Langerhans cell histiocytosis in sequential discordant lymphoma

K Adu-Poku, D W Thomas, M K Khan, C S Holgate, M E F Smith

CASE REPORT

A 52 year old white woman first presented with right inguinal lymphadenopathy. There was no other lymphadenopathy and no hepatosplenomegaly. She had no B symptoms. Her blood count, erythrocyte sedimentation rate, lactate dehydrogenase, bone marrow examination, and computed tomography scans of the thorax, abdomen, and pelvis showed no soft tissue or bony abnormalities. The underlying stimulus is unknown. A viral aetiology has not been substantiated. However, cigarette smoking is an aetiological factor, especially in pulmonary Langerhans cell histiocytosis. Although some argue that Langerhans cell histiocytosis represents a reactive immune disorder, the relentless progression seen in a proportion of cases and the successful responses to cancer based treatment modalities suggest a neoplastic process. Langerhans cell histiocytosis has a complex relation with other forms of neoplasia. For example, it may be found admixed with lymphoma in the diagnostic biopsy, or may precede or follow the diagnosis of lymphoma.

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The nasopharyngeal biopsies consisted of three irregular tissue fragments, together measuring 17 × 15 × 10 mm. The breast biopsy was fatty tissue measuring 30 × 20 × 10 mm, containing a nodule 10 mm in diameter. Both the nasopharyngeal and breast biopsies showed the histological and immunohistochemical features of B cell non-Hodgkin lymphoma of follicular subtype (grade 3/3), with tumour cells coexpressing CD15 and CD30 (fig 1A–C). In addition, a well defined nodule of Langerhans cells, with scattered eosinophils and central necrosis, measuring 4 mm across, was identified (fig 1D–E). The Langerhans cells showed pale clefied nuclei, inconspicuous nucleoli, abundant pale eosinophilic cytoplasm, and indistinct cell borders. Immunohistochemistry demonstrated strong S100 and CD1a (fig 1F) expression, thereby confirming Langerhans cell histiocytosis.

DISCUSSION

Langerhans cell histiocytosis has a complex association with malignant lymphoma: it may precede, occur with, or follow it. Most commonly, and as was the circumstance in the initial clinical presentation of the patient reported here, the diagnoses are concurrent, with the lymphoma being of Hodgkin type. This association is rare, and has been estimated to be 0.3% for Hodgkin lymphoma.

B cell non-Hodgkin lymphoma of the follicular subtype (grade 3/3) affecting the nasopharynx and breast, and containing foci of Langerhans cell histiocytosis, was diagnosed in a 56 year old white woman who was a longstanding heavy smoker. Four years before this she had developed stage 1a mixed cellularity Hodgkin lymphoma affecting the right inguinal region, which was treated by irradiation and chemotherapy without recurrence. Review of the original Hodgkin lymphoma histology demonstrated a small focus of Langerhans cell histiocytosis. This is thought to be the first recorded case of Langerhans cell histiocytosis occurring in a sequential discordant lymphoma. Its importance is discussed.

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The small size of the initial Langerhans cell histiocytosis focus in the biopsied Hodgkin lymphoma node suggests that the Langerhans cell histiocytosis may represent an abnormal (although possibly neoplastic) stromal response to the Hodgkin lymphoma microenvironment. The identification, four years later, of Langerhans cell histiocytosis within non-Hodgkin lymphoma indicates that the Hodgkin directed radiotherapy and chemotherapy had not eradicated the Langerhans cell histiocytosis, and that the Langerhans cell histiocytosis cells had dispersed far beyond their presumed site of origin within the groin node. In situ hybridisation analysis showed no evidence of Epstein-Barr virus in the two lymphomas.

‘This case suggests a degree of interdependence in the growth of Langerhans cell histiocytosis and the non-Hodgkin lymphoma’

The relative risk of secondary non-Hodgkin lymphoma after treatment of Hodgkin lymphoma ranges from 31.5 to 56.8 times for radiotherapy and radiotherapy with chemotherapy, respectively.9 There does not appear to be a significant increase with chemotherapy alone.9 Given this, no assumption should be made that the Langerhans cell histiocytosis necessarily predisposed to the development of non-Hodgkin lymphoma in our case. However, it should be noted that the distribution of the follicular non-Hodgkin lymphoma (two extranodal sites, oropharynx and breast, without lymph node involvement) is distinctly unusual. In this circumstance, it is reasonable to think that the local environment (that is, the presence of Langerhans cell histiocytosis) may well have had a role in the distribution, and therefore the development, of the non-Hodgkin lymphoma. With regard to the development of the Langerhans cell histiocytosis, its presence in the non-Hodgkin lymphoma biopsies, despite the absence of other clinically detectable Langerhans cell histiocytosis, suggests that the non-Hodgkin lymphoma microenvironment was conducive to Langerhans cell histiocytosis growth. Therefore, this case suggests a degree of interdependence in the growth of Langerhans cell histiocytosis and the non-Hodgkin lymphoma.

In conclusion, we present a case of sequential discordant malignant lymphoma. The presence of Langerhans cell histiocytosis in both types of lymphoma and the patterns of

Figure 1  The Hodgkin lymphoma. (A) Reed-Sternberg and Hodgkin cells positive for (B) CD15 and (C) CD30 immunostaining. (D, E) Nodule of Langerhans cells with eosinophils showing central necrosis (haematoxylin and eosin stain). (F) Langerhans cells with strong CD1a expression.
disease illuminate some of the complex relations between these disease processes.

**Take home messages**

- To our knowledge, we describe the first case of Langerhans cell histiocytosis occurring in sequential discordant lymphoma
- The presence of Langerhans cell histiocytosis in both histologically distinct lymphoma types implies widespread dispersal of Langerhans cell histiocytosis cells from the presumed site of origin
- The findings suggest a degree of interdependence in the growth of Langerhans cell histiocytosis and non-Hodgkin lymphoma

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