Complexity of diagnosing and treating langerhans cell sarcoma: A case report

Difficulté diagnostique et thérapeutique du sarcome à cellules de Langerhans: Cas clinique

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Abstract

Introduction: Langerhans cell sarcoma (LCS) is a very rare malignant tumor of Langerhans cells that may metastasize to many organs. The diagnosis of this tumor is difficult and its prognosis is poor.
Aim: To report the difficulty to diagnose LCS, and discuss therapeutic management of this rare entity.
Case presentation: We report a case of LCS in a 52-year-old man who presented with an axillar lymphadenopathy. The diagnosis of nodular sclerosis type Hodgkin's disease was established after histologic examination. The patient was treated with chemotherapy (ABVD regimen: Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) and radiotherapy with a partial response. However, disease recurrence was observed and histological analysis confirmed the diagnosis of Langerhans cell sarcoma. A revision of the initial histological examination concluded to the diagnosis of sarcoma from the beginning. We chose the ESHAP (Etoposide, Methylprednisolone, Aracytine, Cisplatin) regimen and clinical improvement of LCS was obtained after 2 cycles but the patient had a fatal outcome and died by disease progression.
Conclusion: Because of its rarity, diagnosis is difficult and an optimal treatment strategy for this disease has not yet been identified. Polychemotherapy can be an effective modality for the treatment of LCS.

Key words: Hodgkin lymphoma, Langerhans cell sarcoma, Diagnosis, Chemotherapy

Résumé

Introduction: Le sarcome à cellules de Langerhans (SCL) est une tumeur maligne très rare des cellules de Langerhans qui peut toucher plusieurs organes. Le diagnostic de cette tumeur est difficile et son pronostic est sombre.
Objectif: Rapporter la difficulté du diagnostic du SCL et de discuter de la prise en charge thérapeutique de cette entité rare.
Observation: Un homme âgé de 52 ans a consulté pour l'apparition d'une adénopathie axillaire. L'examen histologique de l'adénopathie a confirmé le diagnostic de lymphome de Hodgkin de type scléro-nodulaire. Le patient a été traité par chimiothérapie de type ABVD (Doxorubicine, Bléomycine, Vinblastine, Dacarbazine) et radiothérapie avec une réponse partielle. Cependant, une rechute de la maladie était survenue et l'analyse histologique a conclu au diagnostic de sarcome à cellules de Langerhans. Une relecture de l'examen histologique initial a conclu au diagnostic du SCL dès le début. Le malade a reçu une chimiothérapie de type ESHAP (Etoposide, Méthylprednisolone, Aracytine, Cisplatine) et une amélioration clinique du sarcome a été observée après 2 cycles de chimiothérapie mais le patient est décédé par progression de la maladie.
Conclusion: Vu sa rareté, le diagnostic du SCL est difficile et une stratégie thérapeutique optimale pour cette maladie n'a pas encore été identifiée. La polychimiothérapie pourrait être une option thérapeutique efficace pour le traitement du SCL.

Mots clés: lymphome de hodgkin, sarcome à cellules de langerhans, diagnostic, chimiothérapie

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INTRODUCTION

Langerhans cell sarcoma (LCS) is a rare malignant neoplasm of dendritic cells, which is characterized by an aggressive clinical behavior with a multiorgan involvement including lymph nodes, liver, spleen, lung, and skin (1). The diagnosis of LCS is difficult because of morphological similarity to other tumors. Given its rarity, there is a lack of evidence regarding the most appropriate treatment for this disease, different therapeutic modalities have been used including surgery, radiotherapy and chemotherapy with variable results (2). We describe in this report a case of LCS arising in an axillar lymph node with lung involvement, treated with ESHAP regimen, initially diagnosed and treated as Hodgkin Lymphoma.

CASE REPORT

A 52-year-old man, with no medical history, presented to the hematology department with an axillary mass developed over a period of six months. There were no associated B symptoms. On presentation the patient was otherwise healthy with a performance status 1. Physical examination revealed only a firm right axillar lymph node of 4 cm. Pathological examination of the excised lymph node revealed a nodular appearance with an inflammatory infiltrate including many large cells sometimes multinucleated with a large nucleoli, reminiscent of Reed Sternberg cells. Given the clinical presentation and the histological features of the lymph node, a lymphoma was suspected. The pathologist performed the immunohistochemical study by testing lymphoma markers CD3, CD20, CD15 et CD30 as well as other markers to exclude other solid tumors. Immunohistochemical staining revealed a weak positivity of large cells for CD30. These cells were focally positive for CD15. The diagnosis of nodular sclerosis type Hodgkin's disease was retained and computerized tomography (CT) scan imaging showed right axillary and retro pectoral lymphadenopathy with no evidence of involvement of other organs. Bone marrow biopsy revealed no lymphomatous infiltration.

According to the treatment protocol of localized Hodgkin lymphoma, the patient was treated with 4 courses of polychemotherapy with Doxorubicin, Bleomycin, Vinblastine and Dacarbazine (ABVD) associated with local radiotherapy at a dose of 36 Gray. At the end of treatment, the evaluation of the disease by a CT scan showed a partial response according to Cheson criteria.

Seven months later, the patient noted a left axillary swelling. Physical examination revealed edema of the right upper limb, right parasternal parietal mass of 5 cm, right supraclavicular lymphadenopathy measuring 2 cm and axillary lymphadenopathy measuring 5 cm.

A second lymph node biopsy was performed. Tumor cells were large, sometimes multinucleated with abundant faintly eosinophilic cytoplasm. Nuclei were atypical. Mitotic figures were numerous (Figure 1).

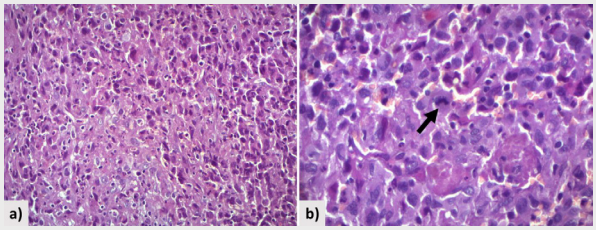

Figure 1. Histological features: a) Hypercellular proliferation of large cells sometimes multinucleated with some eosinophils (HEx200) b) Tumor cells show atypia with increased mitotic figures (arrow) (HEx400).

At immunohistochemical study, tumor cells were negative for Keratin, CD3, CD5, CD15, CD20 and CD30. A second panel of markers including CD1a, CD68 and PS100 was performed. Tumor cells showed a strong positivity for these three markers (Figure 2). These features confirmed the diagnosis of Langerhans cell sarcoma. A staining for CD1a was performed retrospectively for the first lymph node biopsy and showed that tumor cells were positive for this marker. We concluded to the diagnosis of LCS from the beginning of the disease.

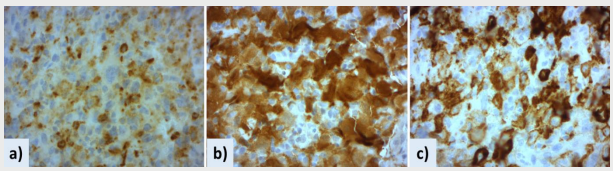

Figure 2. Immunohistochemistry: Tumor cells, including atypical multinucleated giant cells, are positive for CD68 (a), S100 protein (b) and CD1a (c) (x400).

Since the patient had already received an anthracycline-based treatment and due to multiorgan involvement with a recurrent disease, the patient was treated with Etoposide, Methylprednisolone, Aracytine, Cisplatin (ESHAP) and improvement was seen after 2 cycles of chemotherapy with good response at clinical examination. Unfortunately, the patient developed delirium due to hyponatremia after the second course with a good outcome under symptomatic treatment. But he refused to continue chemotherapy courses and died at home due to disease progression 2 months later.

DISCUSSION

LCS is an extremely rare tumor and only few such cases have been reported in the literature.

The rarity of this entity makes its diagnosis challenging and sometimes unrecognizable by pathologists. In our case, the non specific clinical presentation, the histological features of lymph node and the patient's response to Hodgkin lymphoma chemotherapy led to the misdiagnosis. Furthermore, the treatment of LCS is not consensual and there are different therapeutic modalities used in the various cases reported in the literature, depending on the authors' choice.

LCS develops from langerhans cells which are a subclass of antigen-presenting dendritic cells that have different ultrastructural, immunophenotypic, and functional properties (3). There are two entities of tumors arising from langerhans cells as reported by the World Health Organization: Langerhans cell histiocytosis (LCH) and LCS (4).

LCH is benign tumors that mainly affect bone and have a favorable prognosis (5) whereas LCS is an extremely rare and highly aggressive neoplasm that is characterized by localized or multiorgan involvement and affects commonly lymph nodes (74%), followed by skin (48%), lung (28%), liver (16%) spleen (15%) and also bone (1,2).

Histological diagnosis of LCS is difficult due to the rarity of the disease and its morphological similarity to tumors with a pleomorphic component. Based on the morphological appearance, confusion between LCS and other tumors may occur such as malignant melanoma, anaplastic carcinoma, diffuse large cell lymphoma, anaplastic large B-cell lymphoma, T-cell lymphoma and dendritic cell tumors (6). Moreover, there is a difficulty to distinguish LCS from LCH.

These two entities share the same immunohistochemical features with positivity for CD1a, Langerin, S100 protein and Birbeck granules. However, LCS show higher degrees of histological atypia and increased mitotic rates. The weak expression of lysozyme is frequently observed and it can be helpful for the diagnosis of LCS (7). In our case, the review of the first lymph node biopsy concluded to LCS. Indeed, several parameters led to the error: the morphological similarity between tumor cells and Reed Sternberg cells especially with the presence of an inflammatory background, the positivity of CD15 and CD30, the absence of immunohistochemical study for CD1a and S100 protein and the chemosensitivity to the treatment of Hodgkin lymphoma. An optimal treatment strategy for LCS has not been identified and treatment of this disease is not consensual. Several treatments were used depending on the stage of the disease with 3 major categories: surgery, chemotherapy and radiotherapy. Bone marrow transplant has also been performed in rare cases (2). Previous reports showed that surgical excision is a good therapeutic option for localized disease and can lead to complete remission especially in the event of a single organ involvement. Surgery has also been associated with adjuvant chemotherapy and/or radiotherapy in some reported cases of patients with 1 or 2-organ disease with controversial results (2). Radiotherapy alone was reported by Nakayama et al. in a case of localized cervical lymph node disease treated by radiotherapy with a complete remission after a 45-month follow-up (7). However, for patients with disseminated or recurrent disease, other studies found that a benefit could be obtained with chemotherapy. Many chemotherapeutic agents were administered in the reported cases, the most common regimen was CHOP (Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone) chosen for its efficacy in lymphomas but results were controversial (2,8). Several other protocols were used either in first line or after failure of the CHOP regimen; Kaleem et al. demonstrated that EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide and Doxorubicin) was effective for a LCS patient with multi-organ involvement (9). Kwong et al. reported a case with 5-site disease treated using a novel EPIG regimen (Etoposide, Cis-platinum, Ifosfamide and Gemcitabine) and the patient showed good response with complete remission at the end of treatment (10). Yoshimi et al. recommend the ESHAP regimen used as salvage therapy in a patient on progression below 3 cycles of CHOP with good response (3).

In the literature, a small number of patients underwent bone marrow transplant but the results are satisfactory. Howard el al. conclude that bone marrow transplant appears to be an effective treatment in patients with more than 2-organ disease at diagnosis (2). Therefore, this therapeutic modality could play an important role in the management of disseminated LCS.

Due to the poor prognosis of Langerhans cell sarcoma, a more aggressive treatment, including systemic combination chemotherapy and bone marrow transplant may provide a benefit to patients with advanced stage LCS and should be considered even for localized disease in order to improve patient's outcome.

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