

# Development of a calcifying fibrous pseudotumour within a lesion of Castleman disease, hyaline-vascular subtype

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### Abstract

**A nine year old boy with localised Castleman disease of the hyaline-vascular subtype developed a calcifying fibrous pseudotumour. This pathological association does not appear to have been described before. In this case, the development of this very unusual soft tissue tumour-like process was thought to be related to a previous fine needle aspiration biopsy, which was performed because of lymphadenopathy localised to the right inguinal area. This case provides further evidence of the reactive nature of calcifying fibrous pseudotumour and also broadens the pathological spectrum of the stromal cell proliferation that occasionally supervenes within lesions of Castleman disease, hyaline-vascular type.**

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The localised form of Castleman disease, hyaline-vascular type (CD-HV), may occasionally be complicated by stromal cell overgrowths or neoplasms.<sup>1</sup> In this setting, angiomyoid, follicular dendritic cell, or fibrohistiocytic proliferations, as well as various vascular tumours, have been reported.<sup>1</sup> In this paper, we present a unique case of a calcifying fibrous pseudotumour arising within a localised lesion of CD-HV. The pathological findings strongly support the reactive nature of calcifying fibrous pseudotumour.

### Case report

A nine year old boy was examined because of solitary and persistent lymphadenopathy localised to the right inguinal area. This lymphadenopathy, which had recently increased in size, had been noted five years before. At that time, a fine needle aspiration biopsy (FNAB) had been performed and led to a diagnosis of benign reactive lymphoid hyperplasia. Past medical history also included the surgical cure of a right testicular hydrocele at three years of age. Neither clinical nor biological investigations revealed any significant abnormality. The lymph node was excised for diagnostic purposes.

### Methods

Formalin fixed tissue samples from the lymph node were processed and embedded in paraffin, following standard histological techniques. Sections were stained with haematoxylin and eosin. Complementary histological stains included Congo red and Masson trichrome stains for amyloid and connective tissue, respectively.

Immunohistochemical studies were performed on paraffin sections using a Ventana Nexes Staining System (Ventana Medical Systems). Antibodies directed against the following antigens were used: S 100 protein, vimentin, CD68, CD35 (Dako); CD1a, CD34,  $\alpha$  smooth muscle actin (Immunotech SA); desmin (Novocastra Laboratories); and keratins 8, 18, and 19 (CAM 5.2: Becton Dickinson).

To investigate the possible role of Epstein-Barr virus (EBV) infection in the pathogenesis of this fibrosclerotic disorder, an in situ hybridisation (ISH) for EBV encoded RNA (EBER) was performed, using a supersensitive ISH detection system (BioGenex).

### Results

The resected lymph node measured  $3 \times 2 \times 1.5$  cm. A  $2 \times 1.6 \times 1.2$  cm, lobulated, well circumscribed and whitish mass was found on serial sections (fig 1). This had a somewhat gritty texture and a whorled appearance.

Light microscopic examination showed that this mass was composed of a paucicellular and heavily collagenised tissue which contained psammomatous as well as dystrophic calcification (figs 2 and 3). Occasional lymphoid tissue was entrapped within the fibrous process. The tumour cells were spindle shaped, had fusiform or ovoid nuclei with fine chromatin, and did not show any cytologic atypia or mitotic activity. Some scattered small lymphocytes and

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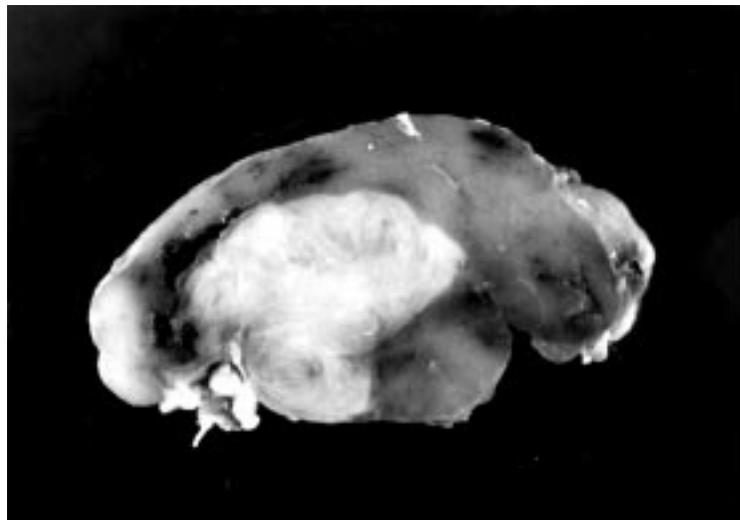


Figure 1 Gross aspect of the lymph node. Note the presence of a lobulated, whitish mass featuring a whorled appearance.

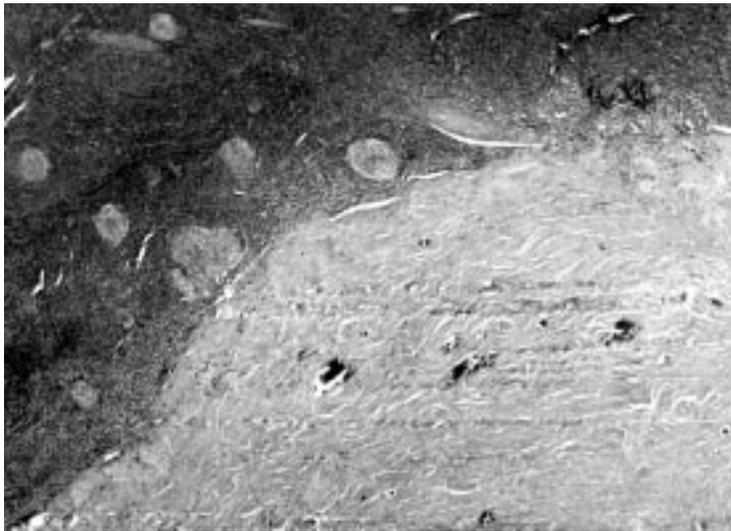


Figure 2 Interface between calcifying fibrous pseudotumour and lymph node tissue. Although the tumour limits are well defined, there is no distinct capsule. Note the appearance of the lymphoid tissue which contains dystrophic follicles (haematoxylin and eosin).

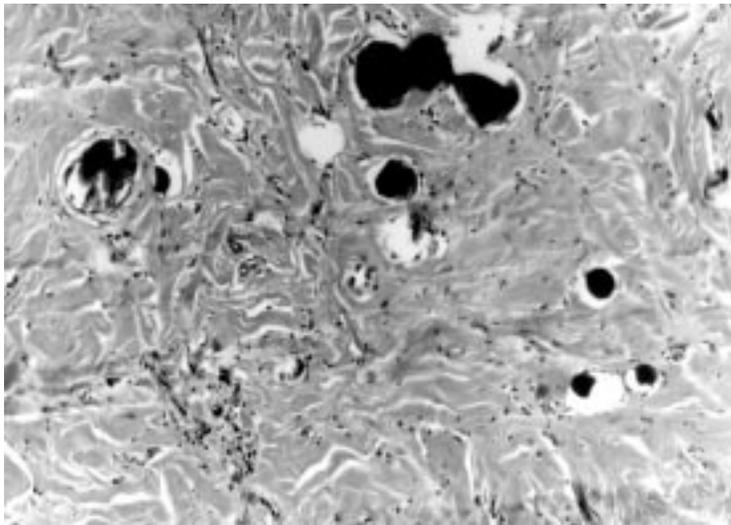


Figure 3 Tumour composed of highly hyalinised collagenous tissue containing scattered, benign looking spindle cells together with psammomatous calcification (haematoxylin and eosin).

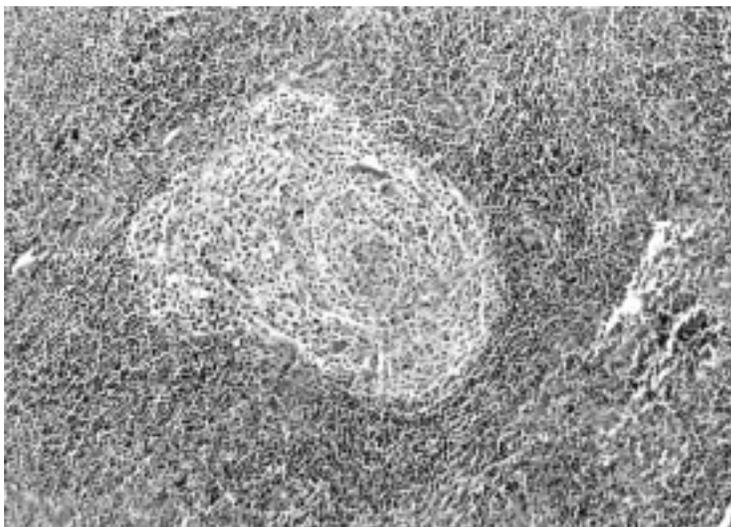


Figure 4 High magnification view of a dystrophic follicle showing a complex configuration with a concentric "onion skin" pattern and abnormal vascularity. There are also some multinucleated follicular dendritic cells (haematoxylin and eosin).

plasmacytes were also seen throughout the tumour process. Congo red stain was negative, whereas Masson trichrome stained the collagen deeply.

The neighbouring lymph node tissue showed all the histological changes that are usually seen in CD-HV.<sup>1</sup> This is characterised by the combination of abnormal follicles (fig 4), hypervascular interfollicular tissue, and the absence of any discernible sinuses. Dystrophic follicles showed a typical onion skin pattern, and occasionally contained multiple germinal centres or multinucleated follicular dendritic cells. In addition, the vessels in the interfollicular areas were occasionally large and featured thick walls.

On immunohistochemical analysis, the tumour cells making up this fibrosclerotic mass were found to be vimentin positive. Occasional weak staining with the antibody directed against CD68 was also seen. By contrast, these cells did not show any immunoreactivity with the antibodies directed against  $\alpha$  smooth muscle actin, desmin, CD34, CD35, cytokeratins, S-100 protein, or CD1a. Immunostaining for both CD34 and  $\alpha$  smooth muscle actin highlighted a rather well developed vascular network throughout the tumour process. In the neighbouring lymphoid tissue, the follicular dendritic cells in the germinal centres showed strong CD35 immunostaining, whereas the reticulum cells in the mantle zones were strongly stained by the monoclonal antibody directed against  $\alpha$  smooth muscle actin. This immunostaining emphasised the impression of an onion-skin-like distribution of the mantle zone lymphocytes. As well as staining some histiocytic and dendritic cells, anti-CD68 antibody also stained plasmacytoid monocytes. The latter were scattered throughout the interfollicular areas.

In situ hybridisation did not reveal any EBER positive tumour cells.

## Discussion

A calcifying fibrous pseudotumour is a rare and benign neoplastic-like disorder of the soft tissues which shows very distinctive pathological features.<sup>2</sup> First described by Rosenthal and Abdul-Karim under the term "childhood fibrous tumour with psammoma bodies,"<sup>3</sup> this fibrosclerotic lesion was later renamed "calcifying fibrous pseudotumour" by Fetsch and colleagues, owing to its possible relation with inflammatory pseudotumours.<sup>2</sup> This pathological condition, which usually involves the soft tissues of extremities, is mostly seen in young patients.<sup>2-6</sup> However, adult cases,<sup>2</sup> as well as other localisations such as pleura,<sup>7</sup> mediastinum,<sup>8,9</sup> peritoneum,<sup>10</sup> or scrotum,<sup>2</sup> have also been reported. Like inflammatory pseudotumours, the precise pathogenesis remains largely unknown but a traumatic aetiology was suggested in at least some cases.<sup>11</sup>

Histologically, this circumscribed but unencapsulated nodular lesion is characterised by paucicellular and heavily collagenised fibrous tissue that contains psammoma bodies as well as dystrophic calcifications.<sup>2-11</sup> In addition, organised lymphoid tissue or a mild lympho-

plasmacytic infiltrate may occasionally be found.<sup>2-11</sup> The immunohistochemical features of calcifying fibrous pseudotumours are not well known as they have been investigated in only a few studies.<sup>5-9,10</sup> According to these reports, the tumour cells were vimentin positive and on some occasions weakly expressed  $\alpha$  smooth muscle actin. In contrast, immunostaining with antibodies directed against cytokeratins, S 100 protein, muscle specific actin, or desmin remained consistently negative.<sup>5,9,10</sup>

Despite the fact that some cases of calcifying fibrous pseudotumour are reported to contain lymphoid tissue featuring changes suggestive of Castleman disease,<sup>10</sup> to our knowledge the occurrence of a calcifying fibrous pseudotumour within CD-HV has not been documented up to now. Although this pathological association may be purely coincidental, we think, however, that it is more than fortuitous, given the extreme rarity of calcifying fibrous pseudotumour, the relative infrequency of Castleman disease, and the known occurrence of various stromal cell overgrowths in association with the latter condition. These neoplasms derive from various vascular and reticulum cell subsets that normally account for the cellular composition of CD-HV.<sup>1</sup> It is conceivable that in the present case, the calcifying fibrous pseudotumour may represent an exaggerated healing process, resulting from the proliferation of a distinct fibroblastic-like reticulum cell which actively secretes collagen, and induced by a traumatic injury such as the FNAB procedure. In addition, the facilitating action of various cytokines produced by the cellular milieu of Castleman disease is also likely.

Whether a calcifying fibrous pseudotumour represents a distinct form of inflammatory pseudotumour or possibly its terminal stage of evolution remains to be determined. In this context, it is worth noting that in lymph nodes, this stage in the evolution of inflammatory pseudotumours is usually characterised by extensive areas of dense sclerosis with minimal inflammatory infiltrate and some residual lymphoid tissue,<sup>12</sup> like a calcifying fibrous pseudotumour. Furthermore, dystrophic calcification can also be found, especially if there is pronounced sclerosis.<sup>13</sup> These histological similarities therefore suggest that calcifying

fibrous pseudotumours and inflammatory pseudotumours are related conditions.

Since EBV has been found to be occasionally associated with inflammatory pseudotumours,<sup>14</sup> its potential role in the development of our calcifying fibrous pseudotumour was investigated by in situ hybridisation. The negative results in both tumour and lymphoid tissues make it unlikely that this virus is implicated in the growth of the pseudotumour described here, and suggest a pathogenesis distinct from that of EBV positive inflammatory pseudotumours.

In conclusion, we document for the first time the occurrence of a calcifying fibrous pseudotumour within a localised Castleman disease, hyaline-vascular type. This particular fibrosclerotic lesion, which probably represents an exaggerated healing process in response to a tissue injury, should therefore be added to the list of stromal cell proliferations that may occasionally occur in Castleman disease.

- 1 Lin O, Frizzera G. Angiomyoid and follicular dendritic cell proliferative lesions in Castleman's disease of hyaline-vascular type: a study of 10 cases. *Am J Surg Pathol* 1997;21:1295-306.
- 2 Fetsch JF, Montgomery EA, Meis JM. Calcifying fibrous pseudotumor. *Am J Surg Pathol* 1993;17:502-8.
- 3 Rosenthal NS, Abdul-Karim FW. Childhood fibrous tumor with psammoma bodies. Clinicopathologic features in two cases. *Arch Pathol Lab Med* 1988;112:798-800.
- 4 Kettani S, François H, Pidhorz L, et al. Pseudo-tumeur fibreuse calcifiante. *Ann Pathol* 1994;14:124-6.
- 5 Fukunaga M, Kikuchi Y, Endo Y, et al. Calcifying fibrous pseudotumor. *Pathol Int* 1997;47:60-3.
- 6 Orui H, Yamakawa M, Ishikawa A, et al. Calcifying fibrous pseudotumor. A case report. *J Bone Joint Surg Am* 1998;80:555-60.
- 7 Pinkard NB, Wilson RW, Lawless N, et al. Calcifying fibrous pseudotumor of pleura. A report of three cases of a newly described entity involving the pleura. *Am J Clin Pathol* 1996;105:189-94.
- 8 Reed MK, Margraf LR, Nikaidoh H, et al. Calcifying fibrous pseudotumor of the chest wall. *Ann Thorac Surg* 1996;62:873-4.
- 9 Dumont P, de Muret A, Skrobala D, et al. Calcifying fibrous pseudotumor of the mediastinum. *Ann Thorac Surg* 1997;63:543-4.
- 10 Kocova L, Michal M, Sulc M, et al. Calcifying fibrous pseudotumor of visceral peritoneum. *Histopathology* 1997;31:182-4.
- 11 Zamecnik M, Dorociak F, Vesely L. Calcifying fibrous pseudotumor after trauma. *Pathol Int* 1997;47:812.
- 12 Moran CA, Suster S, Abbondanzo SL. Inflammatory pseudotumor of lymph nodes: a study of 25 cases with emphasis on morphological heterogeneity. *Hum Pathol* 1997;28:332-8.
- 13 McDermott MB, Swanson PE. Pseudoneoplastic lesions of deep somatic soft tissue and the skeletal system. In: Wick MR, Humphrey PA, Ritter JH, eds, *Pathology of pseudoneoplastic lesions*. Philadelphia: Lippincott-Raven, 1997:377-447.
- 14 Arber DA, Weiss LM, Chang KL. Detection of Epstein-Barr virus in inflammatory pseudotumor. *Semin Diagn Pathol* 1998;15:155-60.