Inflammatory pseudotumour of lymph nodes

N E New, P W Bishop, M Stewart, S S Banerjee, M Harris

Abstract

Aim—to describe the clinical, histological and immunohistochemical features in four cases of an uncommon benign lymph node lesion which may mimic a neoplastic process.

Methods—Four cases of inflammatory pseudotumour of lymph nodes were studied using conventional staining (haematoxylin and eosin, PAS, Gordon and Sweets reticulin stain, and the Ziehl-Neelsen stain) and with immunohistochemical techniques using a variety of antibodies (CD3, L26, CD15, CD21, CD30, KP1, MAC 387, vimentin, aSMA, HHF-35, D33, CD34, and S100).

Results—The lesion comprises a proliferation of spindle cells expanding the connective tissue framework of lymph nodes and is associated with a plasma cell and small lymphocyte infiltrate. There are variable numbers of macrophages, neutrophils and eosinophils, and varying degrees of fibrosis. Vascular changes are common but vary in degree and type.

Conclusions—Inflammatory pseudotumour of lymph nodes is an uncommon benign reaction pattern which may be misdiagnosed as a neoplastic or even a malignant process. Increased awareness of its histological features should help prevent such misdiagnoses.


Keywords: Inflammatory pseudotumour, lymph node.

Inflammatory pseudotumour or plasma cell granuloma is most commonly encountered in the lung where over 200 cases have been recorded. It has, however, been described in many other sites, predominantly as single case reports.1 Recently, a number of examples of inflammatory lymph node pseudotumours have been reported, mainly from the United States. Seven cases were described by Perrone et al2 and three further cases were subsequently reported by the same group.3 Davies et al4 described 14 cases and a further single example was recorded by Kemper et al.3 Here, we report four further cases.

Methods

Three of the cases were identified from the consultation files of one of the authors (MH) and the other was supplied by Dr A J Howat (Royal Preston Hospital). Biopsy specimens were fixed in formalin and embedded in paraffin wax. Sections were stained with haematoxylin and eosin, PAS, Gordon and Sweet’s stain for reticulin (Congo red in case 4), and with the Ziehl-Neelsen technique for acid fast bacilli. Immunohistochemistry was performed by a labelled streptavidin/biotin technique using the antisera listed in table 1. The clinical features of the patients are given in table 2.
Table 2 Clinical characteristics of the cases

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Site</th>
<th>Symptoms</th>
<th>History</th>
<th>Last follow-up</th>
<th>Original biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Young adult</td>
<td>M</td>
<td>Inguinal</td>
<td>Adenopathy</td>
<td>Not known</td>
<td>Not known</td>
<td>? Reactive</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>M</td>
<td>[R] neck</td>
<td>Adenopathy</td>
<td>None</td>
<td>Nodes still palpable (11 months)</td>
<td>? Hodgkin's disease</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>F</td>
<td>1. [R] groin</td>
<td>Adenopathy</td>
<td>Eczema</td>
<td>Alive and well (8 months)</td>
<td>? Hodgkin's disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2. [L] neck</td>
<td>Adenopathy (5 months)</td>
<td>None</td>
<td>Alive and well (16 months)</td>
<td>Inflammatory pseudotumour</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>F</td>
<td>Inguinal</td>
<td>Adenopathy (3 months)</td>
<td>Malignant melanoma</td>
<td>Alive and well (16 months)</td>
<td>Inflammatory pseudotumour</td>
</tr>
</tbody>
</table>

Increased vascularity, predominantly in the form of small vessels, was a feature of all cases. Three of the cases (cases 2 to 4) showed concentric perivascular fibrosis (fig 3A). Case 4 also had areas in which small vessels were rendered prominent by perivascular hyaline material, which appeared to cause luminal obstruction by extrinsic compression in places (fig 3B); this material was not amyloid, being negative on Congo red staining. In case 2 there was a very small focus of necrosis associated with fibrin thrombi in several small intranodal vessels (fig 3C) and a transmural infiltrate of lymphocytes in a single adjacent pericapsular vessel (fig 3D). No acid fast bacilli were observed.

Staining for light chains showed that the plasma cells were polytypic. Most of the small lymphocytes were of T lineage (CD3 positive, CD20 negative). MAC 387 and KP1 (CD68) staining revealed a population of morphologically normal macrophages and also highlighted some of the spindle cells.

The spindle cells stained strongly for vimentin and alpha smooth muscle actin. Weak and focal staining was found with HHF-35 in case 2; no desmin was identified. Staining for CD30 (Ber H2) and CD15 (Leu M1) was absent. Antibodies to S100 protein highlighted a sprinkling of cells at the periphery of the lesions which were thought to represent interdigitating reticulum cells. Staining for CD34 (Q-bend 10) highlighted the blood vessels but did not stain the spindle cells.

Discussion

Inflammatory pseudotumours of lymph nodes have been reported in both sexes in an age range of nine to 82 years. Any of the major lymph node groups may be involved. A single node is usually involved but multiple nodes may be affected simultaneously either within a single nodal group or at different sites. Case 3 in this study presented with involvement of both inguinal and cervical lymph nodes. Symptoms ranged from adenopathy alone to tender adenopathy with fever. A recent abstract recorded cases occurring in splenic, tonsillar, and intestinal lymphoid tissue.

The sine qua non for diagnosis seems to be the presence of spindle cell proliferation expanding the connective tissue framework of the node, often radiating from the hilum. The nodal sinuses may be focally obliterated by the proliferating cells with an associated infiltrate composed of plasma cells and small lymphocytes with variable numbers of macrophages, neutrophils, and eosinophils. Fibrosis is variable and a vague storiform
Inflammatory pseudotumour of lymph nodes

Figure 3
(A) Perivascular fibrosis; (B) perivascular hyalinisation involving small vessels; (C) intravascular fibrin thrombi with adjacent necrosis; (D) transmural lymphocytic infiltrate in a small pericapsular vessel.

The pattern of perivascular fibrosis has been described in some cases, although none of the cases in this study showed such a pattern. Vascular changes are common but vary in degree and type. Proliferation of small vessels is often prominent. Vasculitic changes, with or without microthrombi, were found in all but two of the cases in the literature but were seen in only one of our cases. Case 4 showed a peculiar perivascular deposition of hyaline material, which has not been described previously, but the other features were typical. Necrosis may be present or absent and was seen in only one of our cases where it was associated with vascular microthrombi.

A review of the 25 previously fully reported cases along with the four presented here shows a range of original observations which constitute, for practical purposes, a differential diagnosis (table 3). Roughly one third of cases were correctly diagnosed as having an inflammatory pseudotumour; in a further third some other form of reactive or non-neoplastic proliferation was considered. In the remainder, however, Hodgkin's disease or non-Hodgkin's lymphoma was suggested as a possible diagnosis. The polymorphic cell proliferation in inflammatory pseudotumour, which includes fibroblasts, lymphocytes, eosinophils, neutrophils, histiocytes, and plasma cells, may create an impression of Hodgkin's disease but if strict criteria for identification of Reed-Sternberg and Hodgkin's cells are adhered to, this error should be readily avoided. It is less easy to understand how inflammatory pseudotumour is mistaken for non-Hodgkin's lymphoma as polymorphism, especially the fibroblastic element, is not a feature of most forms of non-Hodgkin's lymphoma. The occurrence of

<table>
<thead>
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<th>Differential diagnosis</th>
<th>Literature (n = 25)</th>
<th>Present study (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory pseudotumour</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Unusual reactive</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Possible lymphoma</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Possible Hodgkin's disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactive [Castleman's disease]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kikuchi's lymphadenopathy</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Kimura's disease</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not given</td>
<td>1</td>
<td></td>
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</tbody>
</table>
Inflammatory pseudotumour is an uncommon cause of lymphadenopathy of uncertain aetiology. In the literature some authors suggest that this condition is reactive in nature and may be akin to granulatous tissue, although the possibility of a benign neoplasm has not been entirely excluded. It has several distinctive features and deserves to be more widely recognised to avoid potentially dangerous misdiagnoses.

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