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Lecture: Histiocytic and Dendritic Cell Lesions

SAMS questions

1. What is the most common site of involvement in patients with Langerhans cell histiocytosis?
   a. Skin
   b. Pituitary gland
   c. Bones
   d. Spleen
   e. Lymph nodes

2. Langerhans cell histiocytosis involving the lungs is associated with which factor?
   a. Smoking
   b. Other sites of Langerhans cell histiocytosis
   c. Young patient age
   d. Absence of *BRAF V600E* mutation
   e. RAS mutations

3. What feature is most characteristic of Erdheim-Chester disease?
   a. Bone lesions composed of eosinophils, histiocytes, and emperipolesis
   b. Histiocytes with an CD1a+, CD68+, factor XIII+ immunophenotype
   c. Bilateral involvement of long bones shown by radiologic imaging studies
   d. "Hairy kidney" as shown by radiologic imaging studies
   e. Absence of *BRAF V600E* mutation

4. What feature is most common in Rosai-Dorfman disease?
   a. Bilateral cervical lymphadenopathy
   b. *SLC29A3* mutation
   c. Involvement of bones
   d. *BRAF V600E* mutation
   e. Histiocytes with a CD1a+, S100+ immunophenotype

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Answers to SAMS questions

1. What is the most common site of involvement in patients with Langerhans cell histiocytosis?

   Answer: C

By far, bones are most often involved in patients with Langerhans cell histiocytosis, in about 80% of patients. The other choices listed are also sites of disease, but at a lower frequency: skin, 30%; pituitary gland, 25%; spleen, 15%; lymph nodes, 10%.

Reference

Emile J-F, Abla O, Fraitag S, et al. Revised classification of histiocytosis and neoplasms of the macrophage-dendritic cell lineages. Blood 2016; 127: 2672-2681.

2. Langerhans cell histiocytosis involving the lungs is associated with which factor?

   Answer: A

Langerhans cells histiocytosis (LCH) of the lungs is strongly associated with cigarette smoking and can resolve once smoking is discontinued. The disease tends to be confined to the lungs without other sites of involvement and patients tend to be adults; children are uncommonly affected. At one time, pulmonary LCH was thought to be benign, but *BRAF V600E* mutations have been identified in many cases suggesting that pulmonary LCH is neoplastic, similar to other types of LCH. RAS mutations are very rare (or perhaps not yet described) in cases pulmonary LCH.

Reference

Roden AC, Hu X, Kip S, et al. BRAF V600E expression in Langerhans cell histiocytosis: clinical and immunohistochemical study on 25 pulmonary and 54 extrapulmonary cases. Am J Surg Pathol 2014; 38:548-551.

3. What feature is most characteristic of Erdheim-Chester disease?

   Answer: B

The lesions of Erdheim-Chester disease (ECD) are composed of histiocytes (often foamy), and commonly associated with Touton giant cells and fibrosis. Eosinophils may be present, but are not prominent, and there is no emperipolesis. Prominent eosinophils, necrosis, and granulomas suggest Langerhans cell histiocytosis, and emperipolesis suggests Rosai-Dorfman disease. The histiocytes of ECD are positive for CD68, CD163, and factor XIII, but are negative for CD1a (unlike Langerhans cell histiocytosis). Over 90% of patients with ECD have osteosclerosis of

long bones, a characteristic finding to support the diagnosis. “Hairy kidney” is also typical of ECD but uncommon, in only a subset of patients. *BRAF V600E* mutations are common in ECD.

Reference

Estrada-Veras JI, O'Brien KJ, Boyd LC, et al. The clinical spectrum of Erdheim-Chester disease: an observational cohort study. Blood Adv 2017; 1:357-366.

4. What feature is most common in Rosai-Dorfman disease?

Answer A.

Patients with Rosai-Dorfman disease (RDD) commonly present with prominent cervical lymphadenopathy and, of the choices offered, this is the most common. However, 43% of patients can have extranodal involvement; about 10% of all patients have bone involvement. There is a rare form of RDD that is familial and associated with *SLC29A3* mutations, but this mutation has not been reported in the more common sporadic form of disease. Instead, about one third of cases of RDD have mutations involving *KRAS* or *MAP3K1*. The histiocytes of RDD have typical cytologic features with oval nuclei, central nucleoli, and abundant, pale, plate-like cytoplasm. These histiocytes are positive for S100 protein, but are negative for CD1a and CD207/langerin.

Reference

Garces S, Medeiros LJ, Patel KP, Li S, Pina-Oviedo S, Li J, Garces JC, Khoury JD, Yin CC. Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai-Dorfman disease. Mod Pathol 2017; 30:1367-1377.