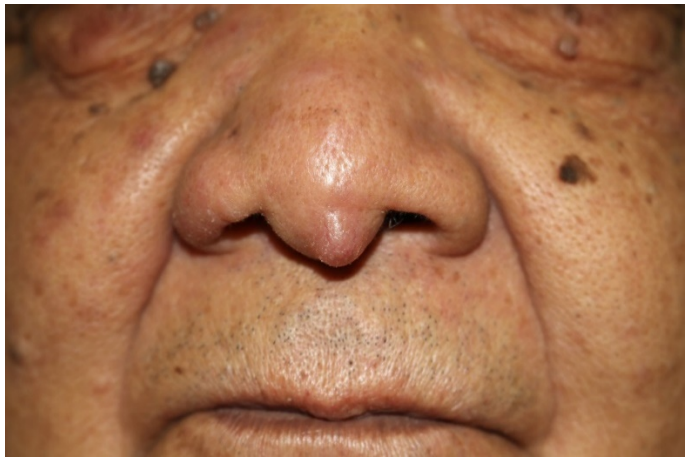
Case 17
A 75 year-old Thai man from Trat
Chief complaint: Asymptomatic erythematous papules on tip of the nose for 1 year



Present illness:

He was suspected of pulmonary Langerhans cell histiocytosis (PLCH) since October 2015 (bronchoalveolar lavage cytology: increased Langerhans cells with the differential diagnosis including smoking related lung disease and PLCH). He has been prescribed with Salmeterol xinafoate/ fluticasone propionate nebulizer, prednisolone orally, and then taper off.

Last year, he noticed that there was an erythematous papule on tip of the nose. It slowly enlarged with no associated pain or pruritus. He denied the history of weight lost, malaise, fever, bone pain or dyspnea.

Past history:

- He had hypertension and colonic polyps (pathological diagnosis tubular adenoma and tubulovillous adenoma).
- He was treated as pulmonary tuberculosis smear negative during February – December 2015.
- History of heavy smoking since age of 20.

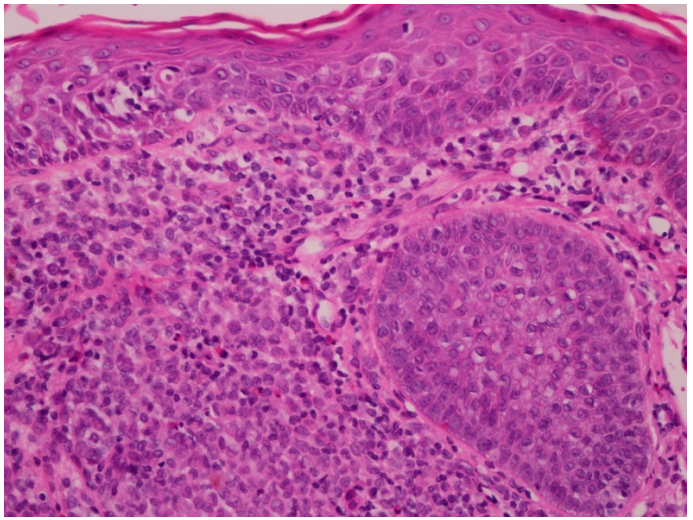
Dermatological examination:

- Ill-defined solitary erythematous firm papule size 0.4 cm. protruding from the tip of the nose.

Physical examination:

HEENT: Not pale conjunctivae, anicteric sclerae
Heart and lung: Normal
Abdomen: No hepatosplenomegaly
Lymph node: No lymphadenopathy

Histopathology: (S16-15492A, tip of the nose)



- Dense diffuse inflammatory cells infiltrate of atypical histiocytes admixed with lymphocytes, eosinophils and a few

plasma cells in the entire dermis and some exocytosis to the overlying epidermis. Atypical histiocyte is characterized by eccentrically kidney-shaped nuclei and abundant eosinophilic cytoplasm.

Immunochemistry: Shows positive CD1a and S100 but negative CD68 of the tumor cells.

Laboratory:
CBC: WBC 8,210 (N 69%, L 13%, M 13%, E 3%, B 2%), Hb 14.5 g/dL, Hct 46.8 %, Plt 222,000
LFT: ALP 179 U/L GGT 268 U/L AST 30 U/L ALT 30 U/L
TB 0.8 mg/dL DB 0.3 mg/dL
LDH 297 U/L
CT neck: No thyroid mass, multiple osteolytic lesion at left C1 arch, C2 to C7 vertebrae
CT chest and whole abdomen: Increase size of multiple small cysts at both lungs. Few nodules at apical segment of right upper lung. Increase size of spleen.
Bone marrow biopsy: Pending
Bone marrow aspiration: Diffuse infiltration with large immature cell 90%
Bone marrow flow cytometry for acute leukemia: No evidence of acute leukemia

Diagnosis: Multisystem LCH (lungs, skin, ± bone marrow)

Management: Pending for bone marrow results

Presenter: Ploychompoo Srisuwanwattana, MD
Consultant: Piyatida Prasertvit, MD

Discussion:

Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disease of Langerhans cells in various organs including bone, skin, lymph node, hypothalamic-pituitary/cental nervous system, lungs, hematopoietic system, liver, spleen and less common thyroid and gastrointestinal tract.

LCH occurs more in children, the incidence of LCH in adults is estimated 1 – 2 per million.[1] LCH has been found more in males. The etiology and pathogenesis is unknown. LCH cells are clonal indicating that LCH may be more neoplastic disease rather than reactive disorder.[2] Association between adult LCH and malignant tumor or hematologic malignancy has been reported.[3] Adult LCH shows in the skin associated with increased risk of a second haematological malignancy, including myelodysplastic syndrome, acute myelomonocytic leukemia, diffuse large B-cell lymphoma, peripheral T-cell lymphoma and histiocytic sarcoma.[4]

Various cutaneous presentation have been reported ranged from solitary/multiple papule(s), tumor(s) or ulcerating lesion(s) to generalized reddish-brown papules. Site of involvement are scalp, nose, shoulder, chest, back, trunk, knee, skin folds and oral cavity.[4]

Differential diagnosis of cutaneous LCH includes seborrheic dermatitis, insect bites, leukemia/ lymphomas cutis, urticaria pigmentosa and non-Langerhans cell histiocytoses.

Diagnosis based on histologic and immunophenotypic examination. Typical papule may reveal proliferation of LCH cells in the papillary dermis admixed with eosinophils, neutrophils, lymphocytes and plasma cells. Epidermal infiltration by Langerhans cells and secondary features such as crusting, pustule formation, hemorrhage or necrosis may be found. LCH cells show positive immunostaining for CD1a, Langerin (CD207), S100 and negative for CD68 and Factor XIIIa or demonstration of Birbeck granules on electron microscopy.

Laboratory and imaging evaluation for all LCH patients

should be evaluated to define organ involvement, including completed blood count, blood chemistry, coagulogram, thyroid stimulating hormone, freeT4, morning urine osmolarity, chest x-ray, skeletal survey, skull x-ray series and ultrasound (liver, spleen, lymph-nodes, thyroid gland). Further investigations are based on the patient's symptoms and findings of basic tests.

The risk organs are hematopoietic system, spleen, liver or CNS which indicate a less favorable prognosis. The disease was stratified into 1) Single System LCH defined as one organ/system involved (uni- or multifocal): bone, skin, lymph node, hypothalamic-pituitary/ CNS, lungs and others (e.g. thyroid, gut) 2) Multisystem LCH defined as two or more organs/ systems involved: with involvement of "Risk Organs", without involvement of "Risk Organs".[5]

Treatment recommendations are based on site and extension of the disease. Surgical excision should limit in solitary skin lesion. Cutaneous LCH treatment includes phototherapy: Psoralen plus ultraviolet A and narrow band ultraviolet B, Thalidomide, Azathioprine and Methotrexate.[5] Multisystem LCH or single systemic with multifocal lesions or with special site lesions should be treated with systemic treatment. Vinblastine/prednisolone has never been proven effective for adults. Some experts prefer monotherapy with cladribine, cytarabine or etoposide.[5]

From the investigation outcomes, our patient was diagnosed with multi-sytem LCH (cutaneous and lung). Nevertheless, the proper treatment plans are still waiting, depend on the bone marrow biopsy involvement.

References

1. Arico M, Girschikofsky M, Genereau T, Klersy C, McClain K, Grois N et al. Langerhans cell histiocytosis in adults. Report from the International Registry of the Histiocyte Society. Eur J Cancer. 2003;39:2341-8.
2. Willman CL, Busque L, Griffith BB, Favara BE, McClain KL, Duncan MH et al. Langerhans'-cell histiocytosis (histiocytosis X)--a clonal proliferative disease. N Engl J Med. 1994;331:154-60.
3. Feldman AL, Berthold F, Arceci RJ, Abramowsky C, Shehata BM, Mann KP et al. Clonal relationship between precursor T-lymphoblastic leukaemia/lymphoma and Langerhans-cell histiocytosis. Lancet Oncol. 2005;6:435-7.
4. Edelbroek JR, Vermeer MH, Jansen PM, Stoof TJ, van der Linden MM, Horvath B et al. Langerhans cell histiocytosis first presenting in the skin in adults: frequent association with a second haematological malignancy. Br J Dermatol. 2012;167:1287-94.
5. Girschikofsky M, Arico M, Castillo D, Chu A, Doberauer C, Fichter J et al. Management of adult patients with Langerhans cell histiocytosis: recommendations from an expert panel on behalf of Euro-Histio-Net. Orphanet J Rare Dis. 2013;8:72.