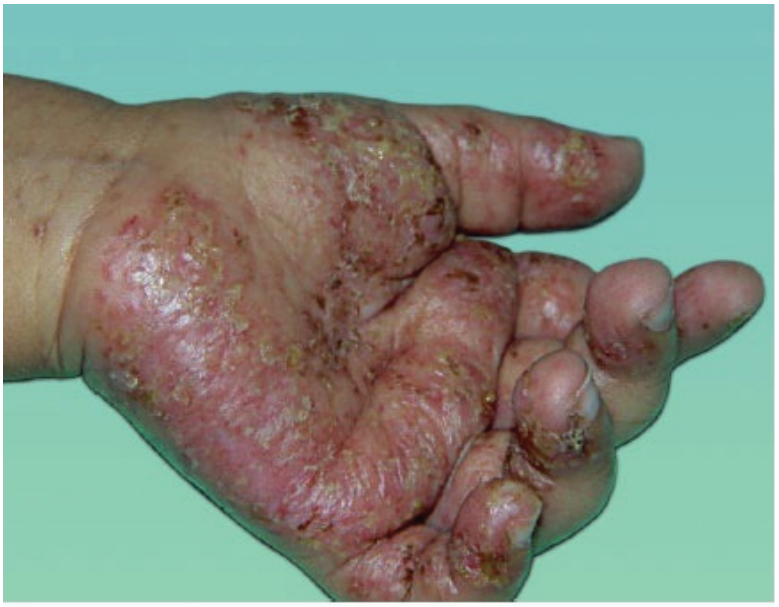
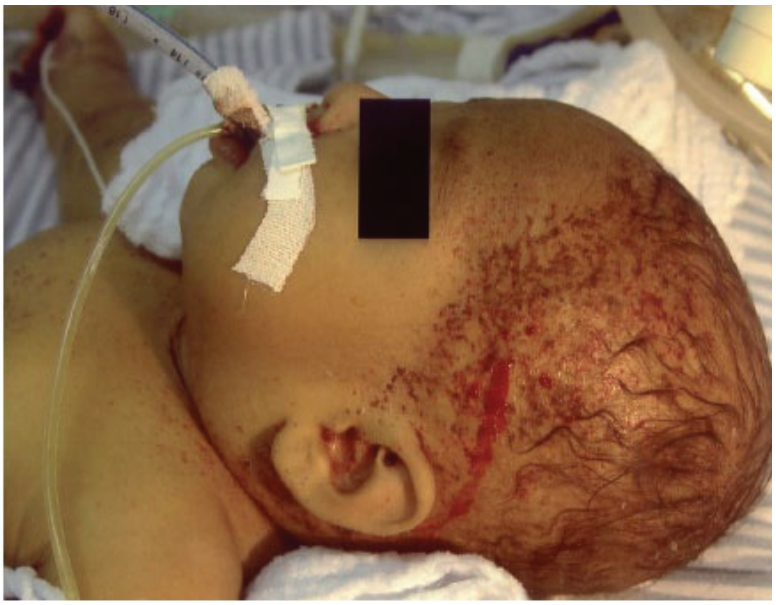


Figure 7: Multiple views of Bone Marrow aspirate showing hemophacocytosis.



Case 1: Typical aspect: "Purpuric Eczema"

Figure 8: Reported case from Brazil.



Case 2: Severe status: note jaundice and purpuric-crusty lesions on scalp and chest

Figure 9: Reported case from Brazil.

Photos of a Reported Case of LSD from Sudan

Ethical Clearance

A verbal consent was taken from the family of the child to take photos and publish the case.

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