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CYTODIAGNOSIS OF LANGERHANS' CELL HISTIOCYTOSIS – XANTHOMATOUS PHASE (A RARE CASE REPORT)

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Abstract:

Cytological findings of xanthomatous phase of Langerhans' cell histiocytosis, a rare self limiting disease is described in a 5-year-old girl who had presented with 4-year history of swellings over the left side forehead and left temporo-parietal regions. She also had one-year history of blood stained discharge from left ear.

Key words: Langerhans' cell histiocytosis, xanthomatous phase, cytodiagnosis.

Introduction:

- The term Langerhans' cell histiocytosis (LCH), earlier known as histiocytosis X, refers to a proliferative disorder characterized by infiltration of one or more organs by mononuclear cells having properties of a unique histiocyte, the Langerhans' cell [LC] [1].
- The LC is a histiocyte with characteristic racquet shaped Birbeck granules visible on electron microscopy [2].
- These cells originate in the bone marrow and travel via the blood to the lymphnode, thymus, lung and skin.
- They are an important component of immune system.
- The severity of the disease is directly influenced by the immaturity of the immune system [3].
- The detection of clonal histiocytes in LCH indicates that this disease is probably a clonal neoplastic disorder with highly variable biological behaviour [4].

LCH can be divided into three groups.

The three classic variants have been described according to the extent of LCH involvement:-

- Unifocal disease (Eosinophilic granuloma) in which the disease is limited to bone in patients who are usually 5-15 years old.
- Multifocal Unisystem disease (including cases of Hand-Schuller-Christian disease) usually seen in children 1-5 years age.

- Multi Focal Multi system disease (including cases of Letterer – Siwe disease) in which there is disseminated involvement of the RES with a fulminant clinical course in children less than 2 years old [5].

Up to 80% of LCH lesions in children are of EG type, and upto 90% occur in bone [6].

Case Report:

- A 5-year-old girl presented with swellings over the left side of forehead, left temporo-parietal region for 4years and blood stained discharge from left ear for one year. The ear discharge was blood stained but not purulent or foul smelling. There was no history of trauma or reduced hearing.
- On examination her vital parameters were within normal limits. The swelling on the left side of forehead measured 5 x 4 cms, was diffuse, cystic, non tender, non- compressible without local signs of inflammation. [Fig 1].
- A similar swelling was noted in the left temporo- parietal region over the pinna of the left ear which measured 4 x 3cms.
- Otoscopy revealed a reddish, polypoidal irregular mass which bled on probing, arising from the roof of the bony left auditary canal. Beyond the mass the ear canal and tympanic membrane were normal. [Fig 2]
- Further ENT and systemic examination did not reveal any abnormality.
- Complete blood counts and bone marrow aspiration of the patient were within normal limit except for mild increase in ESR.
- CT scan of the skull and temporal bones showed lytic lesions corresponding to two swellings [Fig 3]. The dura was intact.
- Fine needle aspiration of both the swellings was undertaken for cytological study using a 23 gauge needle. The smears were stained with Hematoxylin-Eosin (H & E) and Leishman's stain, which revealed moderate cellularity composed of many histiocytes admixed with eosinophils, neutrophils, lymphocytes and multinucleated giant cells [Fig 4]. The cytoplasm of the histiocytes was vacuolated (foamy) in majority of cells, pale blue or pale pink in some and revealed cytoplasmic process in few with well defined borders. The nucleus of histiocytes was large, pale round to oval to kidney shaped and vesicular in some, indented and showed longitudinal grooves (coffee bean) in few. The chromatin pattern was bland and nucleoli were generally small and frequently multiple. Many binucleated and multinucleated histiocytes were also seen. Some of the neutrophils and eosinophils showed hyper-segmentation of the nucleus.[Fig 5,6,7]The diagnosis of xanthomatous phase of langerhans cell histiocytosis was rendered.
- Biopsy of the left aural polyp revealed moderate cellularity composed of similar cells as in FNAC along with focal areas of fibrocollagenous tissue deposition
  [Fig 8]
- The immunohistochemistry showed diffuse S-100 positivity of the histiocytes [Fig.9].
- The patient was subjected for ultrasonographic examination of abdomen and x-rays of chest and long bones to rule out their involvement.

- The patient was then treated with oral methyl prednisolone 2 mg/kg/day for 1month.
- The swellings disappeared and discharge ceased within a week of initiation of the treatment. Since the activity of the disease appeared to have subsided the dosage was changed to an alternate day regimen tapered gradually and stopped after 4 months.
- The patient was on follow-up and one year later there was no recurrence.

Discussion:-

- LCH is currently considered to be a disorder of immune regulation, manifested by abnormal proliferation of histiocytes and granuloma formation [8].
- The LC, a unique histiocyte is the distinctive pathologic component of the disease. LCH can affect every organ.
- The most common sites are bone, skin, lymphnodes, ears, bone marrow, liver, spleen, lung and pituitary.
- Unusual sites include brain, thymus, pancreas, vulva and thyroid [9].
- Solitary LCH may occur in any bone, although there is a predilection for the flat bones with more than half of skeleton lesions occurring in the skull, mandible, ribs and pelvis [8].
- In the present case, lesions were limited to skull bone.
- The disease usually manifests in infancy and early childhood.
- In our case the age of the child is five years.
- The clinical manifestations of LCH are varied and depend on the sites and extent of involvement [1].
- Histopathologic evolution of LCH comprises four different phases.
- The first phase is proliferative phase characterized by the proliferation of histiocytes, eosinophilic leukocytes and other inflammatory cells with in the RES.
- In the second granulomatous phase these cells are intermingled with multinucleated giant cells.
- In the third xanthomatous phase, histiocytes are lipid-laiden and are called foam cells, and overall cellularity is decreased with onset of fibrosis.
- In the last fibrosis phase lesions become more fibrous showing an increased amount of collagen and further decrease of cellularity.
- During the early phase of LCH, lesions are cellular and are marked by aggregates or sheets of LC. Eosinophils are often identified.
- In older lesions, which may be mistaken for chronic osteomyelitis, myelofibrosis or non-specific benign fibrous lesions, are marked by a paucity of LCs and a fibrous background with or without eosinophils [7].
- A relationship exists between the type of histologic phase and the clinical type of disease. In general the proliferative phase is typical of acute disseminated LCH and granulomatous phase is typical of chronic focal or multifocal LCH as the name eosinophilic granuloma suggests.
- The xanthomatous reaction is usually seen in Hand-Schuller-Christian disease [9]. The FNAC in each of these phases is quite distinctive and reveals specific cell types that are described in each phase.

- In our case FNAC revealed many foamy histiocytes admixed with multi nucleated giants cells, eosinophils, neutrophils, scattered lymphocytes and few histiocytes with characteristic coffee-bean nuclear grooving and cytoplasmic processes, indicating the lesion is transiting from late granulomatous phase to xanthomatous phase.
- Histopathology section also revealed similar cells as in cytology along with focal areas of fibrosis and collagen deposition. Immunohistochemistry revealed diffuse S-100 positivity in LCs including giant cells and foamy cells.
- Though the xanthomatous phase is usually associated with Hand-Schuller-Christian disease, the lesions in our case were limited only to skull bone at multifocal areas. No extra-skeletal or multisystem involvement was seen.
- The differential diagnosis includes congenital histiocytomas, Juvenile xanthogranuloma, parasitic infection, and hypersensitivity reactions.
- In addition, or rare occasions, LCH can be associated with some malignancies like Lymphomas, Leukemia's, other solid tumours. Therefore further exclusion of malignancies including Hodgkins disease (HD), malignant melanoma, papillary thyroid carcinoma, malignant histiocytocis (MH) and other tumour cells with nuclear groovings should also be considered.
- Congenital histiocytomas show Birbeck granules only in few cells and are CD68 positive, CD1a negative and S-100 negative.
- In juvenile xanthogranuloma xanthoma cells are S-100 negative, CD68 positive [8].
- Parasitic infections and hypersensitivity reactions lack LCs.
- Malignancies are easily excluded when no malignant cells with obvious cytologic atypia are present in the smear [10].
- One must be aware of different morphologic patterns of LCHs and unusual appearances of Langerhans cells which may lead to diagnostic errors. Electron microscopic demonstration of specific birbeck granules and immunocytochemistry using CDIa & S100 protein are of value in establishing reliable diagnosis. Langerin is a recently identified lectin for which antibodies can be used as immunohistochemical markers of LCs [9].
- As LCH is a self limiting disease and responds relatively well to steroids and antibiotics, phase determination using FNAC without invasive biopsy is important for prediction of patient outcome and for patient management [7].
- FNAC should be done as the first line of investigation in suspected cases of LCH. In our opinion FNAC would not only obviate the need for a more invasive procedure, such as tissue biopsy, but would also provide a prompt and correct diagnosis with less invasive technique.

Conflicts of interest :NIL

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