Welcome to CPD

Presented by

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Histiocytosis Syndromes of childhood

Histiocytosis Syndromes of childhood is a diverse group of disorders in which there is a prominent proliferation or accumulation of cells of monocyte-macrophage system of bone marrow origin characterized by lytic bone lesion, seborrhic eczema like skin lesions, different endocrinopathy, soft tissue infiltration & hepatosplenomegaly.

Classification of Childhood Histiocytoses

Class I: Langerhans' cell histiocytosis(LCH).

"a) Letterer-Siwe disease

b) Hand-Schuller-Christian disease

c) Eosinophilic granuloma"

Class II: a) Familial Erythrophagocytic Lymphohistiocytosis(FEL)

b) Infection-Associated Hemophagocytic Syndrome(IAHS)

Class III: a) Histiocytic lymphoma

b) Acute monocytic leukaemia

Pathology

Class I: LCH

*Hallmark of LCH is presence of Langerhans' cell (antigen presenting cell) in all three form of diseases.

* Birbeck's granule (HX- granule) within LC cytoplasm and CD_1 antigen are diagnostic.

*Variable number of lympho, granulo, monocytes and eosinophils.

* Cells have no malignant characteristics

Staging of LCH:

Stage I - single lytic bone lesion

Stage II – Multiple lytic bone lesions (stage I + II both formerly called eosinophilic gramuloma)

Stage III

III A - Bone plus soft tissue lesion often associated with diabetes insipidus (post pituitary involvement) and exophthalmos (bilateral involvement of the retro-orbit). This stage III A is previously termed as Hand-Schuller-Christian disease.

III B- Only soft tissue involvement, acute disseminated form. This stage III B is previously termed as Letterer-Siwe disease.

Path -contd

Class II:

*Normal reactive macrophages with prominent erythrophagocytosis.

*Occurs in macrophages (antigen processing cells) not in LC (Ag presenting cells).

*No malignant characteristics.

*Cells have no Birbeck's granules or CD_1 antigen.

*Associated with AR inheritance or infective agents (EB virus).

Path- contd

Class III:

*Malignant proliferation of monocytes, macrophages or their precursors.

*Like acute monocytic leukaemia (M_5 type AML)

*Unequivocal malignancies of cells of monocyte-macrophage lineage

Clinical Features

- Fever, malaise, weight loss, irritability
- Skin rashes or eczematous changes
- Nonspecific bone pain, lytic bone lesions
- Lymphadenopathy
- Anaemia, petechae, purpura
- Hepatomegaly/ hepatosplenomagy
- Exophthalmos, polyuria, polydipsia
- Hypothyroidism

C/F- contd

Letterer-Siwe disease:

a) Usually occurs below the age of 2 years (disease of infancy).

b) Acutely disseminated form.

c) mainly affects soft tissue

d) Generalized purpuric rashes, anaemia, leucopenia, thrombocytopenia, jaundice, hepatosplenomegaly, lymphadenopathy, honey-comb appearance at chest X-ray.

e) Mortality is over 60%

C/F-contd

Hand-Schuller-Christian disease:

a) Triad of lytic defect in membrenous bone, DI and exophthalmos.

b) Develops first 6 years of life.

c) Reddish-yellow lumps or yellow crusts on the scalp (lipid laden histiocyte-Xanthomatosis)

C/F-contd

Eosinophilic granuloma:

a) Only bony involvement; no extraskeletal involvement.

b) Occurs in older children or in young adult

C/F- contd

Class II:

a) Fever, weight loss, irritability

b) FEL usually occurs before 4 years and IAHS occurs in older age.

c) Lymphadenopathy, hepatosplenomegaly aseptic meningitis.

d) Autosomal ressecive inheritance or infective agent may be involved

C/F-contd

Class III:

Besides fever, malaise, weight loss, irritability

a) Skin and gingival invovlement

b) Generalized bone pain

c) Hepatosplenomegaly, lymph node invovlement, may have proptosis.

Investigations

a) Complete blood count with blood film
b) Liver function tests
c) CXR (honey comb appearance) and other skeletal survey (lytic bone lesions).
d) Serum and urinary specific gravity and water deprivation test (for DI)
e) Biopsy of the involved organ or affected part.
f) Bone marrow analysis
g) Molecular diagnosis by genetic analysis

Treatment

Specific:

Class I:

Stage I & II- Curettage with intralesional injection of steroid

Stage IIIA & B- Steroid, Multiagent chemotherapy, BMT, Immunomodulating agent (ATG, Cyclosporin)

Class II and Class III: Steroid, chemotherapy, BMT, Antiviral agents.

**Single system disease of LCH and IAHS have high chance of spontaneous remission*.

Treatment- contd

Symptomatic:

a) Analgesic to relieve fever, pain

b) Antibiotic to control infection

c) Topical steroid to treat skin manifestations.

d) DDAVP for DI.

e) HRT for other endocrinopathy.

f) Vaccination (HBV)

Prognosis

Good prognosis if

a) Disease occurs beyond infancy

b) Single system disease

c) Multi-system disease with good response to chemotherapy.

d) Infection-Associated Hemophagocytic Syndrome

Prognosis

Bad prognosis if

a) Disease occurs before infancy.

b) Multi-system disease with acute dissemination.

c) Non response to chemotherapy.

d) FEL and Class III histiocytosis have down hill course.

***Overall prognosis in childhood histiocytoses is favorable.*

Thanks