Inflammatory pseudotumour of lymph nodes

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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, α SMA, 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.

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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 al*² and three further cases were subsequently reported by the same group.³ Davies *et al*⁴ described 14 cases and a further single example was recorded by Kemper *et al*.⁵ 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.

Results

All four cases showed partial node involvement by an apparent inflammatory process which radiated along connective tissue septa (fig 1). In three cases the process appeared to start in the hilum while in case 2 the affected area was mainly restricted to one pole of the node but extended into extranodal adipose tissue. The abnormal area consisted of spindle cell proliferation with a polymorphous inflammatory cell infiltrate (fig 2). The spindle cells were fairly long with attenuated cytoplasmic processes arising from two poles. The nuclei were pale on staining, round to oval in shape, and did not have prominent nucleoli. The inflammatory cell component varied in density and composition between the cases. All contained a predominance of mature plasma cells with a lesser number of small lymphocytes and histiocytes. A moderate number of neutrophil polymorphs were present in case 2 and a heavy infiltrate of eosinophils distinguished case 3. No atypical cells were identified in any of the cases. In one case occasional small giant cell granulomas were present and in another there were a few multinucleated giant cells amongst the other inflammatory cells.

Table 1 Antisera with specificities used in immunostaining

Antiserum	Specificity
CD3 (Dako)	T lymphocytes
L26 (CD20) (Dako)	B lymphocytes
CD15 (Leu M1)	
(Becton Dickinson)	Reed-Sternberg cells, granulocytes
CD21 (Dako)	Dendritic reticulum cells
CD30 (Ber H2)	
(Dako)	Reed-Sternberg cells, Hodgkin's cells
KP1 (CD68) (Dako)	Macrophages
MAC 387 (Dako)	Macrophages
Vimentin (Sigma)	Vimentin intermediate filament
α SMA (Sigma)	Smooth muscle actin
HHF-35 (Biogenix)	Muscle specific actin
D33 (Dako)	Desmin
Qbend10 (CD34)	
(Unipath)	Vascular endothelium
S100 (with trypsin)	
(Dako)	Various including Schwann cells, interdigitating reticulum cells

Antisera sources: Dako, High Wycombe, UK; Becton Dickinson, Oxford, UK; Sigma, Poole, Dorset, UK; Biogenix, Finchampstead, UK; Unipath, Basingstoke, UK.

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Table 2 Clinical characteristics of the cases

Case No	Age (years)	Sex	Site	Symptoms	History	Last follow-up	Original biopsy
1	Young adult	M	Inguinal	Adenopathy	Not known	Not known	? Reactive
2	45	M	[R] neck	Adenopathy (10 months)	None	Nodes still palpable (11 months)	? Hodgkin's disease
3	21	F	1. [R] groin 2. [L] neck	Adenopathy (5 months) Adenopathy (duration unknown)	Eczema [R]foot None	Alive and well (8 months)	? Hodgkin's disease
4	33	F	Inguinal	Adenopathy (3 months)	Malignant melanoma [R]calf	Alive and well (16 months)	Inflammatory pseudotumour

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.⁴ A recent abstract recorded cases occurring in splenic, tonsillar, and intestinal lymphoid tissue.⁶

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

Figure 1 A low power view of whole lymph nodes showing the hilar location of the lesion.

Figure 2 A representative area showing spindle-shaped cells, plasma cells, lymphocytes, and vascularity.

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.

pattern 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 pro-

liferation 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 3 Originally suggested diagnoses on previously reported cases (n = 25) and in this series

Differential diagnosis	Literature (n = 25)	Present study (n = 4)
Inflammatory pseudotumour	8	1
Unusual reactive	5	1
Possible lymphoma	4	
Possible Hodgkin's disease	3	2
Reactive [? Castleman's disease]	1	
Kikuchi's lymphadenopathy	1	
Kimura's disease	1	
Not given	1	

occasional immunoblasts in the infiltrate may have resulted in the overdiagnosis of malignancy.

Kikuchi's disease should be readily distinguished from inflammatory pseudotumour even when necrosis is a feature as the former is characterised by marked karyorrhexis and the absence of polymorphonuclear cells.⁷ Kimura's disease of the lymph nodes may mimic inflammatory pseudotumour because of sclerosis and infiltration of plasma cells and eosinophils in the medullary cords and paracortex. However, Kimura's disease constantly shows florid germinal centres and frequently shows other germinal centre changes, including vascularisation, deposition of proteinaceous material, and polykaryon formation, which are not seen in inflammatory pseudotumour.⁸ A case of nodal angiolymphoid hyperplasia with eosinophilia⁹ showed similar features but the fibrous tissue septa were present in a haphazard arrangement rather than following the nodal connective tissue; the vessels showed the prominent endothelial cell changes typical of this condition. A recently described condition, mycobacterial spindle cell lymph node pseudotumour,¹⁰ also has some similarities although greater nodal involvement is seen and the node is partly destroyed. The lesion is caused by atypical mycobacteria and is observed in immunosuppressed patients; Ziehl-Neelsen staining reveals numerous acid fast organisms. Kaposi's sarcoma may also enter the differential diagnosis but the absence of slit-like spaces and extravasated erythrocytes makes this diagnosis unlikely; mixed polymorphic inflammatory cells are not a feature of Kaposi's sarcoma. Furthermore, the spindle cells of Kaposi's sarcoma stain positively for CD34¹¹ whereas those of inflammatory pseudotumour are negative.

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 granulation tissue,⁴ although the possibility of a benign neoplasm has not been entirely excluded.³ It has several distinctive features and deserves to be more widely recognised to avoid potentially dangerous misdiagnoses.

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