

Langerhans cell sarcoma arising from antecedent langerhans cell histiocytosis

A case report

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Abstract

Rationale: Langerhans cell sarcoma (LCS) is a rare, high-grade neoplasm characterized by overtly malignant cytologic features and a poor prognosis. Herein, we present a rare case of langerhans cell histiocytosis (LCH) that later transformed into langerhans cell sarcoma 11 months after the benign mass was excised from soft tissue in the right groin.

Patient concerns: A 41-year-old patient who presented with a mass in the right groin for 3 years earlier after being bitten by ants.

Diagnoses: The patient was diagnosed with langerhans cell sarcoma arising from antecedent langerhans cell histiocytosis.

Interventions: The patient underwent with 6 cycles of a modified etoposide, cyclophosphamide, vindesine, dexamethasone (E-CHOP) regimen.

Outcomes: The patient is currently receiving follow-up care.

Lessons: LCH transformed into LCS is a rare case. E-CHOP as an effective first-line therapy to treat LCS cases, but, the mechanism is unclear. Due to their rarity, further data on clinical outcomes are necessary to establish the optimal treatment strategy for LCS.

Abbreviations: 2-CDA = 2-chlorodeoxyadenosine, ALK = anaplastic lymphoma kinase, CHOP = cyclophosphamide, vindesine, dexamethasone, E-CHOP = etoposide, cyclophosphamide, vindesine, dexamethasone, ESHAP = etoposide, carboplatin, cytarabine, methylprednisolone, FDG-PET = fluorine-18 fluorodeoxyglucose positron emission tomography, LCH = langerhans cell histiocytosis, LCS = langerhans cell sarcoma, MUM-1 = melanoma associated antigen-1.

Keywords: chemotherapy, langerhans cell sarcoma, surgical resection

1. Introduction

According to the World Health Organization 2008 guidelines, tumors derived from langerhans cells include langerhans cell histiocytosis (LCH) and langerhans cell sarcoma (LCS). LCH is a benign clonal proliferation of langerhans cells, whereas LCS is a neoplastic histiocytosis where cells exhibit overtly malignant features. The 2 disorders have many similarities, including CD1a, S100, and langerin (CD207) expression and the appearance of

typical Birbeck granules.^[1] Occasionally, LCH can undergo malignant transformation into LCS,^[2] and acquire neoplastic cellular characteristics such as atypia, hyperchromatic nuclei, prominent nucleoli, and frequent mitotic figures.

2. Case report

Herein, we describe a case of LCH treated by surgical resection that subsequently transformed into LCS 11 months after surgery. The patient was a 41-year-old male who presented with a mass in

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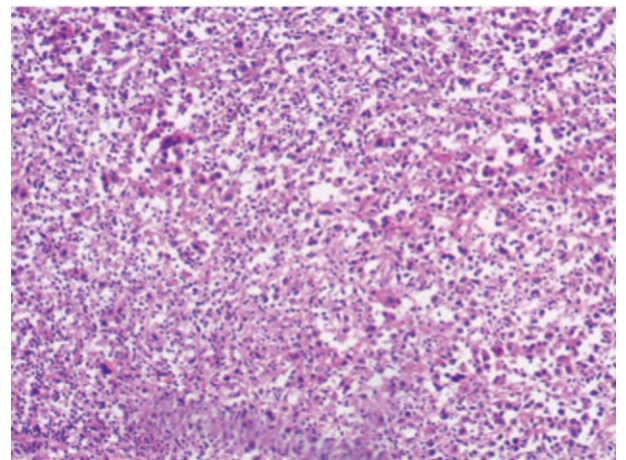


Figure 1. Langerhans cell sarcoma (LCS) cells with malignant cytologic features, including hyperchromatic nuclei, prominent nucleoli, and a high mitotic rate. Cells were stained with hematoxylin and eosin (H&E).

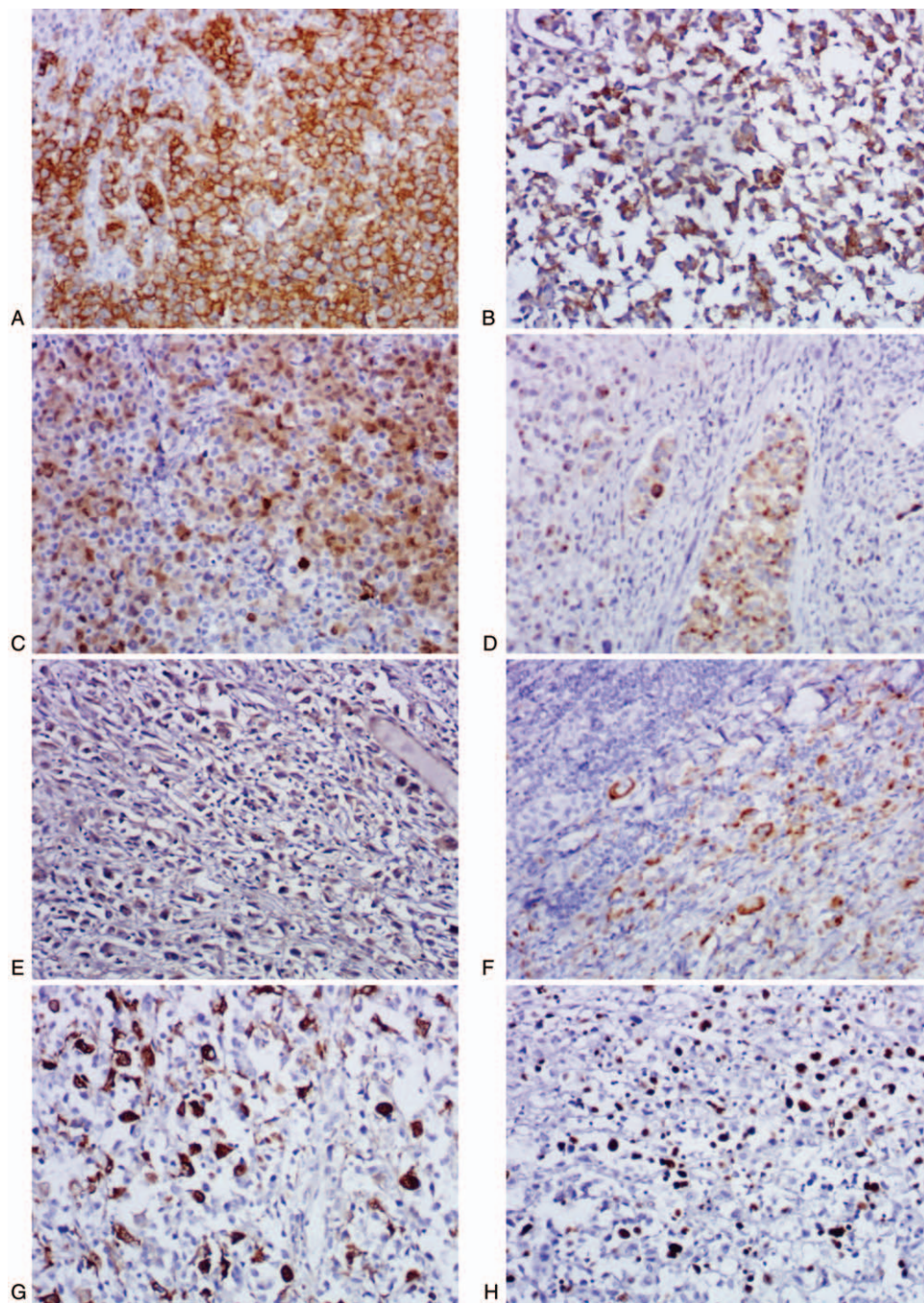


Figure 2. LCS immunophenotyping. Tumor cells were positive for (A) CD1a, (B) CD4, (C) S100, (D) langerin (CD207), (E) vimentin, (F) CD68, and (G) CD163. H, Ki67 proliferation index was ~65%. Magnification, $\times 400$.

the right groin that developed 3 years earlier after being bitten by ants. During this time, he had no symptoms and thus did not seek treatment. One year later, the patient was admitted to the local hospital with a fever fluctuating between 37.8°C and 38.2°C and the soft tissue mass was resected with a wide local excision. Clinical pathology revealed a typical LCH mass consisting of characteristic histiocytes with grooved nuclei surrounded by lymphocytes and eosinophils. In addition, the histiocytes showed membrane staining for CD1, S100, langerin, and CD4, but were negative for CD56, TIA1, CD68, and CD3. The proliferation rate was 15% based on Ki67 expression. There were no surgical

complications; however, the patient was readmitted 11 months after detecting another mass on the right inguinal. Physical examination revealed firm, nontender lymph nodes in both inguinal areas, but no other clinical symptoms. Fluorine-18 fluorodeoxyglucose positron emission tomography revealed multiple enlarged lymph nodes and nodules on the right side of the abdominal aorta, around the right iliac blood vessels, the right side wall of the basin, and the right groin. Clinical laboratory values—including complete blood count, serology, lactate dehydrogenase, and $\beta 2$ -microglobulin—were normal and bone marrow aspiration showed no significant abnormalities.

The histiocytic tissue was resected from the right groin and sent for pathological analysis. The results showed invasive cells with malignant cytological features and an increased mitotic rate (Fig. 1). Immunophenotyping revealed cells positive for CD1a, S100, langerin, CD4, CD163, CD68, and vimentin, and negative for anaplastic lymphoma kinase (ALK), HMB45, melan-A, CD3, CD5, CD20, CD30, and melanoma associated antigen-1 (MUM-1). In addition, the cellular proliferation rate increased to 65% as determined by Ki67 staining (Fig. 2).

The patient was treated with a modified E-CHOP regimen consisting of etoposide (0.1 g/m², days 1–3), cyclophosphamide (750 mg/m², day 1), vindesine (4 mg/m², day 1), and dexamethasone (10 mg/kg/day, days 1–5). A month later, abdominal computed tomography revealed that the hypogastric lymph nodes and nodules had significantly decreased in size. Following these results, the patient was given a total of 6 E-CHOP treatment cycles and is currently receiving follow-up care.

3. Discussion

Langerhans cells are dendritic cells that localize to the skin and mucosa and were first described by Paul Langerhans in 1868.^[3] LCS is extremely rare and has a dismal outcome even with intensive chemotherapy. It is generally considered to be a malignant variant of histiocytosis that can develop de novo or from antecedent LCH. According to the 2008 WHO tumor classification, dendritic cell-derived tumors can be classified as LCH, LCS, finger-like dendritic cell sarcoma, follicular dendritic cell sarcoma, or declassified dendritic cell sarcoma^[4].

The diagnostic criteria for LCS include malignant cytological features—such as atypia, hyperchromatic nuclei, prominent nucleoli, and frequent mitotic figures—and the expression of typical immunophenotype markers, including CD1a, S100, and langerin (CD207). They can also exhibit CD68 and weak lysozyme expression. The appearance of Birbeck granules characteristic of Langerhans cells can also aid differential diagnosis; however, these granules can be damaged during tissue processing prior to microscopic analysis.^[5] It should also be noted that the genetic mutations in the Langerhans cell-specific marker langerin are associated with a lack of Birbeck granules and can also complicate diagnosis.^[6,7] Moreover, CD31 expression has been attributed to an enhanced migratory capacity.^[8] Despite a similar cellular phenotype, LCH cells exhibit lower mitotic rates and cytologically benign nuclei that allow for its discrimination from malignant LCS.

LCS is typically associated with multiorgan involvement, including the skin, lymph nodes, lungs, bone, liver, spleen, and other soft tissues. The disease shows no gender preference and patients vary greatly in age—from 11 months to 81 years based on the reviewed literature.^[5,9] Because of its rarity, an optimal treatment strategy for LCS has not been established, owing to its rarity; however, surgical resection appears to be a good option for localized lesions or confined nodal disease. For instance, Çallı et al reported a case with axillary lymph node involvement treated by curative mass resection. The patient did not receive any other adjuvant therapy and had no evidence of recurrence at annual follow-up.^[10] In addition, radiotherapy may be effective in treating minimally invasive LCS lesions, as Nakayama et al reported on a patient with a localized tumor in the cervical lymph node treated with radiotherapy alone that displayed no signs of recurrence for 45 months.^[11]

The successful treatment of advanced LCS with multiple-organ involvement is feasible with a variety of chemotherapeu-

tic regimens. Systemic combination chemotherapy, such as the CHOP or CHOP-like regimens, may be helpful in some cases.^[12–14] Yoshimi et al used the ESHAP (etoposide, carboplatin, cytarabine, methylprednisolone) regimen to treat a case refractory to the CHOP regimen, and observed a remarkable improvement. Thus, they supported use of the ESHAP regimen as a treatment for refractory disease.^[15] Comparatively, Keklik et al treated a patient with the 2-chlorodeoxyadenosine (2-CDA) regimen but, despite an initial improvement, the disease progressed after the fourth cycle of therapy.^[16] They subsequently administered 2 cycles of ESHAP as a second-line therapy; however, the patient developed advanced disease and died. Nevertheless, current data indicate that the ESHAP regimen may be partially effective in treating relapsed patients.

In conclusion, our case supports E-CHOP as an effective first-line therapy to treat LCS cases that develop from antecedent LCH and display a typical immunophenotype with S100, CD68, CD1a, and langerin expression; but the mechanism is unclear. Further data on clinical outcomes are necessary to establish the optimal treatment strategy for LCS.

Author contributions

WY drafted the manuscript. W-YC made the clinical diagnosis. T-XY made the clinical diagnosis, LWN and J-PL collected the data and helped draft the manuscript.

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