Chediak-Higashi Syndrome

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Chediak-Higashi syndrome is inherited as an autosomal recessive disease. It was described over 50 years ago. Clinical reports have identified mutations throughout the CHS1/LYST lysosomal trafficking gene. The nature of the mutation can be a predictor of the severity of the disease. There are a number of animal models including mouse, cat, cattle, mink and killer whale.

Epidemiology
The condition is rare. The literature tends to be isolated case studies or just a few cases. Family history of the disease is a risk factor but it is uncommon to find a positive history in patients with this condition.

Presentation
- Impaired vision
- Photophobia
- Albinism of the OCA2 type, giving a lighter complexion than unaffected family members
- Silvery sheen to hair which may be fair in colour
- Frequent infections (skin, mucous membranes, respiratory)
- Epilepsy
- Mental retardation
- Enlarged liver and spleen
- Jaundice
- Ataxia causing incoordination and a typical ataxic gait
- Tremor
- Epilepsy
- Peripheral neuropathy causing motor and sensory changes and weakness (if patient survives into adulthood)

Differential diagnosis
Initially the condition may present as one of the varieties of albinism but the recurrent infections should make one suspect the diagnosis. The Hermansky-Pudlak syndrome and Griscelli's syndrome are similar but distinct conditions.

Investigations
- Blood smear shows giant granules in the neutrophils that stain for peroxidases.
- Bone marrow smears show giant inclusion bodies in leukocyte precursor cells.
- Giant granules are also found in cells from biopsy of skin, muscle and nervous system.
- Platelet or leukocyte levels are abnormally low.
- Genetic testing may show mutations in the CHS1 gene.
- Light or polarised light examination of hair shafts can help to diagnose Chediak-Higashi syndrome but cannot differentiate it from the appearance seen in Griscelli's syndrome.
- Fluorescence cytometric analysis of cellular granularity and surface molecules offer useful diagnostic information.
- EEG may be abnormal.
- Brain MRI or CT scan may show small brain due to atrophy.
- Oral radiographs may reveal extensive loss of alveolar bone, often resulting in tooth exfoliation.
- EMG or nerve conduction velocity testing may show delayed nerve conduction.
- A red light reflex is present in the eye (this is frequently seen in albinism).
- There are abnormalities of immune function including reduced level of CD4 lymphocytes.

Associated diseases
- Infection is a constant problem.
- For a better understanding of the visual defects and the problems related to the OCA2, see the separate record on Albinism.

Management
Drug
- Allogenic bone marrow transplantation (BMT) from an HLA-matched sibling is the treatment of choice but does not prevent the neurological disorders.
- If no related donor is available, an unrelated donor or a placental blood graft may be used.
- Haemopoietic stem cell transplant proved an effective treatment in one study.[13]
- Antiviral drugs like aciclovir, high-dose intravenous gamma globulin; and microtubulytic drugs, such as vincristine, vinblastine and colchicine, are effective in the management of the accelerated phase. Cyclophosphamide and prednisolone have been tried but without much benefit. High-dose methylprednisolone and splenectomy have produced temporary respite.[1, 12]
- Frequent infections are treated with antibiotics.

Non-drug
- Abscesses are surgically drained when appropriate.[1]
- BMT appears to have been successful in several patients.[13]

Complications
Frequent infections lead to hypersplenism which in turn causes thrombocytopenia and haemorrhage. About 85 to 90% of patients develop an unusual lymphoma. This is called the accelerated phase and is characterised by generalised lymphohistiocytic infiltrates, fever, jaundice, hepato-splenomegaly, lymphadenopathy, pancytopenia and bleeding.[2, 4]

Prognosis
Without BMT, death before the age of 10 is common.[4] The terminal phase of the illness is not treatable.[2, 4]

Prevention
Genetic counselling is recommended for prospective parents with a family history of Chediak-Higashi syndrome.[14] Examination of hair from fetal scalp biopsy specimens and of leukocytes from fetal blood samples can be used for prenatal diagnosis.[4]

Further reading & references
1. Sondheimer N; Chediak-Higashi syndrome; Medline Plus
2. Chediak-Higashi Syndrome; CHS, Online Mendelian Inheritance in Man (OMIM)
6. Oculocutaneous Albinism, Type II; OCA2, Online Mendelian Inheritance in Man (OMIM)

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