E11. **LANGERHANS CELL HISTIOCYTOSIS: DIAGNOSIS AND CLINICAL APPROACH.**

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Langerhans cell histiocytosis (HCL) is a rare, polymorphic disorder, which can affect any organ or system. Formerly known as "Histiocytosis X" , the disease is due to clonal proliferation of CD1 + histiocytes.
Malignant clone expresses the morphology and phenotype of Langerhans cells, which are specialized dendritic cells found in the skin and mucosa (CD1a, MHC II, Birbeck granules) and also presents markers of activated Langerhans cell (CD54, CD58).

The Working Group of the Histiocyte Society has divided histiocytic disorders in three groups: (1) dendritic cell histiocytosis (2) macrophage-related disorders and (3) malignant histiocytosis. LCH belongs to the first group and includes several forms of the disease (Letterer-Siwe disease - acute disseminated form, Hand-Schüller-Christian disease - intermediate clinical form, eosinophilic granuloma - chronic, indolent disease, Hashimoto-Pritzker disease - congenital self-limiting form).

The pathogenesis of the disease remains unknown - neoplastic process versus reactive process.
In some cases, the diagnosis is purely random, but sometimes the disease begins dramatically , in the early months of life, with leukemia-like image (fever, hepatosplenomegaly, lymphadenopathies, cytopenia) and high mortality.

Clinical presentation of LCH is essentially influenced by the interested organ, the degree of functional involvement and the number of involved sites (unifocal or multisystemic disease). Favorite headquarters are bone, skin and pituitary gland. Lymph nodes, liver, spleen, hematopoietic bone marrow and central nervous system are rarely affected. Pulmonary LCH is common in adults and may announce multisystemic damage.
The diagnosis is based on histologic and immunopnenotypic examination of a lesional biopsy. Accepted criteria for diagnosis include CD1a positivity and / or CD 207 (Langerin) and the presence of Birbeck granules on electronic microscopy.

So far, there is no standard therapeutic protocol accepted. Treatment options depend mainly on the extent and severity of the disease at diagnosis. The Working Group of the Histiocyte Society proposed a risk stratification according to the number of affected systems. Unifocal involvement may benefit from surgical treatment. First-line systemic therapy is indicated in forms with multisystemic involvement, and in cases of unifocal disease unresponsive to treatment.

Current recommendations for systemic therapy (Histiocyte Society / 2008) propose the combination of cytotoxic medication (vinblastine, methotrexate) and corticosteroids. The role of allogeneic stem cell transplantation in LCH has not yet been elucidated; further trials are needed.
Evolution of single system LCH (unifocal) is generally favorable, but if there is multisystemic involvement, the prognosis is variable (60% chronic evolution, 30% complete remission, 10% deaths). Response to chemotherapy in the first 6 weeks of treatment (induction therapy) is the most important prognostic marker for multifocal LCH.