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Clinical Record

Isolated adult Langerhans' cell histiocytosis in cervical lymph nodes: should it be treated?

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Abstract

Objective: We report an extremely rare case of Langerhans' cell histiocytosis involving isolated cervical lymph nodes, and we discuss the diagnosis and treatment of this infrequent disease.

Method: We present a case report and literature review concerning this disease entity.

Results: A 54-year-old man presented with persistent, multiple, left neck masses. Histopathological study of lymph node specimens showed proliferation of Langerhans' cells coupled with eosinophilic and neutrophilic microabscesses. Positive immunohistochemical staining for Cluster of Differentiation 1a (CD1a) in Langerhans' cells confirmed the diagnosis. No other abnormalities were noted on a series of image studies. The patient was managed with 'watchful waiting' without subsequent therapy. The neck lesions regressed gradually over time, and the patient did well over a two-year follow-up period.

Conclusion: The clinical presentation of Langerhans' cell histiocytosis is highly variable, and the choice of treatment depends on the involved organs. Definitive diagnosis depends on identification of characteristic immunohistochemical or ultrastructural features of the biopsy specimen. Watchful waiting may be an effective management strategy in cases of adult isolated lymph node Langerhans' cell histiocytosis, due to its possible spontaneous regression.

Key words: Langerhans' Cell Histiocytosis; Lymph Node; Adult; Immunohistochemistry

Introduction

Langerhans' cell histiocytosis is a rare disorder characterised by proliferation of abnormal Cluster of Differentiation 1a-positive (CD1a) dendritic cells.[1] It may cause local or systemic effects.[1,2] The dendritic cells, together with lymphocytes, eosinophils and macrophages, may be found in various organs and result in a wide range of clinical presentations, including those formerly named eosinophilic granuloma, Hand–Schuller–Christian disease and Letterer–Siwe disease.[3–5]

Langerhans' cell histiocytosis has been categorised into single-system and multisystem disease, depending on the number of organs involved. Single-system disease (the localised form) involves single or multiple sites within one organ system, such as bone, skin or lymph nodes. Multisystem disease (the disseminated form) affects multiple organs, and is further subdivided into a high risk group (with involvement of one or more 'risk organs', including liver, spleen, bone marrow and lung) and a low risk group (without involvement of risk organs).[6] Single-system disease accounts for approximately one-third of patients.[7]

Definitive diagnosis of Langerhans' cell histiocytosis is achieved by histopathological examination of involved organ lesions. We report an extremely rare case of isolated adult Langerhans' cell histiocytosis in cervical lymph nodes, in which no therapy was used but a favourable outcome achieved.

Case report

A 54-year-old man noted multiple masses on his left neck over a two-week period. He denied previous fever, weight loss, night sweats, pulmonary complaints or bone pain. He had been a heavy smoker for more than 20 years. His medical and other histories were otherwise unremarkable.

On physical examination, he was afebrile and had a healthy general appearance. Examination of the ear, nose, throat and neck was unremarkable, except for multiple, elastic, movable, mildly tender lymph nodes in the left neck, despite previous antibiotic treatment.

Blood test results were within normal limits, including those for complete blood count and blood chemistry profile. Computed tomography (CT) scanning of the neck demonstrated multiple cervical lymphadenopathy on the left side at levels II, III, IV and V (Figure 1).

The patient underwent lymph node biopsy. Haematoxylin and eosin (H&E) stained tissue sections demonstrated a proliferation of atypical cells with irregular nuclei, focal nuclear grooving and pink cytoplasm, coupled with eosinophilic and neutrophilic microabscesses (Figure 2). Furthermore, slides stained for S100 and CD1a for immunohistochemical analysis were both positive, as shown in Figures 3 and 4, respectively.

Consequently, a series of chest, abdominal and pelvic CT images and a whole body bone scan were performed, with no abnormal findings.

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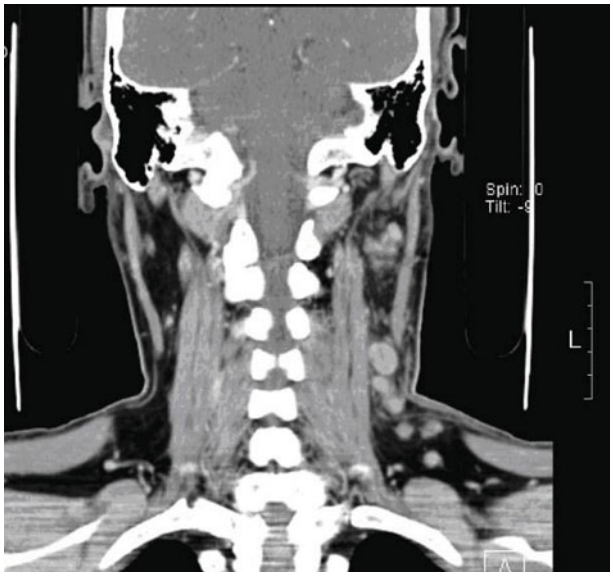

FIG. 1

Coronal reconstruction of contrast medium enhanced computed tomography scan of the neck, showing multiple enlarged left cervical lymph nodes.

As a result, isolated Langerhans' cell histiocytosis of the cervical lymph nodes was diagnosed. The patient was managed by 'watchful waiting', receiving no subsequent radiotherapy or medication but being monitored closely. Two years after presentation, he was quite well with spontaneous disease regression.

Discussion

The aetiology of Langerhans' cell histiocytosis remains a mystery. Ambivalence persists as to whether this disorder is primarily neoplastic, immunodysregulatory, or reactive with both neoplastic and immunodysregulatory characteristics.[3,6] It has been suggested that Langerhans' cell histiocytosis cells may alter their migratory properties through the expression of various chemokine receptors and by releasing inflammatory chemokines, causing not only the retention of the lesional Langerhans' cells but also the recruitment of eosinophils and T lymphocytes. Langerhans' cell histiocytosis may affect any age group, but most patients are aged between five and 20 years. The prevalence of Langerhans' cell histiocytosis in adults is one to two cases per million, significantly lower than that in children.[4] The presenting symptoms may vary depending on the specific organs affected and the extent of involvement. Bone pain, dyspnoea and malaise are the most common symptoms.[8]

The diagnosis of Langerhans' cell histiocytosis is based on identification of characteristic morphological, immunochemical and ultrastructural features of a biopsy specimen of the specific organ lesions. Under light microscopy, the Langerhans' cell resembles a large mononuclear cell with an irregular, lobulated nucleus and homogeneous, granular, eosinophilic cytoplasm. These cells often form granulomas in conjunction with other inflammatory cells. Additionally, immunohistochemical staining using specific markers (i.e. CD1a antigen, adenosine triphosphatase, S100 protein, D-mannosidase and peanutlectin) may assist diagnosis. Furthermore, pentilaminar cytoplasmic inclusion bodies known as Birbeck granules, seen on

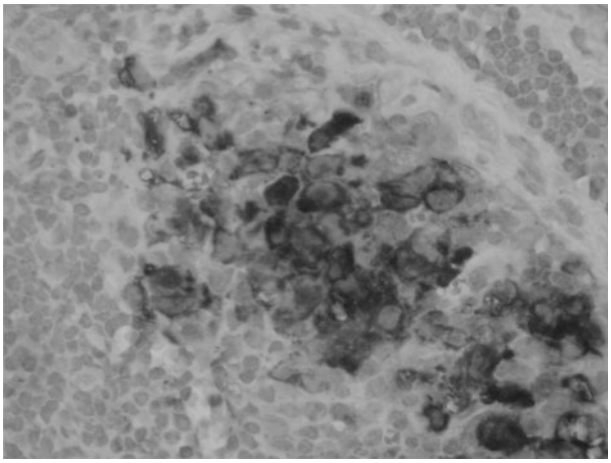

FIG. 3

Photomicrograph with immunohistochemical stain for S100, showing dark staining indicating positivity of Langerhans' cells (×400).

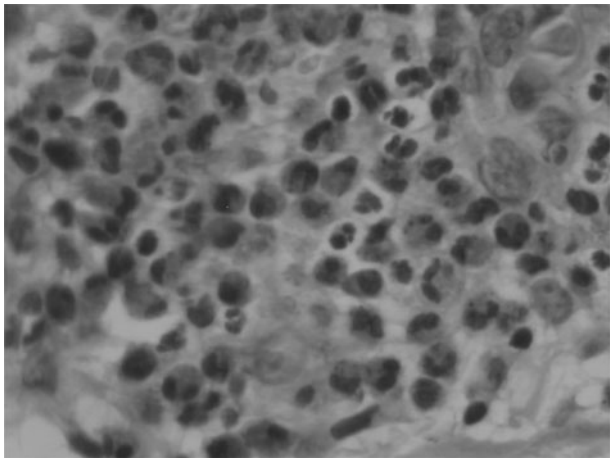

FIG. 2

Photomicrograph of lymph node biopsy showing Langerhans' cells with cleft nuclei and pink cytoplasm, admixed with eosinophilic and neutrophilic microabscesses (H&E; ×400).

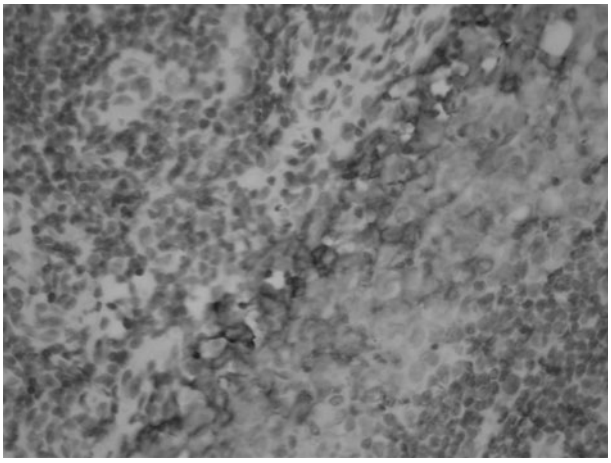

FIG. 4

Photomicrograph with immunohistochemical stain for CD1a, showing dark staining indicating positive membranous pattern in Langerhans' cells (×400).

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ultrastructural analysis, are highly specific to Langerhans' cells. In summary, definitive diagnosis of Langerhans' cell histiocytosis depends on immunohistochemical demonstration of CD1a antigenic determinants on the cell surface, or electron microscopic identification of Birbeck granules in the target cells. The present case demonstrated pathognomonic features of Langerhans' cell histiocytosis, namely Langerhans' cell proliferation on H&E-stained tissue sections and Cluster of Differentiation 1a (CD1a) antigen on lesional cell surfaces on immunohistochemical staining.

- **Isolated cervical lymph node involvement in adult Langerhans' cell histiocytosis is rarely reported, and there is no standard treatment**
- **Definitive diagnosis of Langerhans' cell histiocytosis depends on immunohistochemical demonstration of CD1a antigenic determinants on the cell surface, or electron microscopic identification of Birbeck granules in the target cells**
- **'Watchful waiting' may be an effective therapeutic strategy in adult cases of isolated lymph node Langerhans' cell histiocytosis, due to the possibility of spontaneous regression**

In cases of lymph node Langerhans' cell histiocytosis, coexisting Langerhans' cell histiocytosis is most commonly noted in the bone (62 per cent) and skin (62 per cent), followed by the pituitary gland (38 per cent) and lung (33 per cent). Aricò and colleagues' study of lymph node Langerhans' cell histiocytosis patients found that the disease most commonly involved the head and neck region (6 per cent (18/314)), with involvement of an isolated lymph node being extremely rare (one of 314).[7] In more aggressive cases, liver or bone marrow infiltration is observed.

The clinical course of the disease is unpredictable, varying from spontaneous regression and resolution, to repeated recurrence with chronic sequelae, and even to rapid progression and death. It is possible that cases of isolated lymph node Langerhans' cell histiocytosis present in this way due to previous, spontaneous regression of the true primary site.

Diagnostic investigation of Langerhans' cell histiocytosis should include at least a bone scan, chest X-ray, skeletal X-ray of suspicious bone lesions, abdominal echosonography and routine laboratory tests.[6] Our patient received a battery of imaging studies to exclude the involvement of other organ systems; consequently, a diagnosis of isolated Langerhans' cell histiocytosis in the cervical lymph nodes was able to be made.

Therapeutic strategies are determined by organ system involvement and clinical course, and include watchful waiting, surgical excision, immunomodulation, irradiation, chemotherapy, and organ or stem cell transplantation.[9] The most important indicators of a poor prognosis are involvement of a risk organ (i.e. liver, spleen, lungs or haematopoietic system) and poor response to initial therapy.[10] In contrast, patients with limited involvement may have a fair outcome. It has been reported that patients with isolated bone lesions have the best prognosis, and that adult patients with single-system disease can have a five-year event-free survival of 100 per cent.[7] Treatment strategies for isolated Langerhans' cell histiocytosis in the lymph nodes are controversial, and include surgery, radiotherapy, corticosteroids or a combination of these.[6,11] However, our patient received watchful waiting without subsequent therapy, and had a favourable outcome after two years' follow up.

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