Original Research Paper Pathology

SPECTRUM OF HISTIOCYTIC DISORDERS - CASE SERIES AND REVIEW OF LITERATURE

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ABSTRACT Histiocytic disorders are characterised by infiltration of the tissue with cells of monocyte or macrophage lineage. They range from benign reactive conditions to malignant life threatening diseases like haemophagocytic disorders. Some of the histiocytic disorders can be associated with other malignancies. The present case series is a retrospective analysis of six cases representing various spectrum of histiocytic disorders. It is important to be aware of these benign entities to distinguish it from similar looking malignant lesions to avoid inappropriate management.

KEYWORDS : Histiocytic disorders, Rosai Dorfman disease, sinus histiocytosis with Massive lymphadenopathy, soft tissue sarcoma, kikuchi's, haemophagocytosis.

INTRODUCTION:

Histiocytic disorders are characterised by infiltration of the tissue with cells of monocyte or macrophage lineage (1). Histiocytes are divided into 2 subgroups - antigen-presenting and antigen-processing cells, and all are derived by differentiation of monocytes in the tissues, under the influence of cytokines and possibly physical stimuli. Langherhans cells in the skin and Dendritic and interdigitating reticulum cells are localised to lymph nodes are antigen presenting cells. Antigen processing cells includes those cells which are involved in phagocytosis.

Histiocytic disorders has been recently classified into five groups. a) Langerhans-related b) cutaneous and muco-cutaneous c) malignant histiocytoses d) Rosai Dorfman Disease and e) haemophagocytic lymphohistiocytosis and macrophage activation syndrome (2).

Other way of classifying it is
"L" group: Langherhan cell histiocytosis, Erdheim Chester disease and extracutaneous Juvenile xanthogranuloma.
"C" group : Cutaneous and muco-cutaneous histiocytoses
"M" group: Malignant histiocytoses
"R" group : Rosai-Dorfman disease and miscellaneous non-cutaneous, non
Langerhans cell histiocytoses
"H" group : Haemophagocytic Lymphohistiocytosis and macrophage activation syndrome (2).
Storage disorders are also included under histiocytic disorders.
Here, we provide an overview of benign and reactive histiocytic disorders with a series of cases representing different spectrum of histiocytic diseases.

CASE SERIES:

CASE 1:

1 year old girl presented with cough and dyspnoea since 6 months. CT thorax showed diffuse ground glass opacity in both lungs, extensive small cysts in both lungs - suggestive of LCH. Biopsy of the lung revealed infiltration of the interstitial spaces by neoplastic Langherhans cells which was confirmed by immunohistochemistry for CD1a. Diagnosis of Langerhan cell histiocytosis was made on histology and confirmed by immunohistochemistry for CD1a.

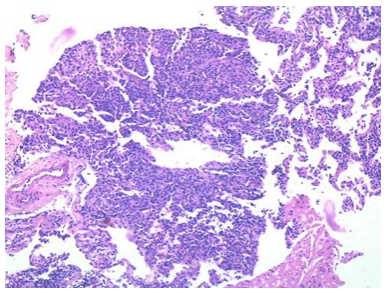

Fig 1: Interstitial spaces infiltrated by neoplastic Langherhans cells (10x)

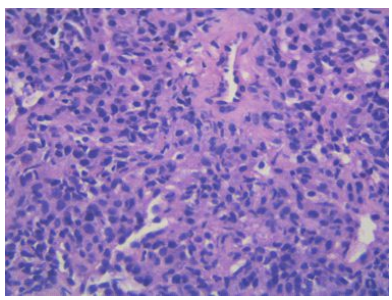

Fig 2: Interstitial spaces by neoplastic Langherhans cells (40x)

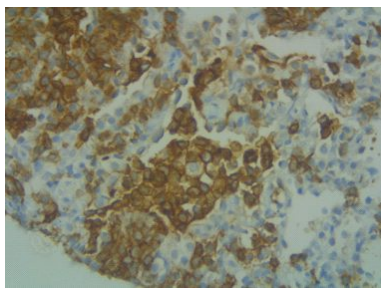

Fig 3: Immunohistochemistry for CD1a showing strong positivity

CASE 2:

25 year old obese female presented with mass in the sacral region

since 4 years. Clinical diagnosis was ? lipoma with fat necrosis/ xanthoma. Excision of the mass revealed a skin covered soft tissue mass with a firm grey white to yellow cut surface.

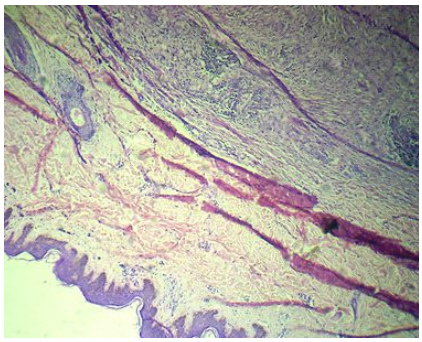

Fig 4: Skin with the dermis showing circumscribed lesion (4x)

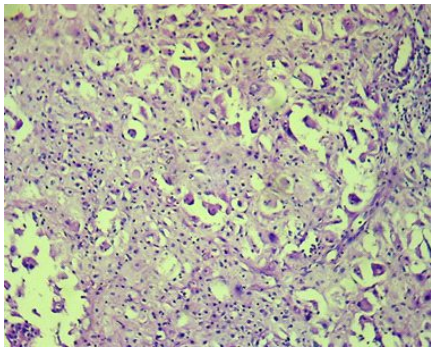

Fig 5: Sheets of foamy macrophages (10x)

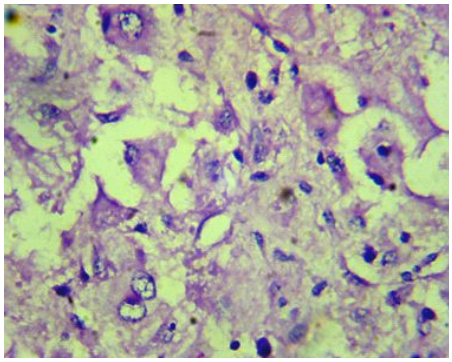

Fig 6: Foamy histiocytes with abundant granular eosinophilic cytoplasm (40x)

Diagnosis of xanthogranuloma was made based on histology.

CASE 3:

55 year old male presented with complaints of dyspepsia. Endoscopy showed nodule in the stomach. Biopsy revealed sheets of foamy histiocytes in the lamina propria.

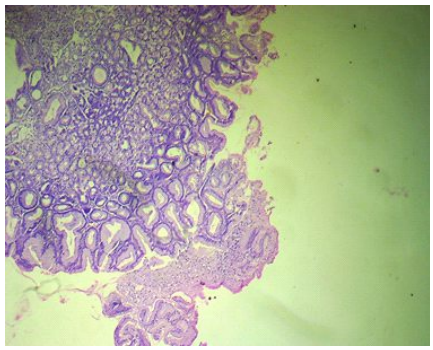

Fig 7: Gastric mucosa with lamina propria showing sheets of foamy macrophages (4x)

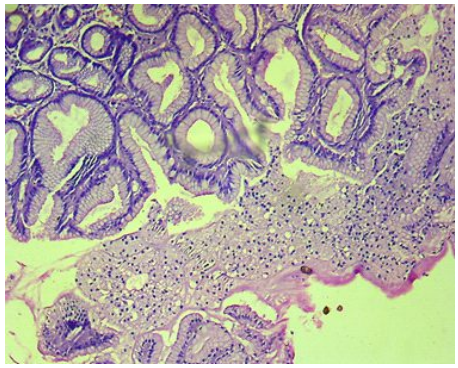

Fig 8: Sheets of foamy macrophages in the lamina propria (10x)

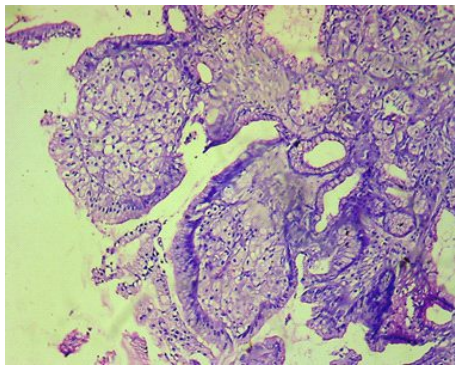

Fig 9: Expanded lamina propria with numerous foamy macrophages (10x)

CASE 4:

Seven month old child with history of developmental delay, failure to thrive and Hepatosplenomegaly.

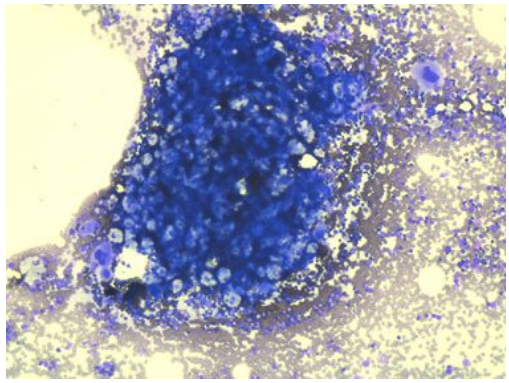

Fig 10: Bone marrow aspirate with cellular fragments

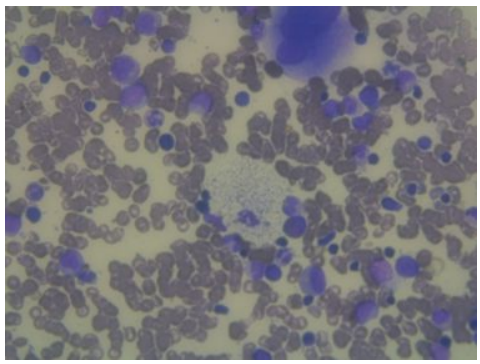

Fig 11: Bone marrow aspirate showing reticuloendothelial cell with foamy cytoplasm

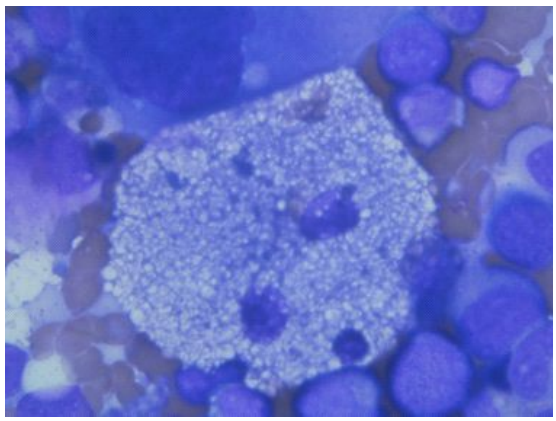

Fig 12: Sea-blue histiocyte containing abundant lipids in the Reticuloendothelial cell

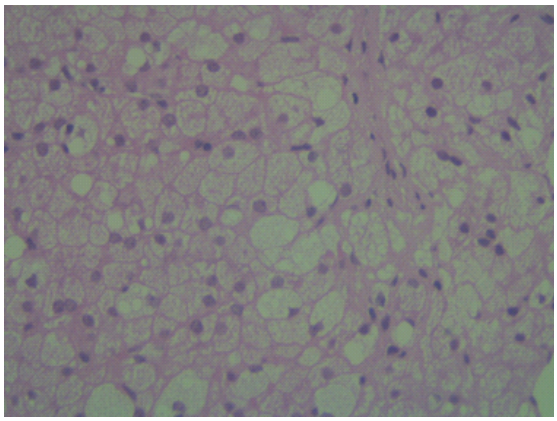

Fig 13: Liver biopsy showing pale staining clusters of foam cells containing sphingomyelin (40x)

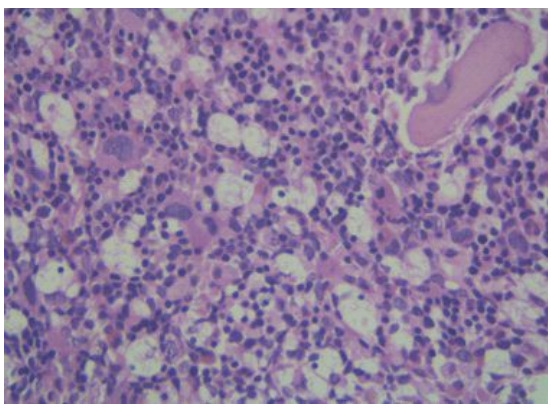

Fig 14: Trephine biopsy showing histiocytes with foamy cytoplasm (40x)

CASE 5:

19 year female who presented with a mass in the back of chest of short duration, clinically mimicking soft tissue sarcoma. MRI showed heterogeneously enhancing soft tissue lesion in the back of chest. The overlying skin and underlying muscle were free of tumour. Clinical diagnosis was soft tissue sarcoma.

Incisional Biopsy was done and sent for HPE which showed polymorphous inflammatory infiltrate with Emperipolesis.

histological examination of excisional biopsy showed polymorphous inflammatory infiltrate with plenty of macrophages with plasma cells. Most of the macrophages exhibit emperipolesis

A Differential Diagnosis of Rosai Dorfman disease / Plasma cell granuloma was considered. IHC showed large histiocytes positive for S-100, moderate numbers of lymphocytes positive for Cd3 & CD20, CD1, CD30 negative - consistent with Rosai Dorfman disease

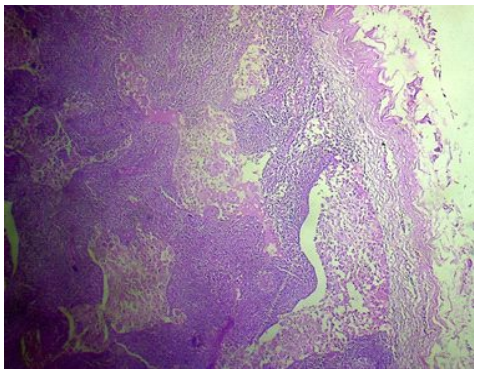

Fig 15: Lymphnode with dilated sinusoids with macrophages (4x)

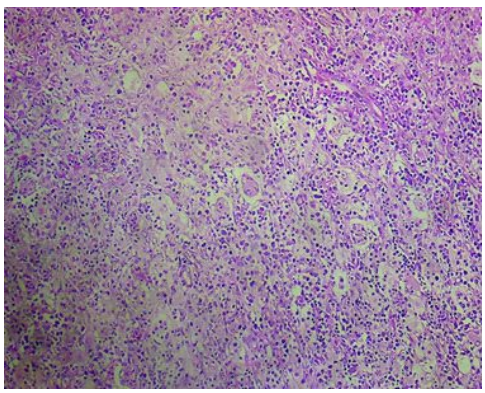

Fig 16: Polymorphous inflammatory infiltrate in the lymphnode (10x)

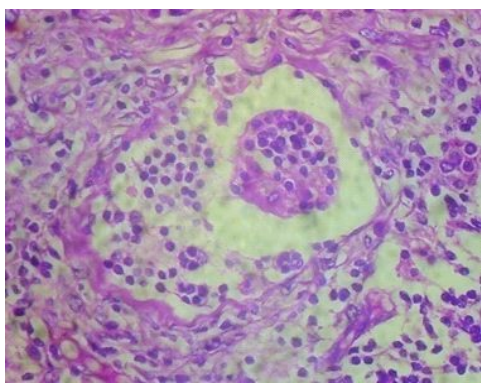

Fig 17: Macrophages exhibiting emperipolesis (40x)

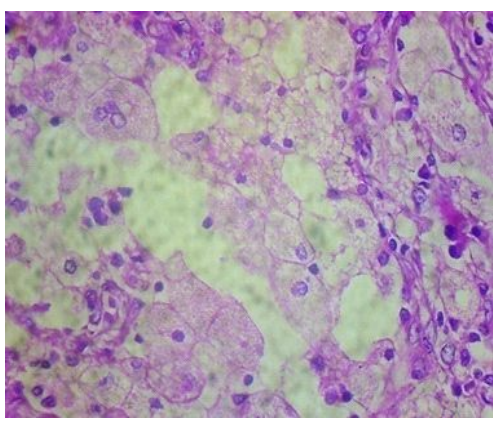

Fig 18 : Sheets of foamy histiocytes (40x)

CASE 6:

29 year old gentleman presented with history of gradually increasing cervical lymphadenopathy. No history of fever, evening rise of temperature.

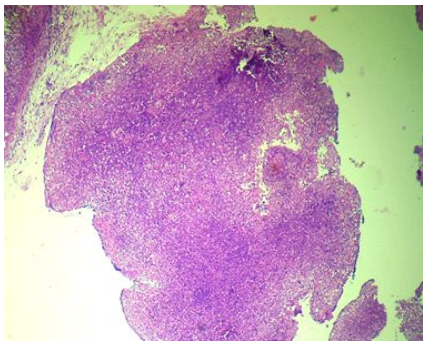

Fig 19: Fragmented lymphnode with karyorrhectic debri (4x)

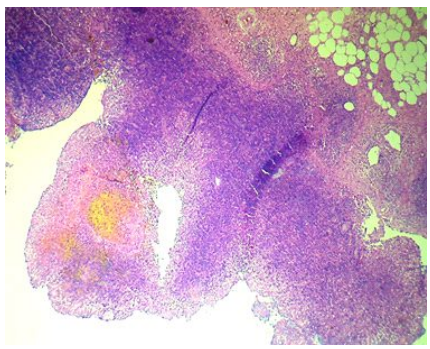

Fig 20: Lymphnode with distorted architecture and fibrinoid necrosis (4x)

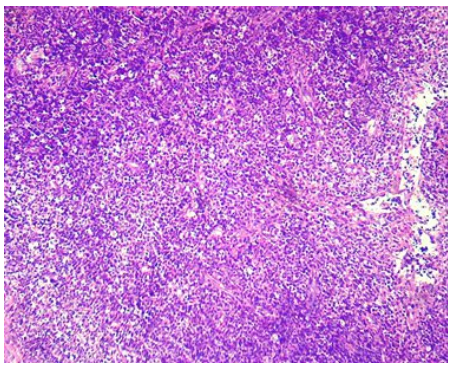

Fig 21: Areas of necrosis and fibrin deposits, apoptosis and histiocytes (10x)

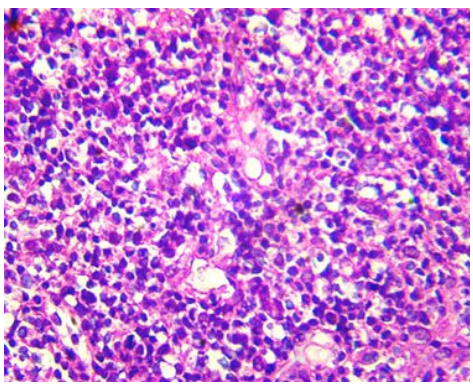

Fig 22: Areas of histiocytic proliferation (40x)

DISCUSSION:

"L" group - Langerhans cell histiocytosis (LCH):

LCH is the most common paediatric disorder of mononuclear phagocytic system. It is a disorder of antigen presenting cells in which there is neoplasic proliferation of pathologic Langerhan cells (3). It can either involve single system or multisystem. Single sytem involvement can be either unifocal or multifocal. LCH usually presents as a lytic bone lesion. The diagnosis is based on histology and immunohistochemistry. Histologically, it can present as a granulomatous inflammation along with pathologic Langerhans cells and other inflammatory cells such as eosinophils, T cells, macrophages and giant cells. The presence of CD1a positivity is in favour of Langherhan cell histiocytosis. On Electron microscopy, Birbeck granules can be identified (4).

The prognosis of LCH confined to skin and involving single system has a good prognosis compared to those having multisystem involvement.

"C" group - Xanthogranuloma:

Juvenile xanthogranuloma is one of the non-Langerhans histiocytic proliferative disorders (5). It usually occurs in the first two decades of life. The most common manifestation is a solitary cutaneous lesion. Juvenile xanthogranuloma can occur in adults. Xanthogranuloma in adults is characterized by absence of extracutaneous involvement (6). Histologically xanthogranulomas are characterized by infiltration of the dermis by histiocytes with foamy cytoplasm, lymphocytes and eosinophils. Giant cells can also be seen (7). Xanthogranuloma usually has a benign clinical course except those with central nervous system involvement.

Mucosal xanthoma:

Gastric xanthomas were first described by Orth (8). Xanthomas are tumor-like lesions. In the gastrointestinal system, they usually occur in the antrum and pyloric region as yellow to white plaques or nodules (9). Histologically, xanthomas are characterized by sheets of foamy histiocytes in the lamina propria. Xanthomas are thought to arise from transformation of macrophages into foamy cells which might be due to phagocytosis of Helicobacter pylori (10). Xanthomas can be associated with precancerous or malignancy.

Storage histiocytosis - Niemann Pick's disease:

It is a autosomal recessive lysosomal storage diseases due to abnormality in lipid metabolism characterized by accumulation of sphingomyelin. It is due deficiency of enzyme Sphingomyelinase (11). There are three types of Niemann Pick disease, Type A&C - neuropathic form and type B - non neuronopathic form. Diagnosis is made by bone marrow examination, liver biopsy. Histologically Niemann pick cells can be seen, which are large cell with foamy cytoplasm (12).

"R" group - Rosai-Dorfman disease and Kikuchi's disease

Also called Massive sinus histiocytosis with lymphadenopathy (SHML) (13), is a rare, non neoplastic histiocytic disorder (14). RDD is classified as Nodal or systemic with latter classified further as cutaneous, respiratory and osseous (15). Lymphnode involvement is usually cervical followed by inguinal, axillary and mediastinal (16). Patients may have fever, leukocytosis, elevated ESR and polyclonal, hypergamma globulinemia (17). Extranodal presentation has been described with most common sites including skin and nasal sinuses. Extranodal disease with soft tissue involvement with only 3% having soft tissue involvement without lymphnode involvement (18).

As these mimic soft tissue sarcomas, histopathological examination of wide excision material and IHC is essential to confirm the diagnosis.

Though our patient had only soft tissue involvement initially, she later developed a lymphnode swelling in neck which showed RDD. Rarely RDD can be associated with auto immune disorders, with

NHL(19), Hodgkin's Lymphoma and solid tumours (20).

Prognosis is fairly good with spontaneous regression, surgical excision if there is no regression and if symptomatic – steroids (21), alkylating agents and IFN α are given. Role of Radiotherapy and chemotherapy is poorly understood. Rarely death has been reported (22) . Our patient presented with a mass in back of chest which was surgically excised and on follow up.

Kikuchis disease:

Kikuchi's disease/ histiocytic necrotising lymphadenitis is a benign self limited lymphohistiocytic disorder characterized by fever with tender lymphadenopathy. It usually affects young adults of Asian descent (23). It can be associated with SLE. Histology shows coagulative necrosis with karyorrhectic debris. There is proliferation of histiocytes and immunoblasts. The characteristic feature is absence of neutrophils. There are three stages in the development of Kikuchi's disease as follows- proliferative, necrotizing and xanthomatous stages (24). To diagnose Kikuchi's the minimum criteria includes the presence of crescentic histiocytes and plasmacytoid monocytes with karyorrhexis. The importance of Kikuchi's lies in differentiating them from other infections like tuberculosis, lymphocproliferative disorders and Systemic Lupus erythematosus. Kikuchi's usually runs a benign course with spontaneous resolution of lymphadenopathy and other symptoms occurring in 1 to 4 months.

CONCLUSION:

Histiocytic disorders can occur in any age group with varied clinical presentations. Differentiation from other histiological mimicks is challenging. Understanding the classification of histiocytic disorders, together with morphology and immunohistochemistry can help in arriving the correct diagnosis. The pathogenesis of most of the histiocytic disorders includes increased levels of cytokines. This case series provides insight into the various histiocytic disorders.

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