

Langerhans Cell Histiocytosis Following Hodgkin Lymphoma in Adult: A Case Report

¹Ali Bawahal, ²Huda O. Basaleem

DOI: [https://doi.org/10.47372/yjmhr.2024\(13\).2.4](https://doi.org/10.47372/yjmhr.2024(13).2.4)

Abstract

Introduction: Langerhans cell histiocytosis (LCH) is a very rare disorder, and usually considered a disease of childhood. It is rarely observed in adults. Its etiopathogenesis remains to be elucidated. One possible etiological cause is a reactive proliferation of Langerhans cells following chemotherapy or radiotherapy for Hodgkin's disease (HD). Eosinophilic granuloma is the benign accumulation of histiocytes located primarily in the bones, but which also affects other organs, including the skin, lungs and lymph nodes. The time interval between LCH occurrence and previous lymphoma is variable. The occurrence of eosinophilic granuloma in a patient with Hodgkin disease has rarely been reported.

Objective: This case report aimed to describe the clinic-pathological, histopathological, immunohistochemical and other features of LCH and to analyze LCH clinical features for improving diagnosis and decreasing misdiagnosis rate.

Case report: In this report, a 38-year-old female presented with LCH twenty-two months after diagnosis and treatment of nodular sclerosing HD. The patient presented with generalized lymphadenopathy and general weakness. The Langerhans cells diffusely infiltrated in the inguinal lymph node and the tumor cells were positive for CD1a and S-100 expression. The patient received chemotherapy and show complete remission.

Conclusion: LCH has a very rare occurrence following HD in adult. The definitive diagnosis depends on pathological biopsy and immunohistochemistry. Although specific therapeutic approach hasn't been well established, combined chemotherapy for multisystem lesions and surgical operation or radiotherapy for unifocal lesions may improve the therapy.

Keywords: Hodgkin Disease, Langerhans Cell Histiocytosis, Immunohistochemistry, Yemen

1 The National Oncology Center-Shabwah, Faculty of Medicine and Health Sciences, University of Shabwah, Aliyaslem2007@gmail.com , +967775901315

2 Aden Cancer Registry and Research Center, Faculty of Medicine and Health Sciences, University of Aden, hudabasaleem92@yahoo.com, +967771263944

كثرة المنسجات لخلايا لانجرهانس بعد سرطان الغدد الليمفاوية هودجكين عند البالغين:
تقرير حالة
علي باوهال¹ ، هدى باسليم²

ملخص الدراسة

المقدمة: كثرة المنسجات لخلايا لانجرهانس هو اضطراب نادر جدًا، وعادةً ما يعتبر مرضًا يصيب الأطفال. ونادراً ما يتم ملاحظته عند البالغين. وما زالت أسبابه المرضية يجب توضيحها. أحد الأسباب المسببة المحتملة هو التكاثر التفاعلي لخلايا لانجرهانس بعد العلاج الكيميائي أو العلاج الإشعاعي لمرض سرطان الغدد الليمفاوية هودجكين. الورم الحبيبي اليوزيني هو تراكم حميد للخلايا المنسجات الموجودة بشكل أساسي في العظام، ولكنه يؤثر أيضًا على الأعضاء الأخرى، بما في ذلك الجلد والرئتين والغدد الليمفاوية. الفاصل الزمني بين حدوث كثرة المنسجات لخلايا لانجرهانس وسرطان الغدد الليمفاوية السابق متغير. نادراً ما تم الإبلاغ عن حدوث الورم الحبيبي اليوزيني في مريض مصاب بمرض هودجكين.

الهدف: يهدف تقرير الحالة هذا إلى وصف الخصائص السريرية المرضية والتشريحية المرضية والكيميائية المناعية وغيرها من خصائص مرض كثرة المنسجات لخلايا لانجرهانس وتحليل السمات السريرية لمرض كثرة المنسجات لخلايا لانجرهانس لتحسين التشخيص وتقليل معدل التشخيص الخاطئ.

تقرير الحالة: في هذا التقرير، أصيبت امرأة تبلغ من العمر 38 عامًا بمرض كثرة المنسجات لخلايا لانجرهانس بعد اثنتين وعشرين شهراً من تشخيصها وعلاجها من سرطان الغدد الليمفاوية هودجكين. المريضة عانت من تضخم عقد لمفاوية في أغلب الجسم وضعف عام. تسلتت خلايا لانجرهانس بشكل منتشر في العقدة الليمفاوية الأربية وكانت الخلايا السرطانية إيجابية بالنسبة لتعبير CD1a و S-100. تلقت المريضة العلاج الكيميائي وأظهرت استجابة كاملة.

الاستنتاج: حدوث كثرة المنسجات لخلايا لانجرهانس نادر جدًا بعد الإصابة بسرطان الغدد الليمفاوية هودجكين عند البالغين. حيث يعتمد التشخيص النهائي على الخزعة المرضية والكيمياء المناعية. على الرغم من عدم وجود نهج علاجي محدد بشكل جيد، إلا أن العلاج الكيميائي المشترك للآفات متعددة الأجهزة والجراحة أو العلاج الإشعاعي للآفات أحادية البؤرة قد يحسن العلاج.

الكلمات المفتاحية: مرض هودجكين، كثرة المنسجات لخلايا لانجرهانس، الكيمياء المناعية، اليمن.

علي باوهال¹ ، هدى باسليم²
¹المركز الوطني للأورام، شبوة و كلية الطب والعلوم الصحية، جامعة شبوة
²مركز تسجيل وأبحاث السرطان، كلية الطب والعلوم الصحية، جامعة عدن

Introduction

Langerhans cell histiocytosis (LCH) is a very rare disorder, and usually considered a disease of childhood. It is rarely observed in adults. Its etiopathogenesis remains to be elucidated [1].

One possible etiological cause is a reactive proliferation of Langerhans cells following chemotherapy or radiotherapy for Hodgkin's disease (HD).

Eosinophilic granuloma is the benign accumulation of histiocytes located primarily in the bones, but which also affects other organs, including the skin, lungs and lymph nodes.

A number of cases of LCH associated with malignant lymphoma had been reported previously: It may follow after the malignant lymphoma [2–5] or occur with it [6].

The time interval between LCH occurrence and previous lymphoma is variable.

The occurrence of eosinophilic granuloma in a patient with HD has rarely been reported. In the present report, we present one case patient who was diagnosed with LCH following chemotherapy for HD.

Diagnosis of HD

In this report, In July 2020, a 38-year-old female presented with two months history of fever, generalized lymphadenopathy and general weakness associated with weight loss and night sweating (B symptoms).

The patient's past medical history indicated no abnormalities. Physical examination revealed conscious, oriented, febrile, pallor, no cyanosis, no jaundice. Chest was clear with good air entry bilaterally. Cardiovascular system S1 + S2 no murmur. Abdomen was soft with hepatosplenomegaly. There was generalized lymphadenopathy.

Laboratory examination revealed that the patient's erythrocyte sedimentation rate (ESR) was 130 mm/1 h (≤ 15 mm/1 h), hemoglobin was 6.7 g/Dl, white blood cells were 13.6×10^3 cell/ μ l and platelets were 197×10^3 cell/ μ l. Liver function showed that total bilirubin was 1.0 mg%, alanine transaminase (ALT) was 31 U/L (≤ 40 U/L), aspartate aminotransferase (AST) was 66 U/L (≤ 50 U/L), albumin was 2.5 g/dl and lactate dehydrogenase (LDH) was 313 U/L (100–300 U/L). Computed Tomography (CT) scans of the neck, thorax, abdomen and pelvic revealed multiple enlarged lymph nodes seen on both sides of the neck largest one more than 1 cm on the left side. There were: enlarged lymph nodes on sublingual and submental region, multiple enlarged lymph nodes on both axillae markedly on the left axilla the largest one measuring about 2.5 x 2.3 cm and multiple enlarged lymph nodes para-aortic the largest one measuring about 1.4 cm and enlarged para splenic lymph nodes. The spleen was enlarged in size more than 15 cm splenomegaly. Enlarged lymph nodes were seen on inguinal area the largest one measuring about 2 cm on right inguinal area (Fig.1).

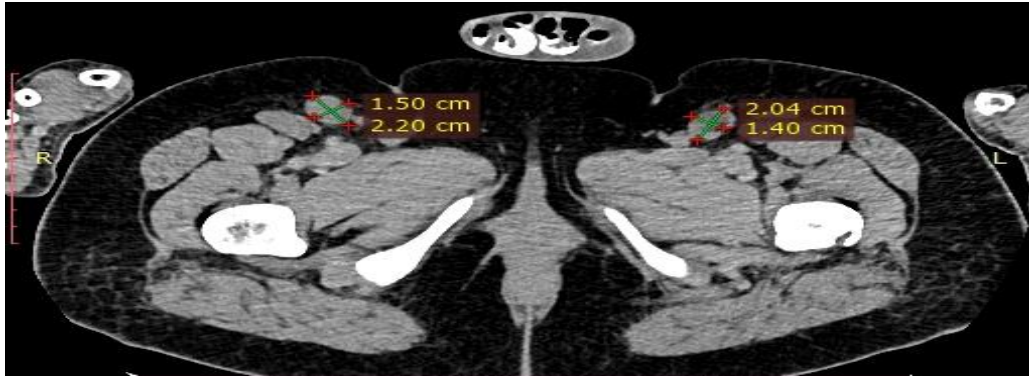


Fig.1: Pelvic CT scan: show multiple enlarged lymph nodes seen on both sides of the inguinal area.

Biopsy was performed from one of the enlarged cervical nodes (measuring 1.5 cm). In histopathologic examination, submitted tissue revealed the presence of losing of nodal capsule with broad collagen bands and lymphoid nodules consist of huge

number of eosinophils and neutrophils with large mononuclear cells looked to be Reed-Sternberg cells- lacunar variant. The findings are consistent with Nodular sclerosing Hodgkin lymphoma. (Fig.2).

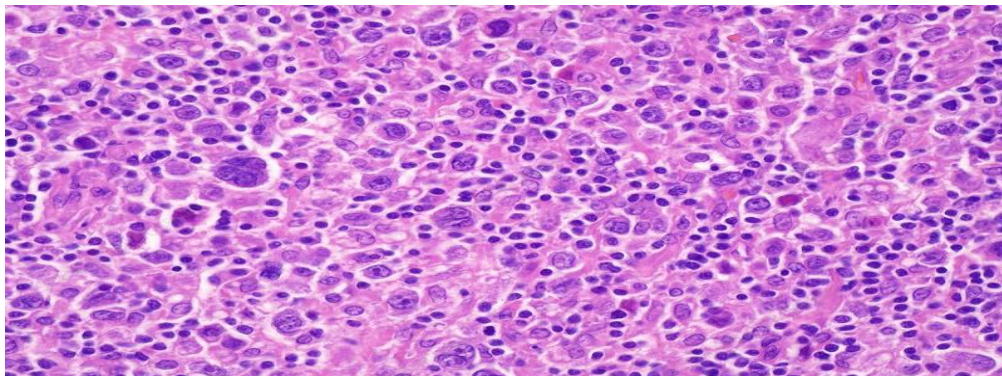


Fig.2: Light micrograph showing numerous Reed-Sternberg cells. The background infiltrate consists mostly.

Immunohistochemical examination (Fig.3) showed that scattered B cell lymphoid follicles (positive for CD20) and T- cell – rich

interfollicular areas (positive for CD3) with sinusoidal aggregates of histiocytes (positive for CD68) and (positive for CD30).

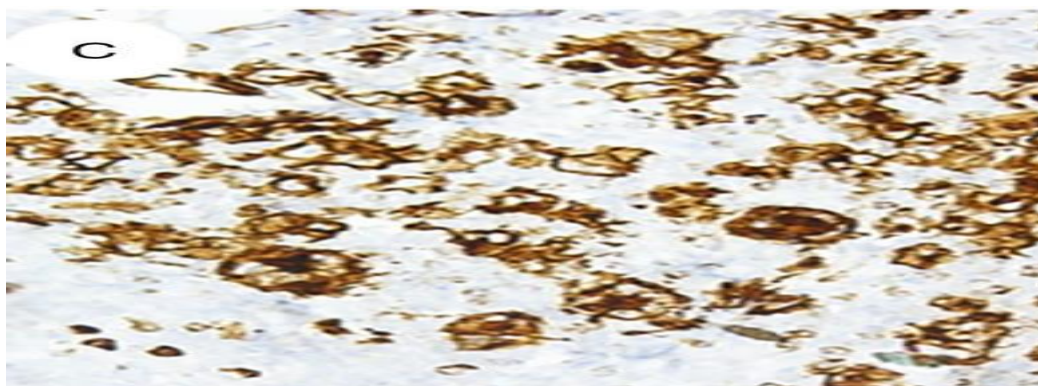


Fig.3: Clusters of CD30-positive cells with membranous and Golgi zone positivity (immunohistochemistry, CD30, $\times 200$)

Diagnosis of LCH

Twenty-two months after the patient entered clinical remission, the patient once again developed generalized lymphadenopathy and skin rash over the left lower limb associated with fever. Physical examination revealed peripheral lymph node enlargement with splenomegaly and skin rash over the left lower limb. The laboratory tests were normal. CT scans of the thorax and abdomen revealed

multiple enlarged lymph nodes on both sides of the neck, axillae and inguinal areas and splenomegaly. An excisional biopsy of the left inguinal lymph node was performed. Microscopic examination revealed lymphohistiocytic cell proliferation. Immunohistochemical examination (Fig. 4) showed that S100, CD1a = positive and CD68 = focally positive.

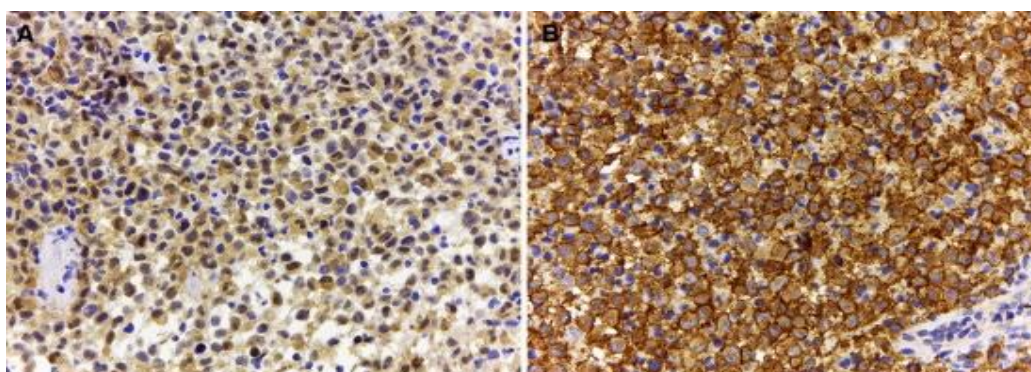


Fig.4: Immunohistochemical profile of Langerhans cell histiocytosis of the head and neck: LCH cells were positive for a S-100 protein (fig.4a), CD1a (fig.4b), (Immunoperoxidase, $\times 400$)

Diagnosis of Langerhan's histiocytosis was made and the patient was treated with two cycles of cytarabine (D1-D5 repeat every 28 days). Then she took the therapy of vinblastine (6 mg / m2

iv once weekly for 6 weeks) + prednisone (40 mg/m2 PO BID X 4 weeks then taper offer 2 weeks). The patient received three cycles of this regimen. Following the

chemotherapy, the patient obtained a remission of the lymphadenopathy, fever and skin rash, and CT scans of the thorax and abdomen revealed a

disappearance of lymph nodes enlargement and splenomegaly. To date, the patient remains in a remission, and keeping on follow-up.

Discussion

LCH, also known as histiocytosis X(HX), is a group of hyperplastic cellular diseases of unknown causes. The Histiocyte Society renamed it as LCH [7].

In 1987 the clinical manifestation varies widely due to the differences among age of onset, the proliferation rate of Langerhans cells and the involved tissues and organs [8].

Braier *et al* [9]. indicated that the incidence rate of rashes in LCH is about 24%.

The patients showed limited invasive nodules and plaques or generalized seborrheic dermatitis-like rashes, which mainly located at torso, scalp, hairline, retroauricular area, skin folds, externalia and etc. Face and feet may also be involved. Besides, it may manifest as ulcers, scabby and granuloma at crissum, groin, armpit or other frictional area as well. Oral and genital mucosae are the most common involved regions. Some patients can appear xanthoma disseminatum that may occur at oral mucosa and conjunctiva. Rash is a common and specific symptom in LCH, and different period rashes which repeatedly occur in batches can be simultaneous developed at a single patient.

It is also the initial symptom which promotes the patient to see a doctor in most cases.

The rashes can occur together with other organ damages or appear as the only symptom. Sometimes the rashes

can be complicated with malignancy [10].

The definitive diagnosis of LCH was based on the histological and immunohistochemical analysis of the lesional biopsy specimens.

The strong positivity for both of the most significant markers used to detect the disease, S-100 and CD1a, made the ultrastructural examination unnecessary.

A presumptive diagnosis of LCH may be made based upon light microscopic findings and a compatible clinical picture, but a definitive diagnosis requires that lesional cells exhibit positive staining with S-100 and CD1a, and the subsequent identification of Birbeck granules upon electron microscopy.

Although the “gold standard” for identification of LC has been detection of Birbeck granules by transmission electron microscopy, this technique is rarely performed today [11].

An association between LCH and a variety of other tumor types has been recognized, and LCH has been described in association with a variety of other tumor types. The malignancies may precede, occur concurrently with, or follow the diagnosis of LCH. The most common associations are with malignant lymphoma and acute lymphoblastic leukemia (ALL) [12].

Lymphoma and ALL more often occur prior to the diagnosis of LCH,

although they may be diagnosed within 5 years following LCH [13]. The association between tumor formation and LCH has yet to be fully elucidated. Dehkordi *et al* (3) discussed the association between the conditions of LCH and HD, and proposed various possibilities: i) HD induces LCH; ii) radiotherapy and/or chemotherapy for HD leads to the development of LCH; iii) LCH may represent a specific cell-mediated immune response to HD; and iv) a common etiological agent induces HD and LCH.

Conclusion

LCH has a very rare occurrence following HD in adult. The definitive diagnosis depends on pathological biopsy and Immunohistochemistry. Although specific therapeutic

Treatments of LCH include surgery, radiotherapy, topical corticosteroids or Mechlorethamine Hydrochloride aqueous solution, thalidomide, systemic chemotherapy and combination therapy. With the progress of chemotherapy, the prognosis of LCH is much better than before.

In the present case, systemic chemotherapy was instituted and after three cycles of chemotherapy, the patient obtained a remission. To date, the patient remains in a remission, and keeping on follow-up.

approach hasn't been well established, combined chemotherapy for multisystem lesions and surgical operation or radiotherapy for unifocal lesions may improve the therapy.

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