Benign fibrous lesions masquerading as sarcomas

Clinical and morphological pitfalls

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Although Konwaler et al. (1955) 40 years ago described nodular fasc iitis, the most common of what is at present known as the pseudosarcomatous proliferative lesions of soft tissue, these benign fibroblastic-myofibroblastic lesions still are misdiagnosed as sarcoma. The misinterpretation of these lesions as malignant is due to their often rapid growth, their infiltrative manner, pleomorphic cellular pattern and the often high mitotic rate.

To this group of "pseudosarcomas" belong, besides nodular fasciitis, proliferative fasciitis and myositis and two rare lesions related to nodular fasciitis; cranial and intravascular fasciitis.

Nodular fasciitis

Nodular fasciitis (NF) is the most common of these lesions and may be regarded as the prototype of the pseudosarcomas. Nodular fasciitis is predominantly found in young or middle-aged adults but also in children, which is important with regard to its misinterpretation as sarcoma. The most common sites are the extremities and trunk but NF is also found in the head and neck region.

The duration of symptoms before the first consultation is in typical cases short: 1 week–month and at the physical investigation the tumours average 2–3 cm in size and appear as firm, deep subcutaneous, often tender masses. At microscopic examination NF is localized in the subcutis, along fasciae or within muscles. A wide variety of morphologic features are observed: NF has been categorized in cellular, fibrous, myxoid or cystic variants, a storiform as well as a loose vascularized tissue-culture like pattern can also be found. Often there is a mixture of patterns. A common finding is inflammatory cells and extravasated erythrocytes. Multinucleated giant cells, sometimes osteoclast-like, are not uncommon. The predominant cells are, however, proliferating fibroblasts and myofibroblasts displaying a wide variation in cell size- and shape. The cells are elongated or fusiform with a variable amount of cytoplasm, uni or bipolar sometimes with long slender cytoplasmic processes or polygonal or triangular with several cytoplasmic extensions in various directions. Binucleated triangular cells with eccentrically placed nuclei, reminiscent of ganglion cells, are found in most cases. Nuclei are spindly, ovoid, rounded or stellate with finely granular chromatin and nucleoli of different size. It is not uncommon to find nuclei with large prominent nucleoli. This cellular pleomorphism with a marked anisokaryosis is common as are numerous mitoses, but atypical mitosis are not seen (Montgomery and Meis 1991).

The majority of NF stain with muscle specific actin, smooth muscle actin, vimentin and CD 68 (an antibody against lysosomal membranes, thought to be a marker for histiocytes). Usually CD68 stains few spindly cells but consistently the giant cells. Desmin is not expressed.

Immunohistochemically as well as ultrastructurally, most cells are of the fibroblastic-myofibroblastic lineage. The CD68 positivity has been considered to favor a histiocytic differentiation and it has been suggested that NF is a fibroblastic lesion where the fibroblasts are capable of differentiaty between fibrohistiocytic and myofibroblastic cell types.

Proliferative fasciitis and myositis

Proliferative fasciitis (PF) and myositis (PM) have many features in common with nodular fasciitis, clinically as well as microscopically. The main differences are location (PF involves fasciae and interlobular fibrous septa of subcutaneous fat and PM is an intramuscular lesion) and the predominance of large mono-or binucleated cytoplasm rich cells, sometimes ganglion-cell like with rounded nuclei often with prominent nucleoli. As in nodular fasciitis, spindly, pleomorphic fibroblast-like cells are present as well as a high mitotic rate. The immunohistochemical profile is the same as for NF. However, the ganglion cell-like cells have been reported to be negative for smooth muscle actin. Ultrastructurally these cells resemble osteoblasts (Lundgren et al. 1992).

When proliferative fasciitis and myositis occur in cildren, they are often extremely cellular and the ganglion cell-like cells seen in solid sheeths with numer-

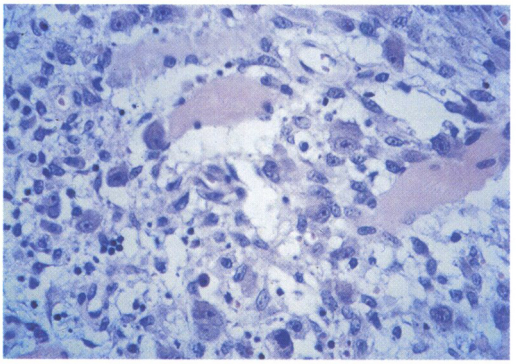

Figure 1. Proliferative myositis. Sheets of ganglion cell-like cells proliferating between muscle fibers. Cellular and nuclear pleomorphism, prominent nucleoli in many nuclei. HE, ×100.

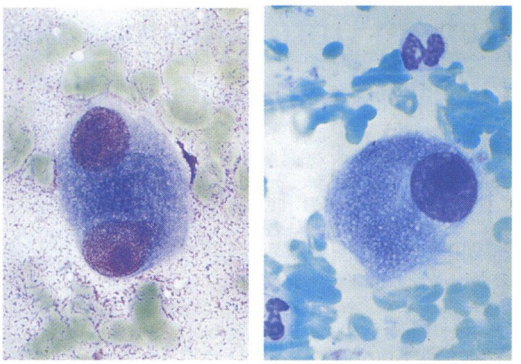

Figure 2. Fine needle aspirate from proliferative myositis. Ganglion cell-like cells with eccentric nuclei with large nucleoli. May-Grünwald-Giemsa, ×250.

ous mitoses together with the cellular pleomorphism and rapid growth have been the source of misinterpretation of these pseudosarcomas as rhabdomyosarcoma (Figures 1 and 2). In a recent study in 6 out of 11 cases of proliferative fasciitis and myositis in children a primary diagnosis of rhabdomyosarcoma was rendered or seriously suspected and chemotherapy was administered to 3 patients (Meis and Enzinger 1992).

NF, PF and PM are closely related lesions and mixed forms occur. The main diagnostic task is not to be able to distinguish the one from the other but to avoid a diagnosis of malignancy.

Cranial fasciitis

First reported by Lauer and Enzinger (1980) this lesion is predominantly found in children during the first year of life. It is a rapidly growing mass involving the deep fascial layer of the scalp and it may erode the bone which at radiographic investigation appears as a lytic lesion with a sclerotic rim. A prominent myxoid matrix is a common finding as are multinucleated giant cells and numerous mitoses.

Intravascular fasciitis

Intravascular fasciitis is a variant of nodular fasciitis, first described by Patchefsky and Enzinger (Patchefsky and Enzinger 1981). Most cases (70%) appear on the upper extremities and the neck region and involve small and medium sized veins. It is common in children and about half of cases reported have ocurred in children less than 15 years.

Clinically it is a superficial, multinodular tumour. The association with a vessel is sometimes difficult to appreciate without the help of special stains. In larger vessels a polypoid intraluminal mass is seen at microscopy. Intravascular fascitis resembles nodular fasciitis but multinucleated giant cells are more common.

Pseudomalignant myositis ossificans

Pseudomalignant myositis ossificans is another pseudosarcomatous lesion, also related to nodular fasciitis and proliferative fascitis and myositis.

This lesion is predominantly found in young people and the lower extremities are commonly affected. Typically, the growth is rapid and there is pain and tenderness.

Most often there is a firm intramuscular mass but it may be subcutaneous. Adjacent bone is not engaged in the process. The histologic appearance is that of a cellular mass composed of proliferating, pleomorphic fibroblasts-myofibroblasts, mixed with the same type of ganglion cell-like cells as in proliferative fasciitis and myositis.

In the typical case this cellular mass is surrounded by mature bone trabeculae and strands of osteoid. Osteoblasts and osteoclasts are seen adjacent to the trabeculae and osteoid and calcified areas are also present. Due to its frequent proximity to bone, the cellular pleomorphic pattern and the presence of osteoid and bone, pseudomalignant myositis ossificans is at risk of beeing misinterpreted as osteosarcoma (Figure 3).

However, the "zone phenomenon" of a soft tissue mass bordered by bone and osteoid gives the lesion a typical appearance on radiographic computerized tomographic or magnetic resonance imaging.

The presence of osteoid, bone and cartilage has also been described in other pseudosarcomas. The formation of bone is, however, disorderly and the radiographic "zone phenomenon" only seen in myositis ossificans.

The etiology of these pseudosarcomatous lesions is obscure. Trauma and infection are known to precede some cases but in the majority they seem to appear without any cause.

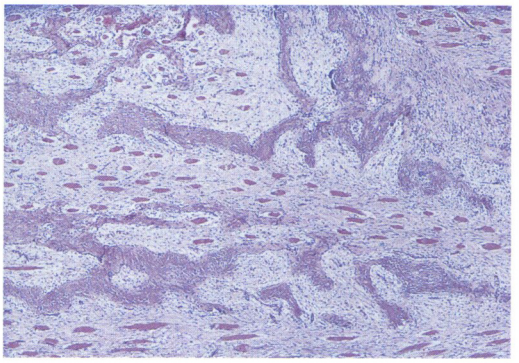

Figure 3. A. Myositis ossificans. Fibrous tissue with bone trabeculae within striated muscle. HE, ×13.

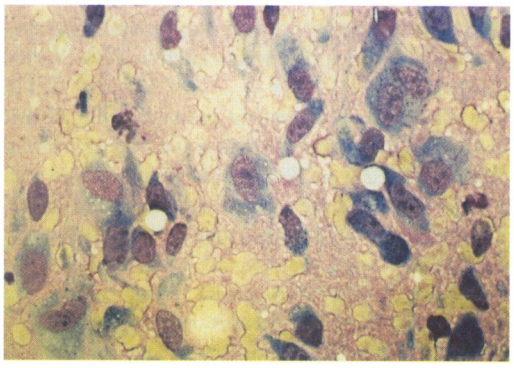

Figure 4. A. The typical appearance of nodular fasciitis in a fine needle aspirate. Proliferating fibroblasts/myofibroblasts in a myxoid background substance. MGG, ×100.

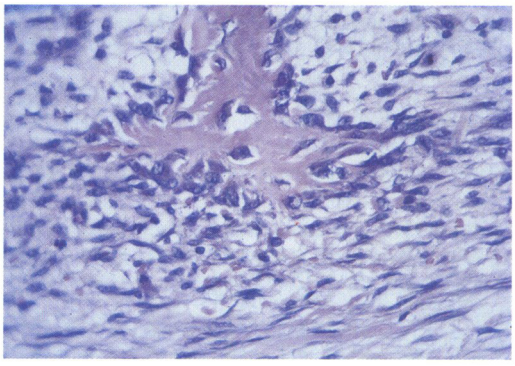

Figure 3. B. The bone trabeculae are surrounded by proliferating osteoblasts. HE, ×100.

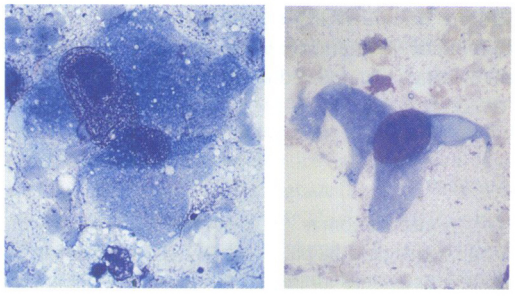

Figure 4. B. Scattered proliferating myofibroblasts may show a considerable pleomorphism. MGG ×250.

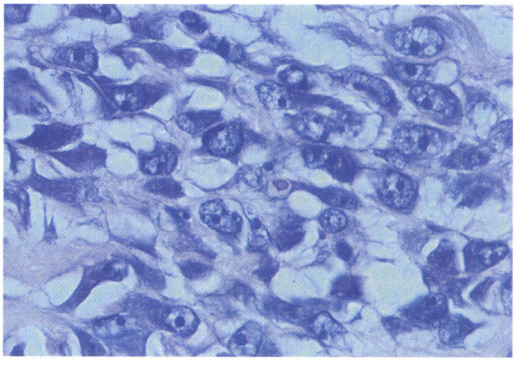

Figure 3. C. High magnification of proliferating osteoblasts. Pleomorphic nuclei with prominent nucleoli. HE, ×250.

Discussion

Pseudosarcomatous lesions of soft tissue are still important pitfalls especially when fine needle aspiration is used as the primary method for a morphologic diagnosis of a soft tissue mass. The pleomorphic cellular pattern together with mitoses may give the impression of malignancy in an aspirate smear (Figure 4). The microscopic appearance of all these lesions have, however, been investigated in fine needle aspirates and reliable diagnostic criteria have been defined for the typical case (Dahl and Åkerman 1981, Lundgren et al. 1992).

In current textbooks of musculoskeletal tumours it is stated that these "pseudosarcomas" almost never recur after radical removal and that cases with spontaneous regression have been reported.

The natural history the "pseudosarcomas" has, however, been clarified after the use of FNA for diagnosis. According to our experience and others, the majority of pseudosarcomas regress in size or disappear completely within 3–4 weeks after the FNA. Stanley and coworkers (Stanley et al. 1991) described 11 cases of NF, diagnosed by the combined evaluation of clinical data and cytodiagnosis, of which all disappeared, the majority 3–8 weeks after the needling.

We have a similar experience at the Lund Musculoskeletal Tumor Centre. Of 46 cases of NF (1985–1994) all 37 not surgically removed lesions de-

creased considerably in size or disappeared completely, most of them within 4 weeks after the FNA (Willén et al. 1994).

In all our cases the patient presented with a short history of a growing, tender mass and the lesions were small, at most 2-3 cm. When patients are referred with a long history and the tumours are large they do not, in our experience, change in size after aspiration and further more large examples of nodular fasciitis do not display the typical diagnostic smear pattern. We have experience of one cases with a long history where the lesion at needling was > 3 cm in size with an abundant myxoid background matrix and composed of a monotonous population of spindly cells of different size and that case was misinterpreted as low grade malignant (Grade1) myxofibrosarcoma at the cytology.

Pseudomalignant myositis ossificans is also a "self-healing" lesion. We have published 5 cases with typical clinical, radiographic as well as cytologic features, all of which disappeared spontaneously (Rööser et al. 1989).

Summary

The "pseudosarcomas" have several features in common: rapid growth, pain and tenderness, infiltrative growth extending along fascial planes or subcutaneous septa or radiating into lobules of adipose tissue. Another common denominator is the pleomorphic pattern of proliferating fibroblasts and myofibroblasts, the presence of more or less ganglioncell-like large cells, uni-or binucleated with prominent nucleoli and a high mitotic rate.

In order to avoid a false diagnosis of sarcoma several factors should be emphasized:

1. awareness of the existence of these lesions,
2. combined evaluation of clinical and morphological data,
3. rapid growth, often noted by the patients, is rare in sarcomas except in some cases of rhabdomyosarcoma. Like wise are the pain and tenderness not typical for sarcoma,
4. the appearance of the lesion at low power,
5. at high power in spite of the cellular pleomorphism, the nuclei are cytologically benign and atypical mitoses never seen.

In doubtful cases immunohistochemistry may be of help as DNA-ploidy analysis. These lesions may be tetraploid but never aneuploid.

Our present work-up of these lesions is primary FNA and when the clinical data and the cytologic features are typical for a "pseudosarcoma" we adopt an attitude of "wait and see" with clinical follow-up. As many of them regress or disappear after the needling there is no need for primary surgery.

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