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MULTISYSTEMIC LANGERHANS CELL HISTIOCYTOSIS IN ADULT – AN UNCOMMON INCIDENCE POSING A DIAGNOSTIC CHALLENGE

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder of Langerhans cells typically seen in infants and children. We report an uncommon case of multisystem LCH in an elderly woman.

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is a localized or systemic clonal proliferative disorder of langerhans cells. This disease is most commonly characterized by single or multiple osteolytic bone lesions demonstrating infiltration with or without histiocytic infiltration of lymph nodes, liver, skin, lungs, spleen, bone marrow, or nervous system. Langerhans' cell histiocytosis [(LCH), histiocytosis X] is a rare disease, which can involve any site and organ of the body. LCH may appear as an isolated lesion or as a widespread systemic disease. LCH has been diagnosed in all age groups, but is most common in children. The incidence appears one to two cases per million adults. We report a rare case of multisystem LCH in an adult patient of 68 years.

A 68 year old male came to our hospital with the complaint of hoarseness, low back ache and a supraclavicular mass. Prior to our hospital the patient was evaluated outside. FNAC done outside was suggestive of a lymphoproliferative disorder ?Hodgkins Lymphoma. Patient was evaluated in our hospital and relevant investigations were done. CT chest done showed left supraclavicular and mediastinal mass, lytic lesions in D10, D11 vertebrae and a small adrenal mass was identified. Histopathological examination of left cervical lymph nodes showed diffuse and sinusoidal infiltration by cells having

ample acidophilic cytoplasm, elongated vesicular nuclei with folds and prominent eosinophilic nucleoli along with scattered eosinophils, plasma cells and lymphoid cells. (Fig 1,2).

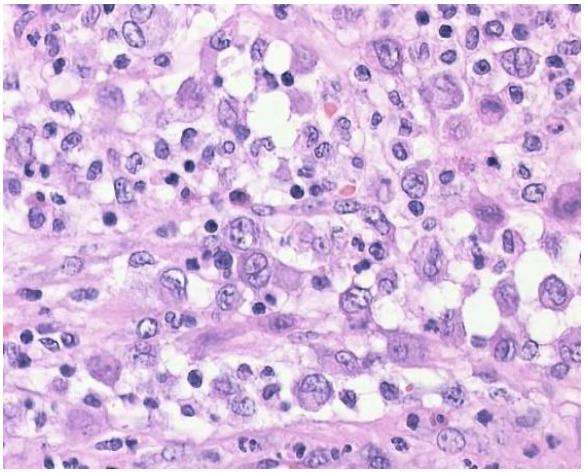

Figure 1: Photomicrograph shows diffuse infiltration by Langerhans cells (cells having ample acidophilic cytoplasm, elongated vesicular nuclei with folds and prominent eosinophilic nucleoli) along with scattered eosinophil s, plasma cells and lymphoid cells. (H&E, 40x).

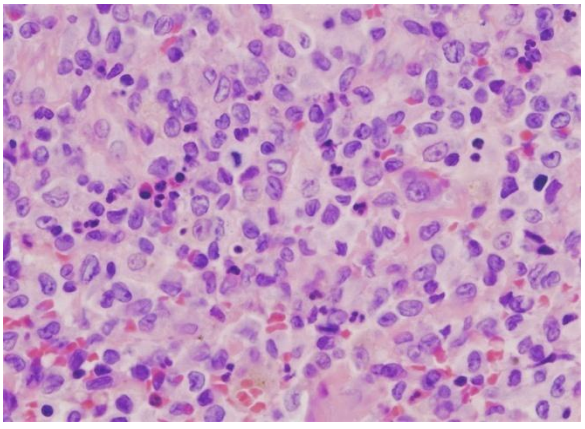

Figure 2: Photomicrograph showing diffuse infiltration bt Langerhans cells along with scattered eosinophils, plasma cells, lymphoid cells mimicking a Hodgkins Lymphoma. (H&E, 40x).

Features were suggestive of Langerhans Cell Histiocytosis. IHC done was positive for S-100, CD-68, Vimentin, HLA-DR (Fig 3,4,5,6) and show equivocal positivity with EMA in occasional cells. CD-15 and CD-30 expression was not seen. IHC diagnosis was compatible with LCH.

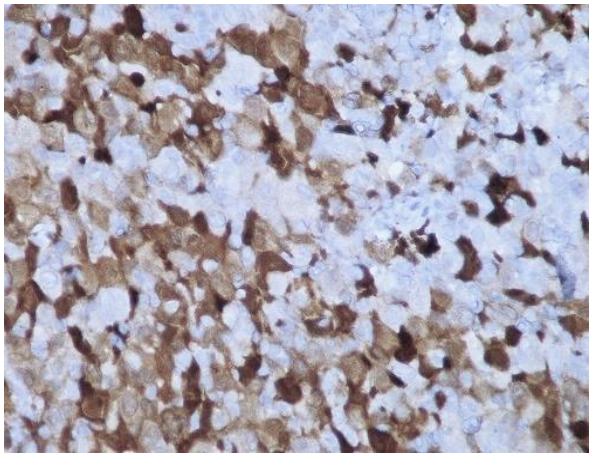

Figure 3: Immunohistochemistry of lymph node showing large cells positive for S-100.

Discussion

Langerhans cell histiocytosis (LCH) is a clinicopathologic entity characterized and defined by proliferation of Langerhans cells. In 1868, Langerhans discovered the epidermal dendritic cells that now bear his name.[1] It affects mainly children from 1 to 5 years. The incidence is 1/20,000 per year with a male predilection (male-to-female ratio of 2:1).[2] Adult LCH is v rare around one to two cases per million people per year.[3] The etiology of LCH is unknown.

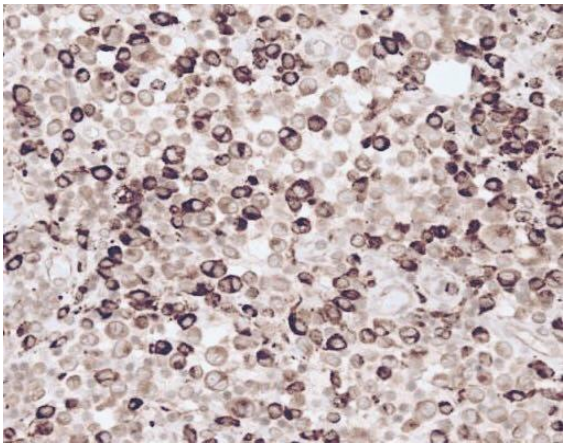

Figure 4: Immunohistochemistry of lymph node showing large cells positive for CD-68.

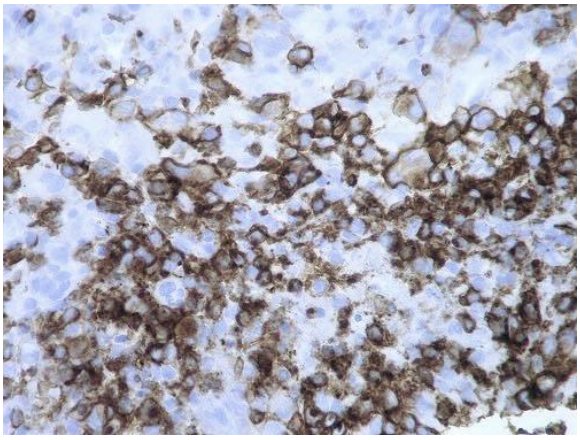

Figure 5: Immunohistochemistry of lymph node showing large cells positive for Vimentin.

A viral cause has been suggested but not substantiated.[4] The Langerhans cells are affected by recurrent cytogenetic alterations.[5] The classification of histiocytic disorders by the Histiocyte Society was made in 1997 and is based on the group of cells present in the lesions. The Histiocyte Society has divided histocytic disorders into 3 groups: dendritic cell histiocytosis, macrophage-related disorders, and malignant histiocytosis.[6] Patients commonly present with pain and swelling of affected bones, fever, night sweats, weight loss and nonspecific symptoms such as fatigue and organ involvement. The diagnosis of LCH is confirmed by histopathology, immunohistochemistry and electron microscopy.

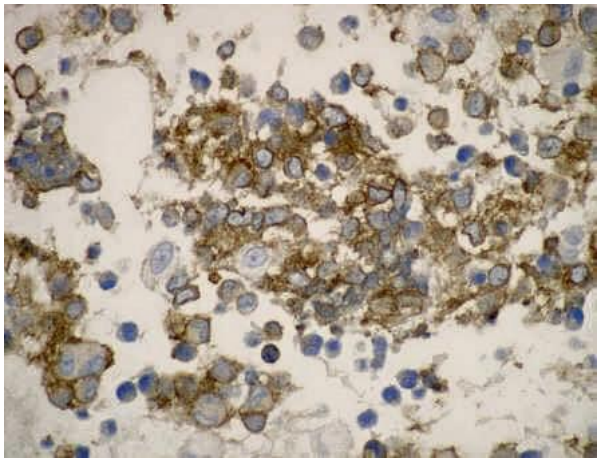

Figure 6: Immunohistochemistry of lymph node showing large cells positive for HLA-DR.

Histomorphologically, the characteristic feature of LCH is occurrence of Langerhans cells in clusters and sheets. The nuclei are typically grooved and irregularly contorted, with a thin nuclear membrane, delicate chromatin, and inconspicuous nucleoli. The cytoplasm is moderately abundant and slightly eosinophilic. The characteristic milieu of LCH includes admixture of large numbers of eosinophils, as well as lymphocytes, neutrophils and plasma cells.

Langerhans cells can exhibit minimal nuclear atypia a relatively brisk mitotic rate with upto 5-6 mitosis per 10 HPF. Involved lymph nodes have a sinus pattern with a secondary infiltration of the paracortex.[7]Langerhans cells have a characteristic immunophenotype CD1a and CD 207/ Langerin membrane positivity, nuclear and cytoplasmic expression of S-100 and CD45 negative immunostaining.[8]

On electron microscopy, the characteristic ultrastructural findings are birbeck granules, which are tennis racquet-shaped or zipper-shaped structures 33nm wide, with central striated lines.[9] LCH can be confused with other causes of lymphadenopathies like sinus histiocytosis with massive lymphadenopathy, dermatopathic lymphadenitis and lymphoproliferative disorders like hodgkins lymphoma due to its polymorphous morphology. However in sinus histiocytosis with massive lymphadenopathy there is a sinusoidal distribution of histiocytes which are much larger with round nuclei, distinct nucleoli and voluminious pale cytoplasm. Emperipolesis can be often seen. These histiocytes are negative for langerin and CD1a but immunopositive for S-100. In dermatopathic lymphadenopathy, large numbers of Langerhans and interdigitating dendritic cells with grooved nuclei are present with predominant paracortical rather than sinusoidal involvement. Greater admixture of lymphocytes, less distinct cell borders, absence of multinucleated forms, intermingling with melanin-laden macrophages and dendritic rather than ovoid appearance of the cells on S-100 immunostaining. Hodgkin lymphoma can pose a diagnostic difficulty with LCH due to large grooved cells with eosinophilic nucleoli in a polymorphous background in case of LCH can resemble HRS cells in hodgkins lymphoma however LCH is typically negative for CD15 and CD30. Also in case of an adult patient with LCH a thorough look for mitotic figures and malignant cytological features must be done keeping a Langerhans Cell Sarcoma in mind which also shows same positivity as LCH, differing only in frankly malignant cytological features as well as mitotic figures and has a more aggressive course and more commonly seen in older age group.[10]

Conclusion

Biopsy and a histopathological examination and immunohistochemical markers are essential to establish the diagnosis and and to confirm the diagnosis of LCH. The Histological appearance of LCH can mimic other lymphoproliferative disorders.

Recognition of the different patterns of LCH is important for recognizing this disease and separating LCH from other more common causes of lymphadenopathy. A differential diagnosis of nodular sclerosis Hodgkin lymphoma should also be considered, whenever a polymorphous population of small lymphocytes, eosinophils, plasma cells, and histiocytes is present in an adult.

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