Langerhans Cell Histiocytosis: osseous and extraosseus manifestations in Children.

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Learning objectives

-To show our experience and recognize the most characteristic imaging features that are sugestive of Langerhans Cell Histiocytosis (LCH) in osseous and extraosseous sites in children.

-To formulate appropriate differential diagnoses for the LCH in each common organs affected.

Background

Introduction

Langerhans Cell Histiocytosis (LCH) is a rare disease, which occurs mainly in children. It is reported to be between 2’6 -5’4 cases per million children in the general population. Frequently children affected are between 1-3 years old and boys are more often affected than girls.

This disorder is due to an uncontrolled monoclonal proliferation of abnormal Langerhans cells, as an immune response triggered by an unknown antigen. Those abnormal Langerhans cells infiltrate nearly any tissue or organ as well as lymph nodes, and associate chronic inflamation and Birbeck bodies.

The most common manifestations of the disease are bone lesions, whereas extraosseous involvement is not as frequent as, so may be more difficult to identify.

A broad range of clinical and radiological manifestations are produced by this disease. So radiologist must recognise the meaning of individual clinical and laboratory findings, as well as the relevance of image features for the differential diagnosis.

In this electronic presentation we will show different examples followed during 5 years since Juny 2005 to May 2006.

Imaging findings OR Procedure details

Osseous Langerhans Cell Histiocytosis
Bones are the most frequently detected area of involvement in LCH.

Clinical manifestations, multiple or solitary, are pain, tenderness, masses but sometimes can be silent.

The radiologic appearance of osseous LCH depends on the site of involvement and the phase of the disease.

Lesions typically are lytic with poorly or well-demarcated margins with or without reactive sclerosis.

**Radiological features**

**SKULL**: Lesions are solitary, typically round and with a well-defined nonesclerotic margin. They may contain a residual bone fragment, acquiring a typical form in "bull's-eye". The bone destruction is produced of the outer to the inner cranial table, looking as a "double-contour appearance".

These lesions can cross sutures, enlarge, coalesce and create an appearance referred as "geographic skull" (Fig.1).

Parietal and temporal bones are used to be affected as orbits (Fig. 2), clivus (Fig.3) mandibule.... (where the alveolar bone is destroyed looking at a "floating teeth") (Fig.4).

In other **FLAT BONES** as ribs or pelvis, lesions initially appear as poorly defined foci of osteolysis, with time they become well defined with or without sclerosis.

In clavicula, they generate a big periostic reaction.

In **LONG BONES**, lesions appear as an area of poorly definided medullary destruction. These defects can enlarge and erode endosteal cortex, with scalloping. (Fig.5)

**Femur** is the most frequently affected, followed by humero (Fig.6) and tibia. Diaphiseal lesions are the commonest (58%) while epiphyseal ones are relative rare.

Later, the lesions can grow down and appear sclerotic, well-defined, or may disappear with little or no deformity.

In spine, the lesions appear in the thoracic vertebral bodies, lumbar region are the next one in frequency.
Vertebral bodies are also affected, lumbar and dorsal ones are the most affected showing the typical appearance of “flat vertebrae”. (Fig.7)

**Extraosseus Langerhans Cell Histiocytosis.**

Extraosseus manifestations may be more difficult to identify and may demonstrate more aggressive behaviour than osseous ones.

It usually appears as a multisystem disease that involves pulmonary, thymic, hepatobiliary, splenic, gastrointestinal, neurologic, mucocutaneous or soft tissue system...

**Radiological features**

**Pulmonary involvement:**

Lesions have been found in 23-50% of those children with multisystem involvement.

The main diagnostic procedures are lung biopsy and bronchoalveolar lavage: >5% CD1 positive.

It is produced by an uncontrolled immune response with a rapid proliferation of Langerhans cells in the bronquial and bronchiolar epithelium. It leads to the formation of aggressive granulomas.

It will be seen as a diffuse, bilateral, symmetric, reticulonodular pattern, with micronodules and cysts. Later, the disease will progress to a honeycomblike pattern. (Fig.8)

Upper and middle lobes are the preferential localization. Costophrenic angles are spared.

It is rare to find pleural effusion, ground glass opacities or hilar lymphadenopathies.

Spontaneous pneumothorax and pneumomediastinum are acute complications of pulmonary LCH.

Differential diagnoses:

- Lymphangioleiomyomatosis: includes small cysts but in lung bases, and nodules will not been seen.
- Emphysema: absence of cystic lesions and nodules.
- Cystic bronchiectasis: Cystic lesions continue the course of the bronchial tree.
- Sarcoidosis: Apical honeycomlike pattern. Adenopathies and perylymphatic nodules.

- Interstitial pneumonia: There are groun glass opacities in lung bases and costophrenic angles.

**Thymic involvement:**

Is rare, and it is usually asociated a multisystemic disease. In many cases it coexists with pulmonary involvement.

We will see a thymic enlargement, which is heterogeneus, with septal contrast-enhancement and cystic areas. Puntate or serpentine calcifications are also typical. *(Fig.9.)*

Diferential diagnoses:

- HIV-related infections, teratoma, thymoma, thimic rebound hyperplasia, confluent lymphadenopathy.

**Hepatobiliary involvement:**

Hepatobiliary involvement is associated in a 50-60% of children with multisystemic disease. It occurs because Langerhans cells directly infiltrate periportal regions of the liver, showing a marked affinity for bile ducts.

In the histopatologic process there are four phases: during the proliferative and granulomatous phases the infiltration of Langerhans cells causes edema and periportal inflammation that we well see as nodular areas of hypoecogenicity and hypoattenuation at CT *(Fig 10).* We will also see hyperintesity at T2WI due to inflammation.

In the xantogranulomatous phase, histiocytes ingest fat-cotaning cells membrane debris so in T1WI MRI we will se the nodules (hypoattenuated and hypoecogenics in CT and US) hyperintense due to fat.

The final phase is respresented by fibrosis and may leads to a sclerosing cholangitis.

Whe it evolucionates to liver failure, the only curative treatment is the orthotopic transplantation.

Differential diagnosis: lymphoma, leukemia, hepatitis or cholangiopathies caused by infectious afents.. ischemia…

**Digestive tract involvement**
It is a rare and aggressive involvement, and its symptoms are not specific. Mostly cases, gastrointestinal lesions will be preceded by cutaneous rash, so cutaneous, mucosal and digestive tract involvement may be considered as a single one.

In conventional barium studies, the findings are no specific, coarsening and cobblestone mucosal pattern, luminal narrowing, increase separation of the loops because of edematous inflammation.

CT and MRI may show few specific features: leading to alternating narrowing and dilatation of the lumen in neighboring segments, edematous infiltration of the mesenteric fat, free fluid..

**Central Nervous System involvement**

It occurs in 23-35% in the most cases are affected by multisystem disease.

Pituitary and hypothalamus may be involved by direct extension from a focus in the sphenoid bone. But Langerhans cells proliferation also may arise from cells of blood vessels that coalesce to form granulomatous masses.

Main MRI imaging features are space-occupying lesions (hypothalamic-neurohypophyseal axis, central nervous system), will be seen as the loss of the normally high signal intensity of the posterior neurohypophysis on T1W images, enlarged pituitary stalk and intense enhancement after i.v. injection.

Intraaxial neurodegenerative changes is the second most frequent pattern of CNS, showing bilateral, symmetric lesions in the cerebellumos (Fig 11), basal ganglia or brainstem, representing diffuse inflammatory brain damage. It will leads to demyelination and gliosis resembling, at the last states that seen in leukencephalopathy.

Differential diagnosis: encephalomyelitis, multiphasic disseminate encephalitis, metabolic and degenerative disorders, metabolic and degenerative leukencephalopathy.

**Head and Neck**

It is a common site of involvement with a reported prevalence of 60-82% among children with a diagnosis of Langerhans cell histiocytosis.

The manifestations may include none, soft tissue lesions, cervical lymphadenopathy... other diseases as lymphoma and Rosai-Dorfman (skin is not affected) disease also presents massive adenopathies and soft-tissue lesions.
Images for this section:

**Fig. 1:** Figure 1. Well-defined lytic lesion in the parietal bone, with geographic margins, crossing the lambdoid suture.

**Fig. 2:** Figure 2. Ovoid, soft-tissue mass in the lateral orbital wall with osseous destruction with intracranial and intraorbit mass effect.
Fig. 3: Multisystemic disease in remission in an 12 year-old girl, with a rerpinginous, and sclerotic lesion involving the clivus with bone destruction.

Fig. 4: Typical imagen in "floating teeth" in the mandibule.
Fig. 5: Fig.5. 3 year-old child, with two lesions in femur and ischium.
Fig. 6: LCH in a 3-year-old girl with shoulder pain. AP view of the shoulder shows a partial well-defined lytic lesion in humerus.

13-year-old boy with a two month history of dorsal pain.

Fig. 7
**Fig. 8:** Pulmonary involvement in multisystem LCH in an 1-year-old girl. CT scan shows thin-walled cystic air spaces and a big mediastinal mass.

**Fig. 9:** Histiocytic infiltration of the thymus associated with pulmonary disease (fig 7). CT scan shows a heterogeneous upper anterior mediastinal mass with multiple and small calcifications.
**Fig. 10:** Figure 9. US and CT scans shows hepatosplenomegaly and small hypoattenuating nodules in spleen representing LCH infiltration in a 1-year-old girl.

**Fig. 11:** Figure 10. Ten year-old-boy with multisystem LCH. MRI shows an hyperintense on T2-weighted images cerebelous lesion.
Conclusion

Due to the broad range of manifestations and its inespecific and uncommon clinical course, the radiologist must know the spectrum of clinical features and radiological appearances that will facilitate an early diagnosis of Langerhans Cell Histiocytosis.

Personal Information

References