Role of imaging in the clinical management of Langerhans Cell Histiocytosis in the brain

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Learning objectives

1) To exemplify the presentation of Langerhans Cell Histiocytosis (LCH) in the brain at different stages, from the acute disease to the late course, including some complications.

2) To discuss the value of the imaging techniques, namely MR, common protocols and possible contribute of the newest techniques.
Background

The spectrum of LCH in the central nervous system (CNS) is diverse and rather well known. In fact, several review articles in the literature have been giving emphasis to this monocyte-macrophage system disease involving the CNS structures [1, 2]. Among these, the Histiocyte Society CNS LCH Study Group has developed a notorious work, namely by recruiting these rare cases and proposing guidelines [3].

However, from the past mysterious denomination of Histiocytosis X, to the latest knowledge about this neuropathological entity [4], a lot issues remains badly understood in terms of clinical importance.

Difficulties arise not only for the clinicians, who have to decide for the appropriated therapeutic and other measures in health care that these patients need, but also for neuroradiologists, who are called to participate in the evaluation of the disease in an integrated way.

The extreme rarity of LCH in the brain and unusual expressions are the major impediments to an easy management of this clinical condition.
To illustrate this Educational Exhibit we used 4 cases of patients with LCH in the brain treated in our institution, all of them males with the diagnosis at childhood or adolescent age (confirmed by electron microscopy in face of the presence of Birbeck granules in tissue samples).

The images were selected in order to show the wide spectrum of abnormalities of the disease affecting the brain and related or contiguous structures. Thinking primarily on the clinical issues to be clarified, the included images were grouped into several phases of the disease, starting from the initial staging, till the late evaluation of neurodegenerative effects.

Usually typified in three types of clinical presentation, with progressive grade of severity: 1) the eosinophil granuloma form, 2) Hand-Schüller-Christian disease and 2) Letterer-Siwe disease; LCH in the brain tends to be observed in patients with craniofacial lesions involving the orbital and temporal regions, also the paranasal sinus and skull-base bones, which probably represent risk factors for CNS lesions [3].

So, examining a patient suspected of having LCH brain involvement, where to look? How to comment? What cautions and general recommendations should be taken?

A) Initial evaluation

- Pituitary / hypothalamic involvement

Usually occurs in patients having diabetes insipidus.

Pituitary abnormalities include: lost of spontaneous hyperintense signal of the neurohypophysis on T1-WI (Fig. 4A), and stalk thickening, above 4 mm or of nodular expression (Fig. 1D; Fig. 4 B-C). Extension to the hypothalamic area is sometimes seen as signal abnormalities, or even local enhancement.

- Parenchymal enhancing lesions

Intraxial lesions can be identified either at supratentorial or infratentorial level, although more commonly in the supratentorial structures (Fig. 1), represented by focal enhancing lesions surrounded by edema in the acute phase (Fig. 2). They may be easily overlooked when "dot-like" (Fig. 5), however their size is usually bigger, ranging from a few millimeters to subcentrimetric lesions.

- Synchronous cranial and skull-base bone lesions
Bone lytic lesions in the cranial vault or in the skull base are in many cases identified by radiographic studies and/or CT before MR evaluation. Lesions affecting the central skull-base, in particular, are sometimes detected in patients having a clinical picture of diabetes insipidus, because of pituitary/hypothalamic commitment, also with multiple lesions in bones or other organs (Hand-Schüller-Christian disease).

Tumefactive lesions in the head (eosinophil granuloma type) are rather easily noticed, and characteristically correspond to focal bone lytic lesions of beveled margins, with epicranial and/or epidural component (Fig 1A, 1C). More subtle lesions should however be searched for.

As above referred, this kind of lesions (with soft tissue component) might represent markers for patients at risk of developing brain LCH, so they should be highlighted.

**B) Monitoring of brain lesions**

- Measure the size of the pre-existing lesions, search for edema, look for new lesions

These 3 points are to be checked when monitoring brain lesions.

The disappearance of edema accompanies the regression of the lesions (Fig. 2).

- Leukoencephalomalacia ("cystic changes")

Areas of leukoencephalomalacia are described in possible relation to the evolution of brain LCH lesions, as very rare findings though. These should be maintained under surveillance, since they may enlarge and even be an indication for drainage by external derivation (Fig. 5 C-D).

**C) Possible complications**

- Cerebral abscess / empyema

It is a potential complication occasionally seen in these multi-medicated and multi-treated patients. At the initial phase the diagnosis could be difficult, so close follow-up is important and advanced MR techniques may be helpful (Fig. 6).

- Intracranial hypertension (ex. from growing "cysts")

**D) Follow-up**

- Observe squealer parenchymal alterations and look for new lesions
This may look superfluous, but recurrences may appear even many years after (Fig. 5).

- Examine the bone reparation, check for new lytic lesions

**E) Neurodegenerative aspects**

- Late parenchymal lesions

These can be either in the white matter, as in the cerebellum (Fig. 9), or in the gray matter, at the basal nuclei or dentate nuclei.

- Vermian atrophy

The relation as a neurodegenerative effect of LCH is easily established when previous lesions in the cerebellum are documented; otherwise other causes have to be ruled out (Fig. 8).

- Leukoencephalopathy

This imaging feature in association to LCH is rare. Pattern of distribution and progression should be examined in long-term patients. Most probably, it related to some neurotoxicity of certain chemotherapeutic drugs (Fig. 7).

**Imaging protocol for a 1.5 T machine (from the Histioyte Society CNS LCH Study Group)**

**Basic Protocol**

- Axial T2-WI (≤ 5 mm slice thickness)
- Sagittal and coronal T1-WI (≤ 3 mm slice thickness), for the pituitary region
- Coronal T1-WI with gadolinium

**Extended Protocol (upon specific indications)**

1) In case of osseous skull lesions and meningeal lesions

- Additional coronal T1-WI with gadolinium and fat saturation (≤ 3 mm slice thickness)

2) In case of neurodegenerative disease

- Axial T1-WI with MTC
- Axial T2-WI SI and Axial T2-WI GRE
3) In case of space-occupying intracranial lesions

- Additional examination of the spinal canal

Possible role for new imaging techniques

Very few studies in the literature make use of the advanced MR techniques to approach patients with brain LCH. It would be interesting though to explore them, in order to document the pathological processes involved in this disease of florid expression.

The neurodegenerative changes especially, might be appreciated in a more precise and comprehensive way, namely using spectroscopy and imaging techniques to picture the brain microstructure [5, 6].
Conclusion

Potential severity of LCH affecting the brain implies the need of serial MR examinations, starting from the staging phase, as to rule out pituitary commitment only, till late evaluations to detect relapsing parenchymal disease and to monitor neurodegenerative effects.

Imaging protocols must be defined, as indicated by the recommendations of the Histiocyte Society that we follow, although the neuroradiologists should be able to analyze these cases in an integrated and adaptive way.

Finally, it is necessary to be aware of the therapeutic procedures in detail, since that these complex cases often depend on the usage of several drugs and require multi-treatments, this way to maximize an accurate diagnostic interpretation.
References


