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### **Atypical haematoma/seroma following treatment for soft tissue sarcoma. Histopathology, 2009;54:505-507**

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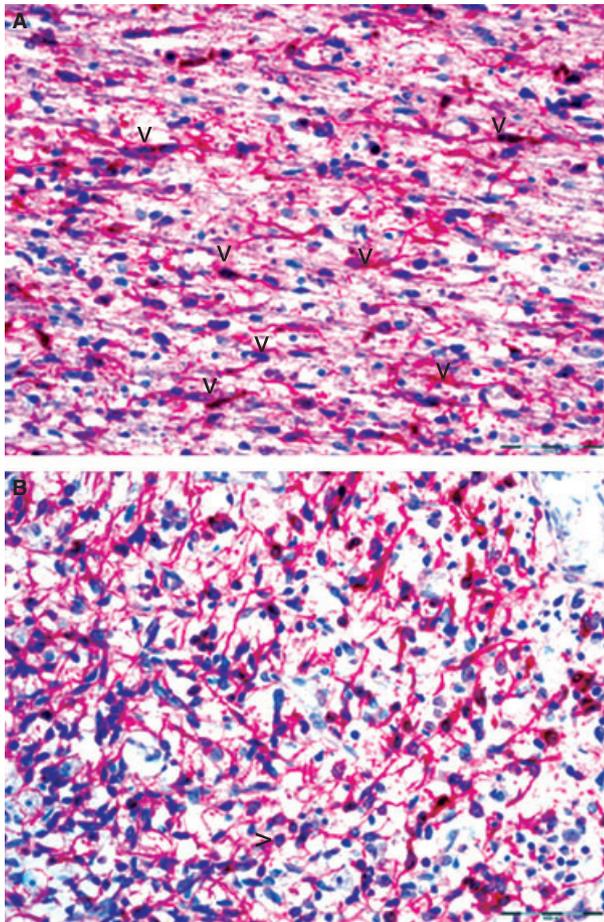
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previously characterized in detail.<sup>4-6</sup> A glioblastoma served as the positive control. Omission of the primary antibody served as the negative control.

MAP-2 was detected in all tumour samples from the seven GC cases, but the amount of positive cytoplasmic immunoreactivity varied from single cells to about 50% of tumour cells (Figure 1). Astrocytic cells showed strong cytoplasmic reactivity. Often the partially ramifying processes were highlighted. Even though the cases described here were predominantly composed of astrocytic cells; three of them also contained individual oligodendroglia-like cells that showed the characteristic perinuclear reactivity without cell processes. Reactive astrocytes were usually immunonegative. The overall pattern of reactivity was identical to that of diffuse gliomas.<sup>1</sup> Interestingly, almost all mitoses in anaplastic tumour areas were immunopositive.



**Figure 1.** A, MAP-2 immunohistochemistry highlights diffuse infiltrating astrocytic tumour cells (v) in the corpus callosum (alkaline phosphatase, scale bar 100 µm). B, Typical process immunoreactivity of astrocytic tumour cells in an area of gliomatosis cerebri with higher tumour cell density; individual cells (>) show an oligodendroglial aspect (alkaline phosphatase, scale bar 100 µm).

Our data demonstrate that MAP-2 is expressed in GC in the same fashion as described for common diffuse gliomas.<sup>1</sup> Thus, MAP-2 has the same diagnostic utility in GC and diffuse gliomas. Furthermore, this study underlines that GC is not a unique entity but represents diffuse gliomas with exceptionally extensive infiltration of large areas of the central nervous system.

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### Atypical organizing haematoma/seroma following treatment for soft tissue sarcoma

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Sir: Fluid collections of lymph (seroma/hygroma) or blood (haematoma), which progressively undergo organization, may develop at the site of soft tissue sarcoma excision. These lesions are more common in the lower extremity at the junction between the subcutaneous fat and the fascia.<sup>1,2</sup> Radiation therapy contributes to their formation by rendering the soft tissues non-compliant and therefore creating a potential space for fluid collection.<sup>2</sup> Due to atypical magnetic resonance imaging findings<sup>2</sup> and progressive increase in size, these lesions may be surgically explored to exclude recurrence or radiation-induced sarcoma. The histopathological findings are usually those of organiz-

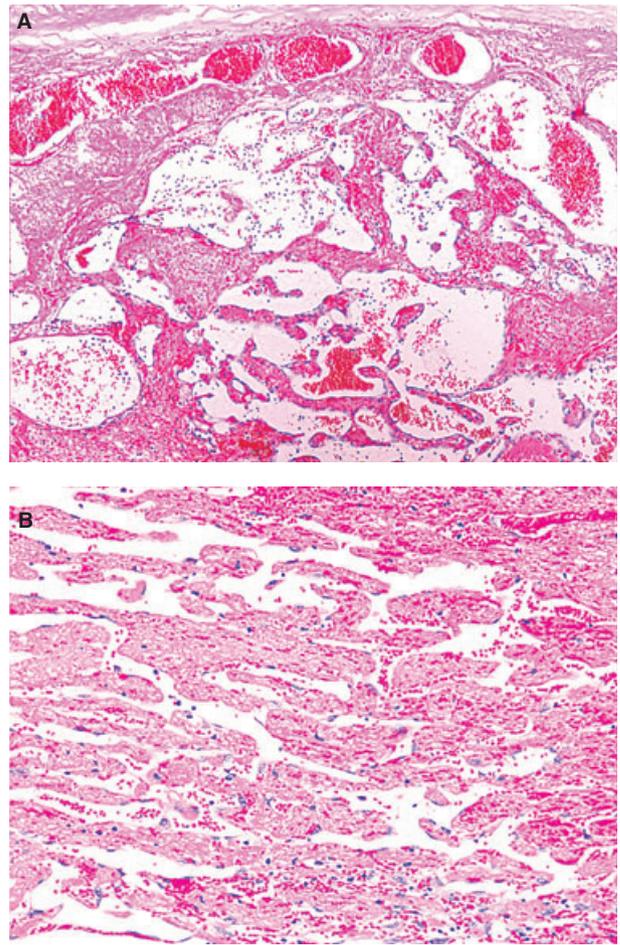
ing haematoma, granulation tissue, foreign body granuloma and fat necrosis,<sup>1,2</sup> but in some cases the lesion may present atypical features. Herein we present the histological, immunohistochemical and ultrastructural features of seven cases of soft tissue haematoma/seroma following treatment for soft tissue sarcoma, which were characterized by alarming histological features, including atypical proliferation of endothelial cells, thereby requiring differential diagnosis from angiosarcoma.

All lesions were located in the subcutis. The initial diagnoses were leiomyosarcoma in four patients, and synovial sarcoma, pleomorphic liposarcoma, and atypical lipomatous tumour in one instance. All patients had been surgically treated and five had received radiation therapy. Six of the seven patients were alive with no evidence of malignant disease at follow-up, whereas the remaining patient had a further biopsy 5 months after the diagnosis of haematoma/seroma, and local recurrence of a pleomorphic liposarcoma was detected.

In the two patients who underwent surgical excision, the lesion was delimited by a pseudocapsule with a mixed inflammatory infiltrate, foreign-body granulomas and calcifications, whereas in four there were areas of granulation tissue. All lesions consisted of fibrin clots partially covered by a single layer of flattened cells, with inconspicuous cytoplasm and oval, sometimes bulging nuclei, either forming interconnected pseudovascular spaces containing erythrocytes, or solid sheets (Figure 1A,B). In three cases, there were focal areas showing papillary architecture. Atypical cells, either lining the pseudovascular spaces (Figure 2A) or within the fibrin cores, were identified in six cases, but no real pleomorphism or mitotic figures were observed. In two of these cases, there were also multinucleated cells, with 2–10 overlapping nuclei similar to those observed in mononuclear cells, which lined the pseudovascular spaces (Figure 2B).

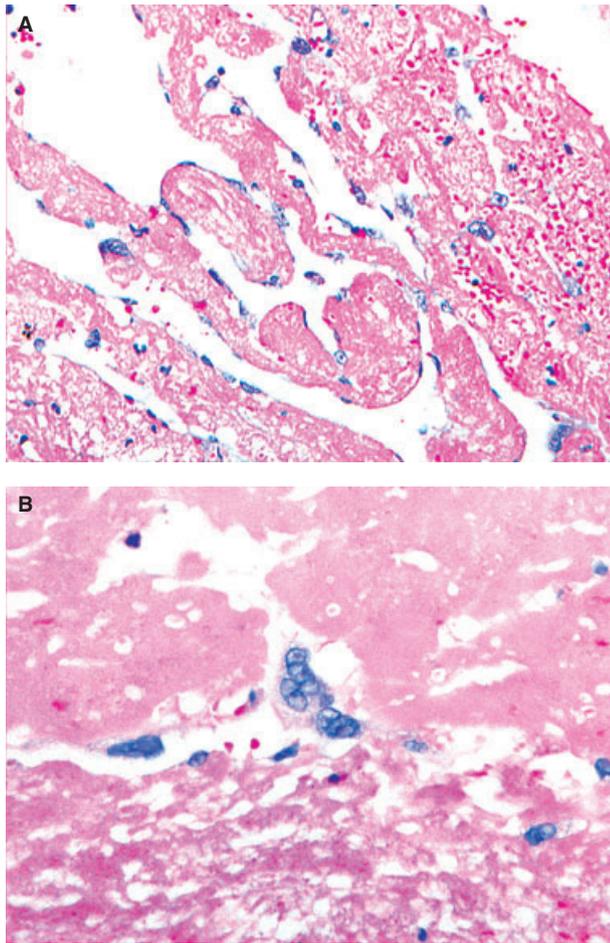
Immunohistochemically, endothelial markers were variably expressed, but at least one was detected in all cases. CD34 was positive in six cases, CD31 in five and D2-40 in four. MIB-1 positivity ranged between 13% and 35% of cells. Ultrastructural analysis was performed in one case. The cytoplasm of lining cells contained mitochondria, few dilated rough endoplasmic reticulum profiles, free ribosomes and intermediate filaments. Several pinocytotic vesicles were detected. Weibel–Palade bodies were not identified. Cells were partly covered by basal lamina-like material and were joined by immature junctions.

Overall, the histological picture observed in these lesions was highly reminiscent of angiosarcoma for the



**Figure 1.** Lesions consisted of fibrin clots partially covered by a single layer of flattened cells, either forming interconnected pseudovascular spaces containing erythrocytes (A,B), or solid sheets.

complex network of interconnected pseudovascular spaces and for the presence of nuclear enlargement of endothelial cells. The possibility of an angiosarcoma was also considered for its association with radiation therapy<sup>3</sup> that had been administered to five patients. Features helpful in this distinction were the presence of a pseudocapsule often containing areas of granulation tissue, inflammatory infiltrate or foreign body granulomas, whereas angiosarcoma has an infiltrative growth. In addition, vascular spaces in angiosarcoma are more irregular, and are lined by neoplastic endothelial cells showing a greater degree of pleomorphism with frequent atypical mitoses.<sup>3</sup> Another feature of angiosarcoma that is diagnostically useful is the 'piling' of neoplastic cells, which bulge into the vascular lumen. In two of our cases, there were scattered multinucleated cells lining the pseudovascular spaces, which mimicked this feature.



**Figure 2.** Atypical cells showing enlarged nucleus with prominent nucleolus lining the pseudovascular spaces (A). In two cases multinucleated cells can be seen (B).

Review of the literature showed a few similar examples of extravascular atypical endothelial proliferation described in the thyroid,<sup>4</sup> but no previous report of similar occurrences in the soft tissues. Three of the thyroid lesions followed a fine-needle aspiration procedure, which presumably resulted in the haematoma accompanied by atypical endothelial proliferation.<sup>4</sup>

It is likely that the present lesions represent a reactive process similar to papillary endothelial hyperplasia and may be interpreted as an exuberant endothelial proliferation occurring within an organizing haematoma/seroma. Adjuvant radiotherapy may contribute to the development of haematoma/seroma by rendering the soft tissues non-compliant and therefore creating the potential space for fluid collection,<sup>2</sup> and by creating vascular damage.<sup>5</sup> By analogy with radiodermatitis, where atypical fibroblasts are characteristic of delayed injury,<sup>5,6</sup> the presence of atypia in the present cases could be due to cellular radiation damage.

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### Activation of NF- $\kappa$ B transcription factor in asthma death

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*Sir:* Bronchial asthma remains a significant cause of mortality at all ages.<sup>1</sup> Inflammation is a central feature of asthma death and is characterized by increased transcription of proinflammatory proteins regulated by the activation of transcription factors such as nuclear factor (NF)- $\kappa$ B.<sup>1,2</sup> So far, no studies have examined NF- $\kappa$ B activation in the lung of fatal asthma. We therefore evaluated by immunohistochemistry the nuclear expression of p65 protein (the major NF- $\kappa$ B subunit), an index of NF- $\kappa$ B activation, in the small airway epithelium and lung parenchyma of patients who died of asthma.

The study was approved by the Royal Brompton Hospital (London, UK) Ethics Committee. Peripheral lung tissues were obtained from eight patients who had died during a fatal asthmatic exacerbation and from five non-smoking subjects with no history of asthma who had died of non-pulmonary causes. Two to four randomly selected tissue blocks were taken, fixed in formaldehyde and embedded in paraffin. Contiguous 4  $\mu$ m thick serial sections were cut as previously