DIAGNOSTIC CHALLENGE Answers

Case 1

Diagnosis

Langerhan cell histiocytosis

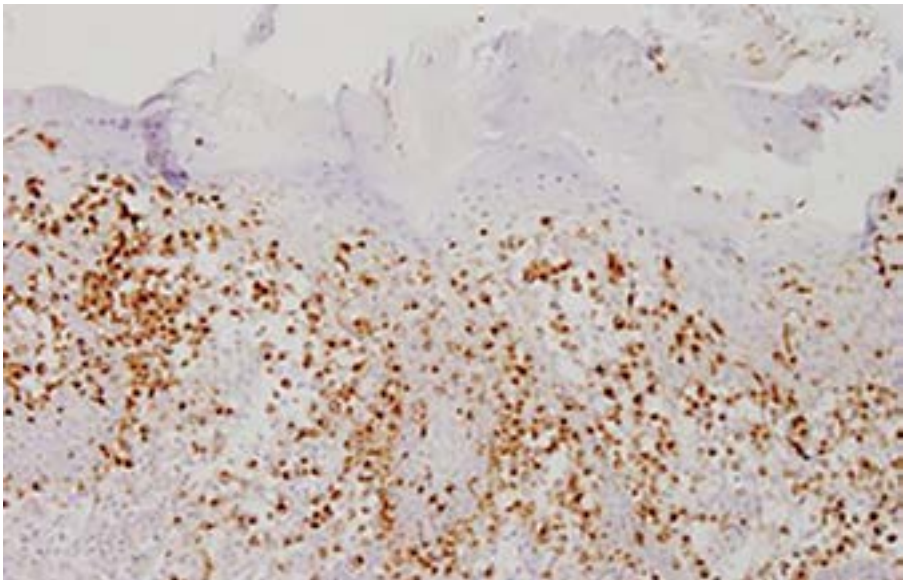

Figure 5

Diagnosis can be confirmed by positive immune histochemical staining of skin biopsy specimen by CD(1a) and langerine (CD 207) as shown in Figure 5.

Discussion

Langerhans cells are immune cells, normally found within the epidermis, where they act as antigen-presenting cells in an early warning system that fights foreign material. Langerhans cell histiocytosis (LCH) or histiocytosis X refers to a reactive increase in the number of Langerhans cells in the skin and other organs. LCH usually affects neonates, infants and young children, being rare in adults.

LCH can be localized, multifocal or multi-systemic. Systemic disease can involve organs such as bone marrow, liver, central nervous system, gastrointestinal tract, lungs and spleen. Systemic forms include Letterer-Siwe disease (with skin, lymph node and visceral involvement) and Hand-Schuller-Christian syndrome whereas a localized disease include eosinophilia granuloma. Self-healing reticulocytosis of infants is another self-limiting benign variant. All of these subtypes overlap and the skin disease is similar in all of them.

The clinical presentation depends upon the extent of organ involvement and symptoms depend upon the function compromised by the pressure effect of the mass of proliferating histiocytes in that organ. Cutaneous involvement presents in the form of an erythematous rash covered with greasy scales and petechiae over scalp and intertriginous areas but can also be widespread. There may be solitary or multiple papules or nodules with ulceration or necrosis. There may be hepato-spleeno-megaly, lung infiltration leading to cough and respiratory difficulty, involvement of the bones leading to lytic lesions on x ray and bone fractures. Involvement of the bone marrow causes pancytopenia leading to pallor, increased risk of infection and bleeding. There may be involvement of the pituitary stalk, causing Diabetes Insipidus.

Answers

LCH is usually diagnosed by characteristic rash and symptomatology of the involvement of a particular organ. The skin biopsy shows a predominant diffuse papillary dermal infiltrate composed of large cells with lobulated, eccentric grooved nuclei with a "coffee-bean shape" appearance and inconspicuous nucleoli. A variable polymorphic infiltrate of eosinophils, lymphocytes, plasma cells and neutrophils is usually admixed with neoplastic cells. Lagerhan cells can be confirmed by immunohistochemical staining with CD1a and CD 207 (Figure 2a & b). When histiocytosis is diagnosed in one organ (e.g., the skin or bone) other organs such as the bone marrow, lungs, liver, and kidneys are investigated accordingly to determine whether they are also affected by histiocytosis.

Treatment depends on the severity of the disease and the number of organs involved. Evidence of damage to the organs is more important than the involvement of the organ as such. Disease limited to the skin only may be treated with topical steroids, PUVA and topical nitrogen mustard. The disease affecting limited areas of the bone may be treated with steroid injections, curettage or radiotherapy. More extensive involvement is treated with systemic steroids and chemotherapy along with supportive treatment according to the dysfunction of the organ involved. LCH may respond to the BRAF-V600 inhibitors, vemurafenib and dabrafenib.

Persons with mild disease confined to one organ, with few or no symptoms, have a good prognosis but the condition may still last for many years and can become worse over time. Not all people with multiple organ involvement will respond to treatment. Children less than two years of age, with LCH affecting many organs, have a mortality rate of 40–50%.

Our Patient

Our patient had Langerhans cell histiocytosis with classical skin involvement, showing diagnostic histological and immune-histochemical features (Figure 1 & 2a/b). There was bone involvement, shown by lytic lesions on the x-ray skull (Figure 3), lung involvement depicted by coarse shadows in lung fields (Figure 4) and hepato-splenomegaly. Bone marrow was involved with pancytopenia and confirmed on bone marrow biopsy. Interestingly the patient also had diabetes insipidus with very low osmolarity of the urine. The patient was referred to a pediatric oncologist for chemotherapy.

Answers

Case 2

Differential Diagnosis

1. Pleomorphic adenoma
2. Warthin's tumor
3. Mucoepidermoid carcinoma
4. Adenoid cystic carcinoma
5. Oncocytoma
6. Metastatic lymph node
7. Sialadenitis

Differential Conditions	Important features
Pleomorphic adenoma	Painless, slow growing, firm mass
Warthin's tumor	Painless, slow growing mass, sometimes bilateral, typically in older adults, often males
Mucoepidermoid carcinoma	Painless or painful mass, possible facial nerve involvement
Adenoid cystic carcinoma	Slow growing, painful, often numbness in face, weakness of facial muscles and difficulty swallowing.
Oncocytoma	Painless, firm, slow growing mass
Metastatic lymph nodes	Often firm, possibly fixed
Sialadenitis	Painful, swollen, tender gland with systemic symptoms.

Diagnosis

Warthin's tumor of Parotid gland

Background

Warthin's tumor also known as papillary cystadenoma lymphomatosum is a benign salivary gland tumor that primarily affects the parotid gland. Etiology is not fully understood but several factors have been associated with it, with smoking being a significant risk factor. Warthin's tumor typically presents as a painless, slow-growing mass near the angle of the jaw. It is most commonly seen in older males.

Diagnosis involves a combination of clinical examination, and imaging studies. MRI and CT typically reveal a well-defined cystic lesion in the parotid gland. Confirmation is achieved through FNA and histopathological examination. The distinctive feature of Warthin's tumor on histopathological analysis is the presence of a double-layered oncocytic epithelium which forms papillary projections into cystic spaces, overlying a dense lymphoid stroma.

Superficial Parotidectomy is typically performed to remove the tumor, while preserving the facial nerve. Total Parotidectomy is considered if tumor involves deeper parts of the parotid gland.

Our Patient

Our patient had the typical features of Warthin's tumor. Superficial Parotidectomy of the patient was performed with regular follow-up visits every 6-12 months.
