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Case Report

Multisystem Langerhans cell histiocystosis in a geriatric patient: case report

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ABSTRACT

Langerhans cell histiocytosis is a condition of exceptional onset characterized by a proliferative event of dendritic cells with mono or multisystem involvement that predominates in the pediatric population and is identified in a smaller proportion in adults. It has a clinical impact and variable prognosis according to its location and number of organs affected. A 68-year-old male patient with clinical and immunohistochemical criteria for Langerhans cell histiocytosis with multisystem settlement with fatal outcome. It is a very rare disease, it is not exclusive to the pediatric population, with little understood pathogenesis and does not have specific treatment. In adults, the clinical impact is more aggressive, with a poorer prognosis and greater short-term complications.

Keywords: Histiocytosis, Langerhans cells, Langerhans cell histiocytosis in adults

INTRODUCTION

Langerhans cell histiocytosis is a proliferative disease of dendritic cells originating in the bone marrow that has a very extensive clinical spectrum, which gives it the potential to affect multiple organs in an isolated or diverse way.[1]

It is recognized for being epidemiologically very rare, affecting around 2 to 10 cases per million inhabitants, starring children, particularly in infants and being identified to a lesser extent in adults. Given its exceptional appearance in a non-pediatric population group, a case of this condition is reported in a geriatric adult with criteria of severity and multisystem settlement where the diagnosis was established thanks to the integration of clinical manifestations and immunohistochemical studies of this nosological entity.

CASE REPORT

This is a 68-year-old male patient, married. Originally from Merida Yucatan. With a history of ethyling until reaching drunkenness for 40 years inactive for 8 years. Operated 6 months ago for choledocholithiasis without post-surgical complications, without known chronic degenerative diseases. He began suffering four months ago presenting unintentional weight loss of more than 11 kilograms and dermatosis characterized by brown papules on the head and trunk, associated with moderate pruritus, with periods of exacerbation and partial remission and that during the last month has intensified. He goes to medical evaluation for presenting abdominal pain in the right hypochondrium, of a stabbing type, intensity 9/10, quantified fever (38°C), dyspnea of small efforts, edema in pelvic extremities and jaundical dye in skin and conjunctivae. If residual litho and/or associated neoplastic agent are suspected, both tomographic and magnetic

resonance imaging of the thoracoabdominal region is carried out, which do not reveal alterations at the intra- and extrahepatic level, but the presence of hepatomegaly and free fluid in multiple cavities stands out: peritoneal, pleural and pericardial. During hospital stay, infectious, hemodynamic, obstructive and metabolic etiologies are ruled out; depletor treatment, oxygen therapy and intravenous analgesia are granted, with torpid evolution. It is evaluated by the dermatology service, which on physical examination observes that throughout the hairy skin acquires an appearance of seborrheic dermatitis represented by traces of scratching, peeling and pruritus, in the anterior thorax they adopt a "V" shape and in the armpits, there are some integral papules and others inflammatory with serous exudate. In less intensity the same lesions are observed in thoracic extremities, palms of the hands and lateral scrotal region where they adopt a petecyform aspect, the percentage of body surface affected is calculated, representing more than 50% approximately (Figure 1 and 2). We proceed to perform biopsy of the lesion where in its approach it was evaluated by three different pathologists who concluded superficial neoplasia of mononuclear cells of histiocytic type not classifiable, so the sample was sent to study by immunohistochemistry through the special stains Fuscina and S100, documenting the following findings (Figures 3-6).

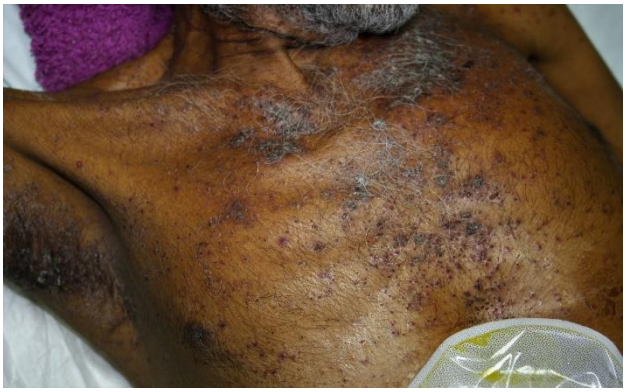

Figure 1: Reddish and brown papulas arranged in a V-shape on the anterior trunk.

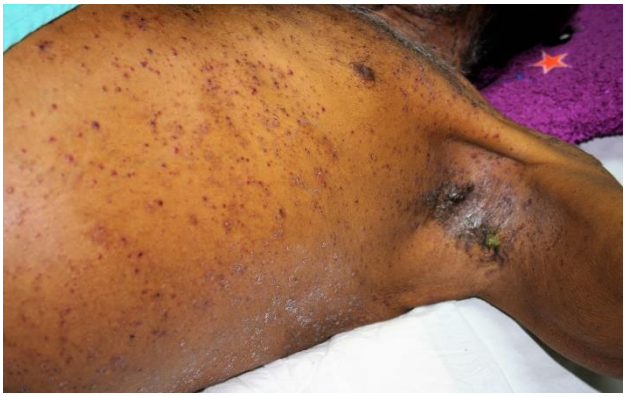

Figure 2: Papulo-scaly lesions of red-brown color arranged throughout the trunk, with affection in the axillary fossa.

Figure 3: Purpuric lesions disseminated in palmar region and phalanges.

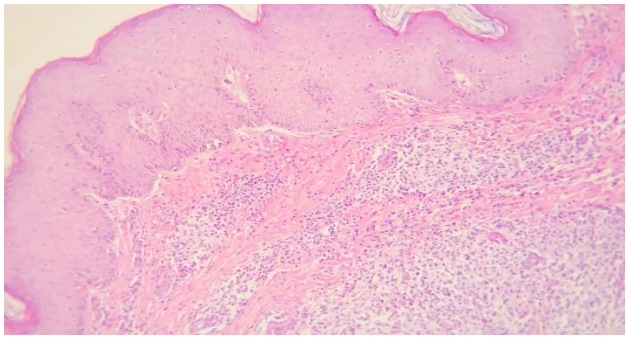

Figure 4: Cutaneous Langerhans cell histiocytosis.

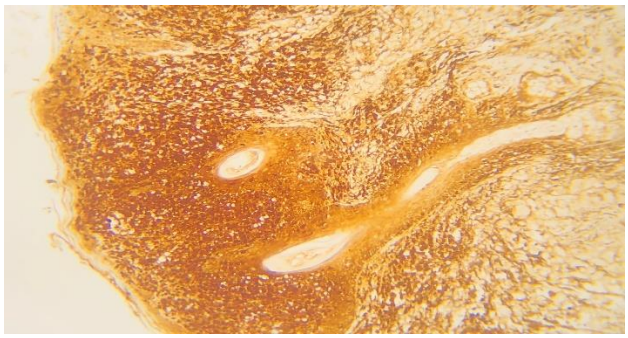

Figure 5: Immunohistochemistry of skin. Findings consistent with S100-positive Langerhans cell histiocytosis.

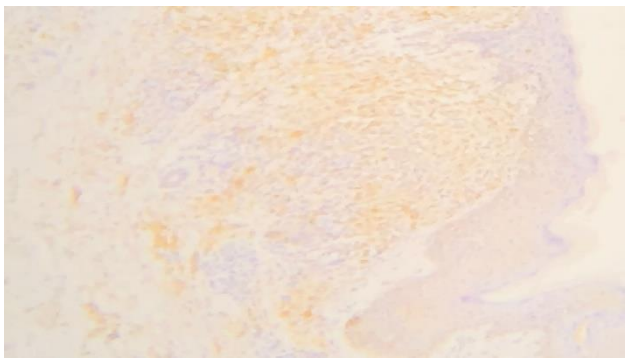

Figure 6: Immunohistochemistry of skin. Findings consistent with Fascina-positive Langerhans cell histiocytosis.

The immunohistochemical diagnosis of multisystem Langerhans cell histiocytosis is declared. After a week of hospitalization despite medical management, the patient has greater clinical deterioration that warranted invasive ventilatory support and vasopressor, leading to multiple organ failure and progressing to a fatal outcome.

DISCUSSION

Langerhans cell histiocytosis refers to a clonal proliferation of myeloid dendritic cells with expression of specific surface markers that are exhibited in different organs in an isolated or generalized manner.[1]

Despite being poorly understood, its initial identification dates from the late nineteenth century, where the first definitive case declared was by Alfred Hand, after finding granulomatous and eosinophilic lytic lesions, diabetes insipidus and exophthalmos in young patients. It took more than half a century, to be named histiocytosis X, a term coined by Lichtenstein where he evidenced the proliferation of these cells in more than one tissue.[1,2] This cell line is part of the family of dendritic cells, recognized for their essential function as antigen-presenting cells whose origin settles in the bone marrow and which are located in the skin, bone, lymphoid organs, extranodal tissues, lung, gastrointestinal tract and cervix.[1-3]

It is a disease whose epidemiological impact has been little recognized, predominantly affecting the pediatric population, estimating an annual incidence of 4-5 cases per million children under 15 years, with a peak age between 1 and 4 years, being more affected the male gender.[1-3] In adults this incidence is reduced to 1 to 2 cases per million debuting between the second and third decade of life, with exceptional occurrence in adults over 65 years.[1,2]

Multiple hypotheses and theories have been born to explain the nature of this mysterious disease. It is insinuated from the active contribution of inflammatory cytokines, to mono or polyclonal proliferation and genetic aberrations, raising the question of whether this disease occurs before an inflammatory, neoplastic or mixed origin.[1,4-6] Lately, the association between mutations of the BRAF gene and V600E has gained strength, being present in the serum of patients who study with this nosological entity.[6] It is well recorded that the only identified risk factor that predisposes to the development of this pathology is prolonged exposure to tobacco, especially when it appears in the clinical context of lung involvement in adult patients.[2,7,8] It has been tried to associate it with personal and family history due to exposure to chemical compounds, benign neoplastic agents, and endocrinopathies without finding a significant relationship.

The clinical presentation is difficult to predict, since it will depend on the location of the lesions and their generalization. According to their classification according to the extension, they are divided into: monosystemic, with involvement in skin, liver, bone, lymph nodes, lung, central nervous system, among others; and multisystem, with invasion of two or more organs or systems. More than half of the cases involve a single organ (usually skin or bone).[9]

If the bone tissue is the affected one (which represents 80% of cases), it usually appears as a lytic tumor with centripetal distribution in large bones, especially at the level of the skull and vertebral bodies, being located in a smaller proportion in the appendicular skeleton; findings that are more solid in the population under 18 years of age, being found only in 20% of adults with this pathology.[6,7,9-11]

When it affects the skin, it is considered the second most affected organ (followed by bone) it appears as a morbiliform rash, the elemental lesion of which is the brown or reddish papule with or without crust. It has a generalized distribution, predominating in the thoracic, scapular, scalp, and sternum.[3,12]

It is often confused with seborrheic dermatitis when it appears in the inguinal and perianal region. When the oral cavity is affected, the lesions arise as ulcers that do not heal in the palatine, lingual or gingival fossa.[13] In this organ, evolution is difficult to predict, since there are several prognostic possibilities; spontaneous regression, reactivation or progression (the latter in pediatrics, where the outcomes are lethal).[3,12]

In the lung, it is observed as a disseminated consolidation in both hemithorax whose main manifestation is dyspnea, which does not improve before oxygen therapy at high flows, with varied radiographic findings, presenting from small intralobular nodules to confluent cystic lesions of diffuse distribution.[2,14]

However, several affected tissues have been found, which are more infrequent and whose epidemiological record has been more limited (larynx, hypothalamus, colorectal territory).[15-17] This condition is also recognized for favoring the accumulation of fluids in virtual spaces causing pleural and pericardial effusion, and ascites.[18]

As is known, its manifestations are very broad but, to identify that it is a multisystem invasion, the most outstanding symptoms are constitutional, accompanied by manifestations of the affected region in question, which in global terms is suspected when cutaneous erythema, dyspnea, polydipsia, polyuria, bone pain, lymphadenopathy, unintentional weight loss, fever, ataxia and alterations in memory. Some studies suggest that diabetes insipidus is listed as the initial manifestation.[2,17]

Currently there are diagnostic criteria provided by the histiocyte society, in order to standardize the components necessary to diagnose this pathology. The confirmatory diagnosis is merely histological and immunohistochemical, usually processed from bone or

skin material, as they are clinically the most obvious and easy to obtain. The evaluation of its presence will depend on the expression of the multiple markers of specific surfaces that have been used for the visualization of the histiocyte in question, among which CD1a+, S-100+, CD68+, CD207+, CD163+, Langerina, Fascina, among others.[1,17]

Its therapeutic approach is controversial and varies according to the type of affectation; in some cases, there is spontaneous regression, others only merit surveillance and some that despite receiving standard treatment have a fateful outcome.

Expectant, conservative or immunomodulatory management is recommended in patients who have involvement of a single organ or system (single lesion in bone, exclusive skin involvement, implementation in a single lymph node).[9]

Chemotherapy is recommended in patients with multisystem invasion; in them the preferred therapeutic scheme is the concomitant administration of steroid (prednisone) and vinblastine, both in induction cycles, subsequently subjected to a maintenance phase that will be determined according to the preliminary therapeutic response.[1]

Those who study with multisystem involvement where it involves skin, bone marrow, lung and/or liver, are those who are classified as high-risk patients with an unfavorable response to treatment and with poor prognostic repercussions.

In case of poor response to conventional management, some patients undergo the administration of cladribine and cytarabine, for a short period, with hopeful results. Of course, there are other modalities that, although not fully supported, have yielded good results, such as allogeneic transplantation of hematopoietic cells, used especially in the scenario of histiocytosis refractory to conventional treatment.[1] Although these therapeutic modalities demonstrate optimistic results in the short and medium term, reactivations are the predominant problem, affecting more than half of the cases treated.[9]

CONCLUSION

Although histopathological and immunohistochemical studies are decisive to confirm the existence of Langerhans cell histiocytosis, it is still considered a challenge to lead to its diagnosis given the complexity of its pathogenesis and the diversity of its clinical behavior, given that most of the documented findings belong to a young population, reported in an extraordinary way in the adult population with very few isolated cases in geriatric patients.

This entity should be suspected in the presence of papular lesions that resemble seborrheic dermatitis that may or may not be accompanied by bone involvement or dysfunction in other organs. Our patient had fever, brown papular dermatosis with scaly area that affected the scalp, face, trunk, folds and extremities in more than 50% of the total body surface, bone changes at the level of thoracic vertebra, serositis in pulmonary, pericardial and abdominal cavities, hepatosplenomegaly and involvement in renal function with progressive elevation of azoados as well as immunohistochemical report compatible with histiocytosis of Langerhans cells and that by its Dissemination was concluded to be multisystemic, which gave it a lethal outcome. The ability of current treatments to achieve functional cures and significantly impact the natural history of this entity is still limited. The lines of research to further understand the terms pathophysiological and therapeutic remain difficult terrain to understand, and constantly offers new studies and cases to consider.

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