Langerhans cell sarcoma – a rare tumour diagnosed by histomorphology and immunophenotyping

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ABSTRACT

Langerhans cell sarcoma is a rare neoplastic proliferation of Langerhans cells that has overt malignant cytologic features. It behaves more aggressively than its counterpart, Langerhans cell histiocytosis. We present here a case of Langerhans cell sarcoma involving the eighth thoracic vertebra in a 31-yr-old man who presented with a two-month history of back pain. In the past, the diagnosis of Langerhans cell sarcoma relied on the demonstration of Birbeck granules. However, with the advent of monoclonal antibodies suitable on routinely-fixed tissues, the Langerhans cell phenotype can be easily confirmed by CD1a protein expression using immunohistochemistry. In this report, we describe the morphological features and the immunohistochemical findings of this tumour diagnosed even in the absence of Birbeck granules. We also highlighted how immunophenotyping is useful in differentiating Langerhans cell sarcoma from other histiocytic and dendritic tumours.

Key words: Langerhans cell sarcoma, morphology, immunophenotyping, CD1a

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INTRODUCTION

The World Health Organization currently classifies Langerhans cell derived neoplasms as Langerhans cell histiocytosis and Langerhans cell sarcoma (Jaffe et al. 2007). Langerhans cell histiocytosis is a proliferating disorder of Langerhans cells, whereas Langerhans cell sarcoma is a neoplastic proliferation of Langerhans cells that have overtly malignant cytologic features (Ben-Ezra et al. 1991, Jaffe et al. 2007). First diagnosed in 1984 (Wood et al. 1984), Langerhans cell sarcoma is a very rare disease that can present de novo or progress from an antecedent Langerhans cell histiocytosis (Lee et al. 2006). The diagnosis relies on malignant cytological features, a typical immunophenotype that consistently shows expression of CD1a, S-100 protein, and Langerin (CD207), and the appearance of the typical Birbeck granules demonstrated by electron microscopy (Ferringer et al. 2006, Jaffe et al. 2007). In practice, Birbeck granules could be demonstrated only in a minority of cases due to the unavailability of fresh tissues for ultrastructural analysis. Furthermore, cells may lose their ultrastructural characteristics as they become less differentiated. In a recent study, Verdijk et al (Verdijk et al. 2005) found lack of Birbeck granules in Langerhans cells to be associated with mutation in the Langerin gene.

Currently, with the availability of antibodies suitable for tissue immunohistochemistry, the identification of the cell of origin of the different types of tumours can easily be performed on formalin-fixed paraffin-embedded tissues. In addition, the use of antigen retrieval techniques has allowed an expanded range of molecules, previously detectable on fresh material only, to be studied in these tissues. Immunohistochemistry on paraffin-embedded tissues now play a major role in the diagnosis of Langerhans cell sarcoma, a diagnosis that has frequently been missed in the past.

In this report, we describe the histomorphological and immunohistochemical findings of a Langerhans cell sarcoma in a 31-year-old man in the absence of ultrastructural analysis.

CASE REPORT

The patient was a 31-yr-old male who presented with localized back pain at the mid-thoracic region for two months. It was associated with poor appetite and weight loss. The disease was progressive and had caused bilateral lower limb weakness and inability to walk. Past medical history showed that the patient had type 2 diabetes mellitus since he was 25 years of age.

A magnetic resonance imaging (MRI) scan revealed a pathological fracture of the eighth thoracic vertebra (T8) associated with a heterogeneous lesion involving the body and both pedicles, and narrowing of the spinal cord canal (Figure 1A and 1B). A computed tomographic (CT) scan guided biopsy of the lesion was performed and was sent for histopathological examination.

Histologically, the biopsy showed fragments of tissue infiltrated by aggregates of large cells with overtly malignant features. The cells contained abundant eosinophilic cytoplasm with markedly pleomorphic nuclei, some displaying prominent nucleoli (Figure 2). Abnormal mitotic figures were frequently seen and many multinucleated giant cells were present. There were scattered neutrophils and eosinophils in the background (Figure 2). Immunohistochemical studies showed that the malignant cells expressed CD1a, S100, CD68 and CD4 (Figure 2). The tumour cells were negative for CD20, CD3, CD15, CD30, CK, MPO, HMB45 and Desmin. The antibodies used and the results obtained are
Figure 1: (A) Magnetic resonance imaging (MRI) shows a pathological fracture (arrow) and a lesion in the eighth thoracic vertebral body with loss of the normal marrow fat. (B) MRI shows a heterogeneous lesion involving the body and both pedicles of the eighth thoracic vertebra with narrowed spinal cord canal (arrow).

Figure 2: (A) The biopsy shows infiltration by pleomorphic cells including binucleated and multinucleated cells in a background of scattered inflammatory cells. (B) High power view clearly shows the malignant features of the cells with abundant eosinophilic cytoplasm. Arrows show two mitotic figures. The neoplastic cells are strongly positive for (C) CD1a and (D) CD68. The neoplastic cells are also positive for (E) S100 and (F) CD4.
Table 1: List of primary primary antibodies used, corresponding cell that express the antigens, antibody source, antibody dilution and results of immunostaining.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Marker</th>
<th>Source</th>
<th>Dilution</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD1a</td>
<td>Langerhans cells</td>
<td>Lab Vision</td>
<td>1:30</td>
<td>+</td>
</tr>
<tr>
<td>S100</td>
<td>Dendritic cells</td>
<td>DAKO</td>
<td>1:400</td>
<td>+</td>
</tr>
<tr>
<td>CD68</td>
<td>Pan-macrophages</td>
<td>DAKO</td>
<td>1:200</td>
<td>+</td>
</tr>
<tr>
<td>CD4</td>
<td>T helper cells</td>
<td>Lab Vision</td>
<td>1:25</td>
<td>+</td>
</tr>
<tr>
<td>CD20</td>
<td>B cells</td>
<td>DAKO</td>
<td>1:1000</td>
<td>-</td>
</tr>
<tr>
<td>CD3</td>
<td>T cells</td>
<td>DAKO</td>
<td>1:200</td>
<td>-</td>
</tr>
<tr>
<td>CD15</td>
<td>Granulocytes</td>
<td>DAKO</td>
<td>1:20</td>
<td>-</td>
</tr>
<tr>
<td>CD30</td>
<td>Activated B &amp; T cells</td>
<td>DAKO</td>
<td>1:20</td>
<td>-</td>
</tr>
<tr>
<td>CK</td>
<td>Epithelial cells</td>
<td>DAKO</td>
<td>1:150</td>
<td>-</td>
</tr>
<tr>
<td>MPO</td>
<td>Myeloid cells</td>
<td>DAKO</td>
<td>1:1500</td>
<td>-</td>
</tr>
<tr>
<td>HMB45</td>
<td>Melanocytes</td>
<td>DAKO</td>
<td>1:150</td>
<td>-</td>
</tr>
<tr>
<td>Desmin</td>
<td>Muscle cells</td>
<td>DAKO</td>
<td>1:150</td>
<td>-</td>
</tr>
</tbody>
</table>

summarized in Table 1. A combination of both the morphological and immunohistochemical findings supported the diagnosis of Langerhans cell sarcoma.

The patient underwent anterior and posterior instrumentation decompression and fusion procedures after which he symptomatically improved. He was subsequently planned for radiotherapy.

DISCUSSION

Langerhans cell sarcoma is a rare tumour and most previous reports have been in the form of case reports with paucity of information from larger series of cases (Mardones et al. 2009, Takahara et al. 2009). Tani et al (Tani et al. 1992) suggested that the diagnosis of malignant Langerhans cell neoplasm should be made on the basis of the presence of proliferation of Birbeck granule-containing tumor cells that have overt malignant cytological features such as nuclear atypia and frequent mitosis.

Ultrastructural analysis using electron microscope to demonstrate Birbeck granules in the cytoplasm of tumour cells however requires fresh tissue that are fixed in suitable fixatives such as glutaraldehyde. Attempts at demonstrating Birbeck granules using formalin-fixed tissue samples were often unsuccessful (Lee et al. 2006, Zhao et al. 2009) due to fixation-related tissue ultrastructural damage. In the present case, the tissue sample was small and was entirely fixed in formalin and paraffin embedded, rendering it unsuitable for ultrastructural analysis. The diagnosis of Langerhans cell neoplasms had been previously made without the demonstration of Birbeck granules in the tumour cells (Ben-Ezra et al. 1991, Lee et al. 2006). Ben-Ezra et al. (1991) could demonstrate Birbeck granules in only three of the nine cases they reported.

Fortunately, with the advent of newer and better monoclonal antibodies for immunohistochemistry, a new marker (i.e., CD1a) that is specific for Langerhans cells is now available (Favara et al. 1997, Krenacs et al. 1993). CD1a represents one of the first phases of differentiation of the CD1 antigen family. It is expressed on cell surfaces of cortical thymocytes and Langerhans cells (Krenacs et al. 1993), but it is not expressed on other non-neoplastic macrophages and dendritic cells such as interdigitating dendritic
cells, follicular dendritic cells and plasmacytoid dendritic cells (Jaffe et al. 2007). The narrow specificity of the antibody (Krenacs et al. 1993) and the ease of the immune staining process renders CD1a immunostaining useful as a routine procedure for the diagnosis of Langerhans cell sarcoma (Nezelof & Basset 1998).

In addition to CD1a, the tumour consistently expresses S100 and Langerin (CD207). Interestingly, it can cause aberrant expression of the T cell marker CD4 (as shown in the present case) but the markers of the B and T cell lineages were absent. The immunophenotype of Langerhans cell sarcoma is identical to that of Langerhans cell histiocytosis (Jaffe et al. 2007). Pathologically, the differentiation between these two conditions is purely morphological. Nevertheless, Langerhans cell sarcoma is associated with an aggressive clinical course and distant metastasis (Ben-Ezra et al. 1991, Misery et al. 2003, Tani et al. 1992) and should be considered as a separate entity from Langerhans cell histiocytosis (Ben-Ezra et al. 1991, Jaffe et al. 2007, Tani et al. 1992).

REFERENCES


