

LANGERHANS CELL HISTIOCYTOSIS: A Case report

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Abstract:

Langerhans cell histiocytosis is a progressive proliferative disorder of mononuclear macrophage system. The clinical presentation of this disease depends on the extent of dissemination, and the clinical course of the disease is usually variable. In this report an eight-year Sudanese female child referred to the Oncology out Patient with multiple swellings in her head and thigh, generalized lymphadenopathy and hepatomegaly. Neurologically she had focal abnormal rapid and regular right upper limb movement, persisting even during sleep. Histopathology examination of the biopsy of the thigh swelling showed fibro-fatty tissue with centrally necrotic collection of cells mainly eosinophils, plasma cells and histiocytic cells which was consistent with LCH. Multiple lytic lesions were noticed on radiological studies. She was treated with a regimen of Vinblastine, Etoposide and Dexamethasone.

Key Words: Langerhans cells, Histiocytosis x, Eosinophilic granuloma, Lettere-Siwe disease, Hand Schuller-Christian disease, Hashimoto-Pritzker syndrome self-healing histiocytosis, pure cutaneous histiocytosis, Langerhans cell granulomatosis, Type II histiocytosis, and the generic term nonlipid reticuloendotheliosis.

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Introduction

Langerhans cell histiocytosis (LCH) is a progressive proliferative disorder of mononuclear macrophage system, described first by Lichtenstein in 1953¹. Historical terms for LCH include "Histiocytosis x, Eosinophilic granuloma, Lettere - Siwe disease, Hand Schuller-Christian disease, Hashimoto-Pritzker syndrome, self-healing histiocytosis, pure cutaneous histiocytosis,

*Langerhans cell granulomatosis, Type II histiocytosis, and the generic term nonlipid reticuloendotheliosis*². LCH is the preferred term, since the cell of origin, "the Langerhans cell (LC)", has been known over 40 years and is increasingly better characterized. The key issues are whether the disease is unifocal or multifocal in a single-organ system with or without other non-risk organs involved. The risk organs are liver, spleen, bone marrow, and lungs. The LC are derived from stem cells, which are found in the skin, lymph nodes, bone marrow, spleen and probably the brain. These cells have characteristic surface proteins, which identify them as "immature" or "mature". Within the LC is a five-layered structure, a Birbeck granule, first seen by electron microscopy³. The gene coding for this infolded surface protein has been identified and called "Langerin".⁴ Now the diagnosis of LCH can be confirmed by staining biopsy tissue specimens with anti-Langerin, as well as the standard marker anti-CD1a⁵. The absolute best therapeutic approach has not really been carefully studied, but clearly most people agree that the treatment in these situations should not be worse than the disease.



Figure 1: Photo of the patient showing proptosis on the right eye.

Case report: An eight-year Sudanese female child referred to oncology out patient with multiple swellings in her head and thigh. Her parents stated that her illness started two years back with symptomatic anaemia which necessitated blood transfusion. She was quite well for one year duration, when they noticed multiple painless swellings in her head and thigh which increased gradually in size. Her mother could recall that four months before her recent presentation, the child was reluctant to walk following a

minor trauma to her left thigh. The condition deteriorated with attacks of severe headache, convulsions and loss of consciousness. This clinical scenario accompanied by increased amount of urine and loss of weight.

On examination: the patient was ill, pale, not thriving well and with bilateral proptosis Fig. (1). She has multiple scalp swellings, which were firm, not tender; the biggest one was 5x3 cm Fig. (2). She had generalized lymphadenopathy. Chest was clear, cardiovascular examination showed tachycardia and haemic murmur. Abdomen was soft with hepatomegaly of 6 cm below costal margin. Left thigh examination revealed a healed scar of the excisional biopsy and a hard swelling of 4x4 cm on the upper aspect which was not tender. No neurological signs apart from a focal abnormal rapid and regular right upper limb movement, persisting even during sleep. Complete blood count showed anaemia. X-rays films of the skull and lower limbs showed multiple lytic lesions (Fig.3 and 4). Histopathology examination of the biopsy of the thigh swelling showed fibro-fatty tissue with centrally necrotic collection of cells mainly esinophils, plasma cells and histiocytic cells which was consistent with LCH (Fig. 5). The general situation of the patient was initially treated then she received a regimen of vinblastine, etoposide and dexamethasone.



Figure 2: Photo of the patient showing scalp swelling

Discussion

LCH is a disease of infancy and early adulthood. More than 50% of patients are affected when they are below the age of 2 years and more than 70% below 20 years of age. It is rarely seen in middle and old age. LCH of bone is slightly more prevalent in male⁵. However, for LCH involving other organ systems, a female

predominance was reported⁶. No racial differentiation was reported. Incidence rate is one case per 200000 population. Little is so far known about definite aetiological factors³. Infections, malignancy, immunological disturbances and genetic causes are implicated as causative factors⁷.

The definitive diagnosis of LCH can be made by demonstrating CD1a positivity of lesional cells. The two major diseases among the Class II histiocytosis have indistinguishable pathologic findings. One is familial erythrophagocytic lymphohistiocytosis (FEL) which is the only inherited form of histiocytosis and it is autosomal recessive. Most recently several specific gene mutations underlying FEL have been discovered. In contrast, the Class III histiocytosis is unequivocal malignancies of cells of monocyte-macrophage lineage. By this definition acute monocyte leukemia and true malignant histiocytosis are included among the Class III histiocytosis⁸.



Figure 3: Photo of the patient showing patient showing skull lesions

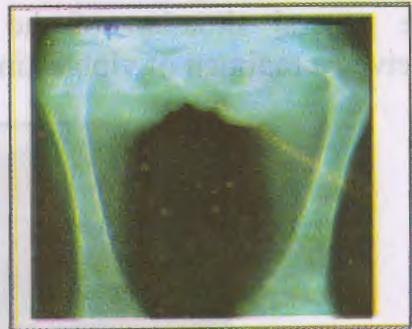


Figure 3: Photo of the bone lesions

Clinically LCH has divergent course from totally asymptomatic to fulminating acute symptoms. Presentation mainly depends upon whether it is localized disease or has organic dysfunction, like pituitary dysfunction due to involvement of the sella turcica. Bony lesions may cause otitis media due to destruction of temporal and mastoid bones and proptosis secondary to orbital masses. Patients with acute disseminated (LCH) present with fever, anemia thrombocytopenia, pulmonary infiltration, skin lesions and enlargement of the lymph nodes, spleen and liver. Cutaneous abnormalities are present in almost 80% of patients with characteristic weeping eruption mimicking seborrheic dermatitis. Neurologic involvement may produce seizures, headache, ataxia and vertigo.

Recommended baseline diagnostic evaluation includes CBC, LFTs, RFTs, Urine examination (routine and for osmolarity) and also hormonal studies of the hypothalamic-pituitary axis.

The radiological manifestations, using different imaging modalities (X-ray, CT, radio-isotope and MR) are rarely pathognomonic. Nevertheless, familiarity with the imaging findings may be essential for the diagnosis⁹ considering the fact that it presents in many ways, mimicking other conditions and affects many organs¹⁰. Chest x-ray may show parenchymal infiltration (usually nodular), honey comb appearance and tissue fibrosis. Skeletal survey (skull x-rays, spine, chest, abdomen, pelvis and limbs) shows typical lytic lesions. Usually there are no accompanying peripheral sclerotic rims. Skull x-rays show lytic lesions in the diploic spaces of the parietal bone, rounded or ovoid punch out lesions with beveled edges (hole within a hole) and button sequestrum (bony sequestrum with lytic lesion). Sclerotic margins are only seen during healing phase^{9,10}.

Tissue diagnosis is the hallmark for diagnosing LCH. Bone trephine biopsy, lymph node biopsy (preferably excisional biopsy rather than FNAC), upper gut biopsy, biopsy from mucocutaneous lesions are the recommended procedures. Infiltration of the involved structures with LCH of different maturity is essential for diagnosis.

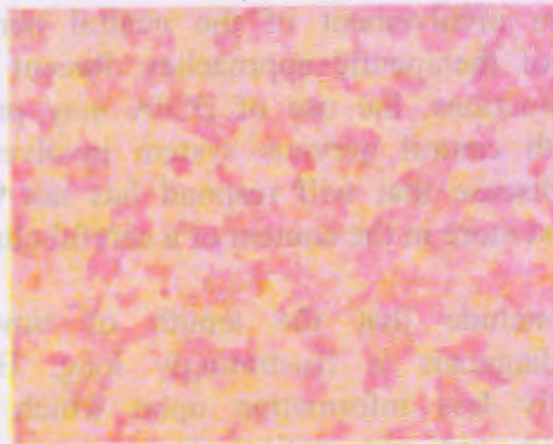


Figure 4: histopathology appearance of the biopsy.

Presently the staging system in use is Lahey's¹¹. This system depends on the patient's age, number of organs involved and if any organ dysfunction present or not. This system counts points for age (less than 2 years =1, more than 2 years = 0), numbers of organ involved (less than 4 sites = 0, more than 4 organs or sites =

1) and organ dysfunction (no organ dysfunction =0, organ dysfunction exists =1). Stage is then calculated accordingly: stage 1, 2, 3 and 4 scoring 0, 1, 2, 3 points respectively.

LCH may in some instances regress on its own without treatment. In other situations, very minimal treatment will result in the resolution of symptoms and regression of the disease. One must therefore often try to balance the extent of medical intervention with the severity of the disease involvement. For patient, with more extensive disease there is general agreement, based on many published studies that systemic chemotherapy will be beneficial. The exact type of chemotherapy that is best has not been completely worked out. Such chemotherapeutic agents include steroids (eg. prednisone), vinblastine, vincristine, etoposide or VP-16, 6 - mercaptopurine and methotrexate. While all of these agents have demonstrated good activity in treating LCH, their very best scheduled and combination are still being explored. One of the major challenges currently faced is what type of treatment should be used for patients with extensive and/or progressive disease that is not responding to the "regular" recipe. Here, one faces significantly less information upon which to make the best decision¹². An area of particular need is how to manage patients with chronic, progressive involvement of the liver, lung and central nervous system. In the case of liver and lung involvement a variety of immuno- suppressive treatment can be used, but no curative therapy has been developed. For patients with progressive involvement of the central nervous system, there is also a lack of therapeutic approaches. Recent work is suggesting that in some situations, the use of 2CdA may provide some benefit for patients with central nervous system involvement, but the type and extent of disease that will respond has not been clarified. This need to be studied more in the context of a careful clinical trial¹².

Conclusions:

We can conclude that the length of time from presenting symptoms to diagnosis is frustratingly long. Here we are faced with significantly less information upon which to make the best decisions, as we put our patient in a regimen of Vinblastine, Etoposide, and steroids but unfortunately she showed no improvement

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