Neuroimaging of Langerhans Cell Histiocytosis

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I. INTRODUCTION

CASE REPORT
OUR PATIENT: PRESENTATION

• 23y/o M without significant PMHX.
• He had a MVA with a head to steering wheel trauma. He suffered a left forehead laceration. Thereafter he had progressive swelling of the affected eye, peri-orbital redness and sensation of sinus fullness. No fevers/chills/sweats/wt loss. He went to see an internist one month after the MVA. Ointment was prescribed.
• The patient felt this helped so he continued to use the ointment for about a month.
• With time, the patient’s eye was more swollen, so he presented to an ophthalmologist two months post-MVA. The ophthalmologist prescribed oral antibiotic and requested a CT scan. The scan was performed at an outside hospital.
OUR PATIENT: CT SCAN

• CT posterior fossa and orbits:
  • Exophthalmos, inhomogeneous mass 3.5x3x2cm with rim enhancement and low-density center, which is centered on the posterior roof of the orbit.

• Referred to BIDMC and admitted.
OUR PATIENT: HISTORY

• PAST MEDICAL/SURGICAL HISTORY:
  • None

• SOCIAL HISTORY:
  • born/raised in Arizona
  • moved to Massachusetts 2 years ago
  • works as photo lab supervisor
  • lives in Halifax with parents and son (22 months old)
  • active, camps, fishes. Travel to Mexico once, years ago.
  • no smoking, rare etoh, no ivdu
  • lots of tattoos, about 2 per year. always in tattoo parlors.
  • sexually active with women. currently monogamous.
OUR PATIENT: HISTORY

• PAST MEDICAL/SURGICAL HISTORY:
  • None

• FAMILY HISTORY:
  • healthy son.
  • no diseases in mom/dad/siblings

• ALLERGIES:
  • NKDA

• MEDICATIONS at home:
  • po abx (cannot ascertain from history)
OUR PATIENT: PHYSICAL EXAM

- PHYSICAL EXAM:
  - Gen: NAD, normal respiratory effort.
  - Mental status: Awake and alert, cooperative with exam, normal affect.
  - Orientation: Oriented to person, place, and date.
  - Speech intact.
  - CN: Left peri-orbital swelling and erythema; mild proptosis, chemosis; no audible bruit; no pulsation;
  - II: Pupils equally round and reactive to light bilaterally. Visual fields are full to confrontation.
  - III, IV, VI: Extraocular movements intact except for discreet limitation in extreme upward gaze on left.
  - V, VII: Facial strength and sensation intact and symmetric.
  - XII: Tongue midline without fasciculation.
  - Sensation: Intact to light touch bilaterally.
OUR PATIENT: MRI

T1 Isointense lesion

MRI: Sagittal T1 C(-)
MRI: Axial T1 C(-)
MRI: Coronal T1 C(-)

(PACS, Beth Israel Deaconess Medical Center. 2009.)
OUR PATIENT: MRI

**Heterogeneous**

**Enhancement**

MRI: Sagittal T1 C(+)
MRI: Axial T1 C(+)
MRI: Coronal T1 C(+)
OUR PATIENT: SURGERY

• Surgery:
  • Left-sided 1.5 craniotomy for dissection and decompression
  • Intra-operative image guidance with BrainLab
  • Microscopic dissection and decompression of middle temporal fossa, anterior skull base and orbital roof
  • Intra-orbital decompression, dissection and evacuation of lesion that looks like chronic hematoma/abscess
  • Fresh frozen analysis confirmed PMN infiltrate consistent with chronic inflammation and abscess
  • Intra-operative cultures were sent off for gram-stain, culture and sensitivity
  • Pericranial autograft for repair
  • Autologous cranioplasty
OUR PATIENT: MANAGEMENT

• Management of the orbital abscess was started by the infectious disease team with Cefepime, AmBisome and Vancomycin.

• All cultures negative!

• ...and the pathology examination...
OUR PATIENT: PATHOLOGY

• Pathology Examination, ten days later:

• SOFT TISSUE, RETRO-ORBITAL/CRANIAL FOSSA REGION, BIOPSY:
  • ATYPICAL HISTIOCYTIC AND EOSINOPHIL RICH INFILTRATE
  • “Overall, this is an unusual lesion, with histiocytic and eosinophilic rich infiltrate. The eosinophils form almost an abscess, while the histiocytes are in an organized bundles and display an unusual immunohistochemical profile characteristic of Langerhans Cell Histiocytosis”

• Patient began LCH study, looking for other foci...
OUR PATIENT: LCH STUDY

Whole body BONE SCAN with Tc-99m

Skull BONE SCAN with Tc-99m and X-RAYS

Whole body BONE SCAN with Tc-99m

(Unifocal involvement)

(PACS, Beth Israel Deaconess Medical Center. 2009.)
OUR PATIENT: DIAGNOSIS

SO, THE PRELIMINARY DIAGNOSIS WAS:

**UNIFOCAL ORBITAL LANGERHANS CELL HISTIOCYTOSIS**

... *and, what is LCH???
II. Langerhans Cell Histiocytosis

DEFINITION
LCH: DEFINITION

• *Histiocytosis X* is a rare disease of unknown cause.

• It is an uncommon proliferative disorder of bone marrow-derived antigen-presenting cells of the dendritic cell line, also known as *Langerhans cells*.

• The basic pathological feature of this disease is to form tumor masses or granulomatosis with destruction of the surrounding tissues.

*Electron Microscope: Langerhans Cell*

LCH: TERMINOLOGY

• In 1953 L. Lichtenstein grouped three distinct clinical syndromes that show indistinguishable histology, under the term “Histiocytosis X”.
  • Eosinophilic Granuloma
    • Limited to bone (5-15y)
  • Hand-Schüller-Christian disease
    • Multifocal bone lesions and extraskeletal involvement of RES and pituitary gland (1-5y)
  • Letterer-Siwe disease
    • Disseminated involvement of the RES with fulminant clinical course (<2y)
• The actual term for these disease is “Langerhans Cell Histiocytosis”
III. Langerhans Cell Histiocytosis

EPIDEMIOLOGY
LCH: EPIDEMIOLOGY

• LCH is more common in children than in adults, with most cases being diagnosed before the age of 15 years.
• The incidence is estimated at between 0.2 and 2 per 100,000 children under 15 years of age.
• Large series tend to demonstrate a preponderance in males, sometimes as high as 60% to 70% of cases.
• Is more common in whites of northern European descent.
IV. Langerhans Cell Histiocytosis

CLINICAL PRESENTATION
LCH: SITES OF INVOLVEMENT

• Unifocal (65%)
  • Bone (90%)
    • Skull
    • Femur
    • Pelvis
    • Ribs
    • Vertebrae
      – T > L > C
  • Others (10%)
    • Lung
    • Lymph node
    • Skin

• Multifocal (45%)
  • Bone (60%)
    • Skull (>50%)
  • Bone + Soft Tissue (25%)
  • Soft Tissue (15%)
LCH: SIGNS AND SYMPTOMS

- **Skull**
  - Painful, immobile scalp mass that may have recently enlarged.
- **Spine**
  - Local pain, back stiffness, torticollis, or kyphoscoliosis.
- **Pituitary**
  - Diabetes insipidus, panhypopituitarism
- **Soft tissue and RES**
  - Fever, hepatosplenomegaly, lymphadenopathy, pancytopenia, skin lesions
V. Langerhans Cell Histiocytosis

PATHOLOGY
LCH: PATHOLOGY

• The key feature is the *presence of Langerhans cells*.
• They show positive immunohistochemical staining for **CD1a** and **S-100**
• The diagnostic gold standard feature is the ultra-structural identification of **Birbeck granules**, which are 34nm wide tubular or tennis-racket-shaped intra-cytoplasmic penta-laminar structures with a zipper-like central core.
LCH: PATHOLOGY

**PATHOLOGY: Langerhans Cell (s100, CD1a)**

**ELECTRON MICROSCOPE: Langerhans Cell (Birbeck granules)**
(Hasegawa K, Mitomi T, Kowa H, Motoori T, Yagisita S. A clinico-pathological study of adult histiocytosis X involving the brain. J Neurol Neurosurg Psychiatry.1993 Sep;56(9):1008–1012)
VI. Neuroimaging

CALVARIA
LCH NEUROIMAGING: CALVARIA

- In the calvarium, the lesions are round or oval lytic lesions, and have a characteristic beveled edges.

LCH NEUROIMAGING: CALVARIA

• On MRI, lesions are:
  • T1: isointense to gray matter
  • T2: Isointense or hyperintense
  • Variable enhancement after gadolinium administration

VII. Neuroimaging

SKULL BASE
LCH NEUROIMAGING: SKULL BASE

- Radiologic findings:
  - Destructive, lytic “punched out” bone lesions

LCH NEUROIMAGING: SKULL BASE

- On MRI:
  - T1: variable signal intensity
  - T2: hyperintense
  - Homogeneous enhancement on CT and MRI after contrast administration

VIII. Neuroimaging

CRANIOFACIAL
LCH NEUROIMAGING: FACIAL SWELLING

- LCH typically presents as rapidly progressive facial swelling

LCH NEUROIMAGING: MANDIBLE

• The mandible is the second most common location of LCH
• Mandible lesions tend to destroy alveolar bone, which produces the radiologic appearance of “floating teeth”

LCH NEUROIMAGING: ORBITAL

- Orbital LCH is characteristically:
  - Isointense to gray matter on T1, T2, and proton density sequences
  - Enhance avidly on CT and MRI after contrast administration.

(PACS, Beth Israel Deaconess Medical Center. 2009.)
IX. Neuroimaging

CENTRAL NERVOUS SYSTEM
LCH NEUROIMAGING: CNS

• The most common CNS locations involved are the hypothalamic–pituitary axis and cerebellum.
• Diabetes insipidus is the most common endocrine manifestation of LCH.
LCH NEUROIMAGING: CNS

- MRI findings in central diabetes insipidus are characterized:
  - Lack of high signal intensity of the posterior pituitary on T1-weighted images
  - Often associated with enhancement and thickening of the pituitary stalk of greater than 3 mm

LCH NEUROIMAGING: CNS

• Neurodegenerative changes are the second most frequent pattern.
  • Bilateral symmetric lesions in the cerebellum and basal ganglia of variable signal quality on MRI

LCH NEUROIMAGING: CNS

- Other more rare lesions includes parenchyma, meninges, pineal gland, choroid plexus...


X. Neuroimaging

SPINE LESIONS
LCH NEUROIMAGING: SPINE

- The lesions are similar to skull lesions.
- More than 80% involves the vertebral body, and is usually limited to a single vertebral level.
- Vertebra can be partially or completely collapsed (*vertebra plana*)
LCH NEUROIMAGING: SPINE

MRI: Sagittal T1 C(-)  
MRI: Sagittal T1 C(-) 

XI. Langerhans Cell Histiocytosis

DIFFERENTIAL DIAGNOSES
# LCH: Differential Diagnoses

<table>
<thead>
<tr>
<th>Chronic Osteomyelitis</th>
<th>Bone Metastases</th>
<th>Aneurysmal Bone Cyst</th>
<th>Fibrous Dysplasia</th>
<th>Bone Infarct</th>
<th>Acute Pyogenic Osteomyelitis</th>
<th>Osteosarcoma, Variants</th>
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LCH: DIFFERENTIAL DIAGNOSES

X-RAY: Lateral view
CT: Axial, Bone Window
CT: Axial, Bone Window

(Chronic Osteomyelitis. PACS, Beth Israel Deaconess Medical Center. 2009.)

MRI: Sagittal T1 C(-)
MRI: Coronal T1 C(+)

Renal Cancer Metastasis

(Osteomyelitis)

(Skull Metastasis. PACS, Beth Israel Deaconess Medical Center. 2009.)
CONCLUSIONS
CONCLUSIONS

• LCH is a rare disease which mainly affect bone
• The neuroimaging of LCH is, in most of the cases, non-specific and it can vary depending on the location, specially on MRI
• LCH should be considered as a differential diagnosis of craniofacial tumors
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REFERENCES

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