Case 13
A 3 month-old male infant from Bangkok

Chief complaint: Solitary erythematous punched out ulcer on right cheek for 1 month.

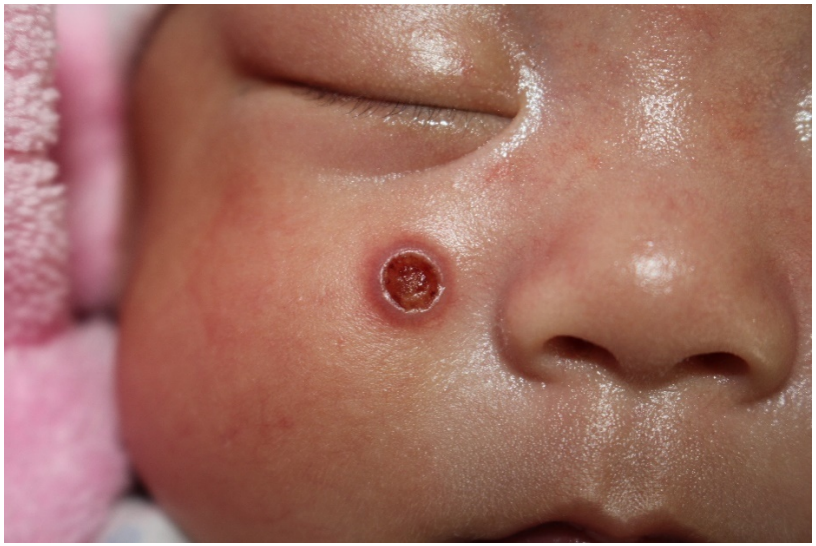

Fig. 13.1

Present illness:
The patient presented with a one-month history of solitary vesicle located on right cheek. The lesion progressed into a pustule which then ulcerated prior to presentation. After a one-week course of oral cephalexin the lesion worsened.

Past history:
- Pre-term GA 31^{+2} weeks, birth weight 1030 g, delivery by cesarean section due to pre-eclampsia.
- History of bilateral inguinal hernia status post bilateral herniotomy at 2 months

Family history: No family history of skin disease.

Dermatological examination: (Fig. 13.1)
Solitary well-defined erythematous punched out ulcer on the right cheek

Physical examination: Other systemic examination revealed no abnormalities.

Investigations:
- **CBC**
  - WBC 22,730/mm^3 (N 16, L 79, M 5, Eo 0, B 0%)
  - Hb 12.1 g/dL Hct 36.2 %, MCV 73 fL
  - Plt 567,000/mm^3
- **Coagulogram:** PT 13.3, PTT 31.2, INR 1.14
- **Liver function test:** AST/ALT 55/28 U/L, ALP/GGT 446/62 U/L, TP/Alb 58/36.2 g/L, TB/DB 1.2/0.4 mg/dL
- **Renal function:** BUN/Cr 3/0.23 mg/dL

Histopathology: (S17-032079A, skin, right cheek) (Fig. 13.2, 13.3)

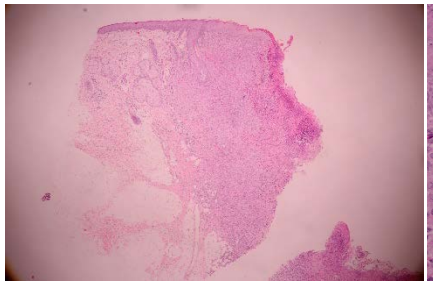

Fig. 13.2

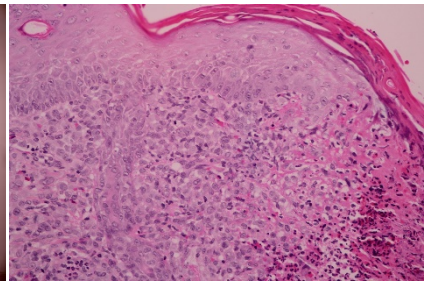

Fig. 13.3

- Dense diffuse mixed inflammatory cells infiltrate in the whole dermis and subcutaneous tissues.

- Infiltrates are composed of lymphocytes, neutrophils, eosinophils and numerous large cells with lentiform nuclei and pale eosinophilic abundant cytoplasms.

Immunohistochemistry: (Fig. 13.4, 13.5)

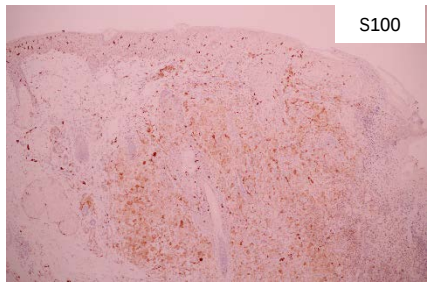

Fig. 13.4

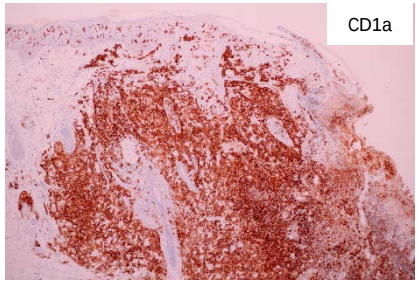

Fig 13.5

- Positive immunostaining for S100 and CD1a

Diagnosis: Congenital self-healing Langerhans cell histiocytosis

Treatment:
- Chloramphenicol ointment apply twice daily
- Complete resolution

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Discussion:
Langerhans cell histiocytosis (LCH) is a rare non-inherited clonal proliferative disease of langerhans cell, first described in 1953.[1] LCH has a wide clinical spectrum characterized by papules, papulovesicles, necrotic papule, eczematous seborrheic-like eruption, nodule and petechiae. LCH usually develops in children ages 1-3 years, with incidence in adults less than one-third of children and male to female ratio of 2:1.[1,2]

The pathogenesis of LCH remains unknown. The first hypothesis proposes that the condition is reactive in nature and may be induced by viruses such as HHV-6, CMV, adenovirus and parvovirus. These viruses are believed to stimulate immune mechanism and proliferation of LCH cells. The second hypothesis describes an abnormal bone marrow with chromosome 7 instability and abnormal p53 protein causing increased clonality of Langerhans cells. Consistent with this hypothesis, it was found that over 50% of Langerhans cells in LCH had BRAF mutation. This hypothesis strongly suggests that LCH is associated with neoplastic disease.[3]

The differential diagnosis of LCH is based on clinical presentation. In the papulosquamous variant, the differential diagnosis includes seborrheic dermatitis, lichen nitidus. In the vesiculopustular pattern, varicella must be excluded. And lastly in xanthomatous pattern, juvenile xanthogranuloma should be considered.[4]

Three main histological patterns of LCH follow its clinical progression, which include proliferative, granulomatous, and xanthomatous. The proliferative pattern clinically presents with papules, with histology consisting of lichenoid infiltration in the epidermis and upper dermis. The deep dermis shows localized infiltration around blood vessels. The granulomatous pattern, which is seen in chronic stages of LCH, consists of aggregation of Langerhans cells with multinucleated histiocytes and a varying number of eosinophils, neutrophils, lymphocytes and plasma cells. The xanthomatous pattern is seen clinically in HSC (Hand-Schüller-Christian) and consists of numerous foam cells composed of Langerhans cells and eosinophils. Multinucleated giant cells are frequently seen. Lipid accumulation is found later as a secondary phenomenon. LCH cells show positive immunostaining for S100 protein, CD1a and Langerin (CD207) the latter being the most specific for LCH cells. They also show negative

immunostaining for dermal dendrocyte markers (factor XIIIa) and macrophage/monocyte markers (CD68, CD163 or HAM56).[5]

Recently, LCH is reclassified into two groups.

1. Single-system disease - composed of single site (localized involvement of bone, skin or lymph node) and multiple sites
2. Multisystem disease - composed of low-risk group mainly affecting the skin, bone, lymph node and pituitary; and high-risk group which commonly affect the hematologic system, lungs, liver and spleen

It is recommended that the clinician approaches LCH based on the above classification system by first identifying organs of involvement, which may significantly impact the course of the disease and its prognosis.[6]

In our patient, we identified the organ of involvement to be skin only. Thus, it is a single-system disease (formerly called congenital self-healing LCH or Hashimoto-Pritzker disease) which is self-limited, often presents at birth or neonatal period and spontaneously resolves by 2-3 months. It must also be noted that, up to 33% can progress to multisystem disease.[7,8]

Treatment of choice for isolated cutaneous LCH is close observation. Symptomatic treatment, such as topical steroids, tacrolimus, or imiquimod are also important to facilitate good quality of life. Surgical resection is reserved for single lesions. Systemic steroids, vinblastine and phototherapy are not necessary in severe cases or cases with complications. Long-term monitoring for recurrence and involvement of other organs is recommended.[2,9]

Our patient is a 3-month old male infant who presented with a solitary erythematous punched out ulcer on the right cheek. There was no other organ involvement at the time of presentation.
Histopathology was consistent with proliferative pattern. Immunohistochemistry was positive for CD1a and S100. All of the above are compatible with the diagnosis of cutaneous langerhans cell histiocytosis.
The lesion spontaneously regressed within 1 month after presentation. Long-term follow-up is planned and to date, there is no recurrence or other organ involvement.

References:

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