Hemepath Case 51: 3-Year-Old Boy

HISTORY

A 3-year-old boy is brought in by his mother. He has experienced recurrent seizures and has a limp when he walks. The child has had frequent respiratory tract infections and skin rashes ever since he was born. He burns quickly in the sun, and bleeds easily with mild injuries. He is delayed developmentally. The child's parents are first cousins.

On physical examination, the child is noted to have hypopigmented skin patches throughout his body, and pale, almost silvery, hair. He is very sensitive to light from the ophthalmoscope; fundoscopy reveals pale retinae. Neurological examination shows reduced sensation in his left foot. The boy walks with an abnormal gait, and seems to have trouble coordinating his movement.

CBC

Hgb (g/L)	Low
MCV	N
WBC	Low
Plt	N

DESCRIPTION OF SLIDE

Peripheral Blood Smear

RBCs and platelets are unremarkable. Neutrophils show markedly abnormal granulations (see circles) that are large and blocky. Somewhat similar granules may be seen in other white cells, including lymphocytes and monocytes.

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MORPHOLOGICAL DIAGNOSIS

Chediak-Higashi syndrome

DISCUSSION

Chediak-Higashi syndrome (CHS) is a rare, autosomal recessive disorder with defect in the *CHS1/LYST* (lysosomal trafficking regulator) gene. This gene is involved in fusion of

cytoplasmic lysosomes, and a mutation leads to increased aggregation and thus abnormally large granules in multiple cell types.

The giant granules in immune cells (neutrophils, monocytes, and natural killer cells) contain a decreased level of hydrolytic enzymes. Destruction of microbes is delayed, and patients therefore have an increased susceptibility to infections, particularly of the skin, respiratory tract, and mucous membrane. In addition, the large lysosomes also prevent chemotactic movement of neutrophils – that is, they cannot "squeeze" between the endothelial cells to migrate to the site of infection.

Hypopigmentation of the skin, hair, and eyes ("oculocutaneous albinism") is due to an uneven aggregation and distribution of melanosomes. Patients also exhibit progressive neurologic dysfunction (e.g. abnormal gait, ataxia, delayed mental development, peripheral neuropathy, seizures, etc.), although the mechanism for this is not well understood.

An accelerated phase occurs later in life, at which time lymphocytes infiltrate multiple organs, including the bone marrow, liver, and spleen. This worsens the existing pancytopenia and is often lethal.