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Review article

Histiocytoses

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Abstract

Histiocytoses are an important group of dermatoses characterized by histological infiltrates predominantly rich in cells of monocyte-macrophage origin. The present review focuses on the salient clinical, diagnostic and therapeutic features of different entities included in this group.

Introduction

The histiocytoses are a heterogeneous group of diseases characterized by the accumulation of reactive or neoplastic histiocytes in various tissues. The majority of the signs and symptoms of the histiocytoses may be the result of functional activity of these cells. An abnormal or altered regulation of histiocyte activity may be presumed to be important in the pathogenesis of these disorders. The present article aims to present the diverging spectrum of these diseases in a simplified and tabulated version.

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Table 1

Histiocytoses [1-10]

Tumor	Clinical aspects	Histopathology	Prognosis	Work up
Class – I Histiocytoses				
Langerhans cell histiocytosis (LCH)	***Skin:*** • Seborrheic dermatitis like rash on scalp, abdomen, groins • Yellow brown, scaly, purpuric papulonodules • Erosions, ulceration, scarring ***Hashimoto-Pritzker variant:*** • Neonatal period • Resemble healing varicella • Generalized, self-limiting ***Nails*** • Paronychia • Onycholysis • Subungual expansion • Nail plate loss ***Oral*** • Periodontal involvement • Mandibular mass ***Ears*** • Polypoids in external ear • Discharge, deafness	• Lymphohistiocytic infiltrate • Mixed cellular infiltrate • Pautrier's like microabscesses ***Markers*** • S 100 protein • Peanut agglutinin • Placental alkaline phosphatase • Alpha–D mannosidase • CD 1 ***Ultrastructure*** • Birbeck granules	***Poor if*** • Age > 2 years • Widespread	***For diagnosis*** • Detailed history • Thorough examination • Skin biopsy • Marker studies • Electron microscopy • Non invasive work up ***For extent*** • Based on symptoms ***For follow up*** • Disease itself • Opted therapies ***Treatment options*** *Skin limited LCH:* • Topical 20% nitrogen mustard • PUVA therapy • Thalidomide *Multisystem LCH:* • Prednisolone 2mg/kg x 2 months

Table 2

Histiocytoses [1-10] ***(Cont'd....)***

Tumor	Clinical aspects	Histopathology	Prognosis	Work up
	Neuroendocrine • Cerebellar involvement • Diabetes insipidus • Short stature • Hypogonadism • Thyroid involvement ***Lungs:*** • Pneumothoraces • Non specific and rare ***Gastrointestinal Tract:*** • Hepatomegaly • Ascites • Cholestatic jaundice • Malabsorption • Diarrhea ***Bone:*** • Osteolytic lesions • Pathological fractures • Vertebral collapse ***Bone Marrow:*** • Pancytopenia • Splenomegaly			• Chemotherapy with vinblastine, methotrexate, 6–mercaptopurine, etoposide, cyclosporine • Alpha interferon • Combination

Table 3

Histiocytoses [11-13] ***(Cont'd....)***

Tumor	Clinical Aspects	Histopathology	Prognosis	Work Up
Class – II Histiocytoses				
Dermatofibroma	• Firm yellow brown nodules • Dimple sign • Limbs	• Storiform pattern • Factor XIIIa staining	• Good	• Surgical excision • Intralesional steroids
Juvenile xanthogranuloma	• Onset in infancy • Asymptomatic • Sudden appearance • Spontaneous regression • Firm reddish yellow macules, papules, plaques • Upper half of the body • Surface telangiectasia • Ulcers, atrophic scars ***Complications:*** • Iris hemorrhages • Secondary glaucoma • Iritis, uveitis, proptosis • Visceral involvement ***Associations:*** • Leukemias • Urticaria pigmentosa • Neurofibromatosis • Neimann–Pick disease	• Touton giant cells • Lymphohistiocytic infiltrate • Mixed cellular infiltrate	• Resolves in 1–5 years	• As for LCH class–I • No treatment needed for skin disease • Surgery, radiotherapy for ocular lesions

Table 4

Histiocytoses [14-23] ***(Cont'd....)***

Tumor	Clinical Aspects	Histopathology	Prognosis	Work up
Benign cephalic histiocytosis	• Resemble juvenile xanthogranuloma • No mucosal or visceral involvement	• Same as juvenile xanthogranuloma	• Good	• As for LCH class–I • No treatment needed
Necrobiotic xanthogranuloma	• Periorbital noduloulcerative lesions • Xanthomatous plaques, ulcerations, atrophy • Ocular involvement • Associated paraproteinemia	• Touton cells • Necrobiosis • Palisading granulomas	• Depends on the extent of disease	• As for LCH class–I • Treatment of paraproteinemia • Systemic steroids • Chemotherapy • Radiotherapy • Plasmapheresis
Multicentric reticulohistiocytosis	***Arthropathy*** • Rheumatoid arthritis like ***Skin involvement*** • Yellow brown papulonodules • Extremities, face, scalp, ears • Nail dystrophy, pruritus ***Mucosal infiltration*** ***Internal malignancies*** ***Fatal cardiac involvement***	• Same as in necrobiotic xanthogranuloma	• Depends on the extent of disease	• As for LCH class–I • Systemic steroids • Immunosuppressives
Diffuse plane xanthomatosis	• Large, flat, plaque like xanthomatous lesions • Head, neck, trunk, flexures • Associated paraproteinemia	• Xanthomatous element • Foamy macrophages • Mixed cellular infiltrate	• Depends on the extent of disease	• As for LCH class–I • Treatment of paraproteinemia • Plasma exchange

Table 5

Histiocytoses [14-23] ***(Cont'd….)***

Tumor	Clinical Aspects	Histopathology	Prognosis	Work up
Generalized eruptive xanthoma	• Yellow brown papules • Generalized distribution • Diabetes insipidus	• Lymphohistiocytic infiltrate • Mixed cellular infiltrate	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications
Xanthoma disseminatum	• Yellow brown papules • Generalized distribution • Mucosal involvement • Systemic involvement • Diabetes insipidus	• Lymphohistiocytic infiltrate • Mixed cellular infiltrate	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications
Familial hemophagocytic lymphohistiocytosis (Autosomal recessive)	• Fever maculopapular rash • Signs of meningeal irritation • Lymphadenopathy • Hepatosplenomegaly • Anemia • Thrombocytopenia	• Lymphohistiocytic infiltrate • Lymphopenia in lymphoid tissues	• Depends on the extent of disease	• As for LCH class–I • Splenectomy • Exchange transfusion • Chemotherapy • Marrow transplantation • Treatment of complications
Familial sea blue histiocytosis (Autosomal recessive)	• Pigmentation • Upper half of the body • Stippled deposits on macula • Systemic involvement	• Histiocytic infiltrate	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications
Hereditary progressive mucinous histiocytosis (Autosomal dominant)	• Red brown papules • Acral parts • Progressive	• Histiocytic infiltrate • Mucinous component	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications

Table 6

Histiocytoses [14-23] ***(Cont'd....)***

Tumor	Clinical Aspects	Histopathology	Prognosis	Work Up
Sinus histiocytosis with massive lymphadenopathy (*Klebsiella, Brucella, EBV*)	• Massive adenopathy • Cervical adenopathy > 90% • Yellow purple papulonodules • Nasal polyps • Constitutional symptoms • Systemic involvement	• Dilated sinuses • Reactive germinal centers • Lymphophagocytosis	• Depends on the extent of disease	• As for LCH class–I • Chemotherapy • X-rays • Treatment of symptoms • Treatment of complications
Virus-associated hemophagocytic syndrome (Herpes, adenovirus, EBV)	• Sudden onset • Generalized macular rash • Constitutional symptoms • Hematological abnormalities • Other systemic involvement	• Histiocytic infiltrate • Erythrophagocytosis	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications
Malakoplakia (Soft plaque, an immunodeficiency disease)	• Papulonodules • Abscesses, sinuses, ulcers • Mucosal involvement • Systemic involvement	• *Hansemann cells* (histiocytes with eosinophilic granules) • *Michaelis Gutmann* bodies (histiocytes with basophilic inclusions)	• Depends on the extent of disease	• As for LCH class–I • Treatment of symptoms • Treatment of complications

Table 7

Histiocytoses [24-26] ***(Cont'd....)***

Tumor	Clinical aspects	Histopathology	Prognosis	Work up
Class – III Histiocytoses				
Monocytic leukemia (M5 of FAB classification)	• Constitutional symptoms • Red brown, violaceous macules, nodules • Gum involvement • Hematological abnormalities • Extramedullary disease • Organomegaly	• Malignant histiocytic infiltrate • Adnexal involvement	• Poor	• As for LCH class–I • Blood and marrow studies • Chemotherapy • Radiotherapy • Electron beam therapy • Marrow transplant
Malignant histiocytosis	• Same as in monocytic leukemia	• Same as in monocytic leukemia	• Poor	• Same as in monocytic leukemia
True histiocytic lymphoma	• Same as in monocytic leukemia	• Same as in monocytic leukemia	• Poor	• Same as in monocytic leukemia

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