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Cytology of Soft Tissue Tumors

Venkateswaran K Iyer*
Department of Pathology, AIIMS, New Delhi, India

Introduction

Soft tissues are the supportive tissue of various organs as well as the nonepithelial, extraskeletal structures. They include adipose tissue, fibrous connective tissue, skeletal muscle, blood vessels, and the peripheral nervous system. Soft tissues are almost entirely derived from the mesoderm except for the peripheral nerves. Soft tissue tumors, being a large heterogeneous group of neoplasms, are classified according to histogenesis, as detailed below. [1] Most have benign and malignant counterparts; some are of borderline malignant potential with aggressive local invasion. The incidence of benign soft tissue tumors is about ten times that of malignant ones. Benign deep masses in adults are usually due to intramuscular lipoma. Extremity masses larger than 5-7 cm and deeper than subcutaneous tissue, favour the diagnosis of a malignant soft tissue tumor. Benign tumors are usually superficial and well defined or encapsulated masses showing slow growth. [1] Of the imaging methods commonly used for evaluation, magnetic resonance imaging best defines the relationship between a tumor and its adjacent anatomic structures, such as compartment boundaries, nerves, vessels, and muscle. [2]

WHO (2002) Classification of Soft Tissue Tumors

Soft tissue tumors are divided into the following four categories: Benign: These usually do not recur locally, and if they do, the recurrence is nondestructive and almost always readily curable by complete local excision. Morphologically benign lesions which are extremely rare, may give rise to distant metastases that cannot be predicted on the basis of routine, histological evaluation. Cutaneous benign fibrous histiocytoma is the best example. Intermediate (locally aggressive): These tumors show an infiltrative and locally destructive growth pattern; however, they do not metastasise. The example in this category is fibromatosis. Intermediate (rarely metastasising): These tumors are often locally aggressive but in some cases, they also have a tendency to produce distant metastases (usually in a lymph node or lung). This risk is low (< 2%). The classic examples are plexiform fibrohistiocytic tumors and angiomatoid fibrous histiocytoma. Malignant: Soft tissue sarcomas are locally destructive with the potential to recur; the risk of distant metastasis is significant. (Depending on the histological type and grade, the potential ranges from 20 to almost 100%).

Fine Needle Aspiration Cytology

Benign soft tissue tumors usually present with superficial small swellings, usually in the subcutaneous tissue, and are best assessed by FNAC. [3-6] Although numerous histopathological entities are currently known, the majority are rare and can only be diagnosed on histology. The commonly encountered soft tissue tumors and lesions and their FNAC appearance are described below.

Lipoma: This is the most commonly encountered swelling that is subjected to FNAC. Clinical findings of the swelling are essential in its differentiation from subcutaneous fibroadipose tissue, accurate needle placement within the mass being the most important criterion. Lipomas are usually solitary but may be multiple, and the swelling slips under the examining hand.

Aspirates show adipose tissue which is indistinguishable from normal fibroadipose tissue (Figure 1). Delicate vessels without much fibrous tissue are the rule. [7,8] The fat cells are univacuolated with nuclei pushed to the periphery. Intramuscular lipomas may be admixed with skeletal muscle. These have to be differentiated from myxomas which also occur in this location, the aspirates of which have myxoid material with stellate cells.[9] The presence of atypical nuclei may be indicative of benign lesions such as atypical lipoma or a well differentiated liposarcoma. Lipoblasts in the aspirate usually indicate a well differentiated liposarcoma. However, lipidladen macrophages may mimic lipoblasts making cytological identification difficult. The presence of these findings indicates the necessity for histological examination for proper evaluation, which can be recommended on FNAC. **(Figure 1)**

Benign Nerve Sheath Tumor: Schwannomas and neurofibromas may be solitary or multiple (in neurofibromatosis) and are commonly aspirated for diagnosis. Aspiration from neurofibromas is usually painful. Aspirates are cellular and show spindle cell morphology with moderate cellularity. A fibrillary background is common in both schwannomas and neurofibromas. [10] Nuclei of both tumors are long with pointed ends and have a ìbuckledî or twisted appearance (Figure 2). The presence of nuclear palisading (or Verrocay bodies) favors a schwannoma over a neurofibroma but FNAC cannot help make this distinction cannot be reliably made in its absence. Some aspirates show nuclear enlargement and pleomorphism. [11] This is a common finding in large benign nerve sheath tumors that warrants a careful search for mitotic figures and histological examination of an excision biopsy is essential for proper evaluation. The presence of mitotic figures even in aspirates not showing nuclear pleomorphism, may indicate transformation to a malignant peripheral nerve sheath tumor. **(Figure 2)**

Fibromatosis: This is a locally aggressive tumor and is currently classified in the intermediate WHO grade. However, this is a common tumor which is frequently assessed by FNAC. It has site predilections which should be taken into account before the interpretation of the FNAC findings. Aspirates from fibromatosis have variable cellularity. [12,13] Those with low cellularity are benign in appearance (Figure 3) and are composed of spindle-shaped fibroblasts arranged in groups interspersed with collagen (and not fibrillary material as with nerve sheath tumors). Single cells are seen in the background; mitotic figures are rare.

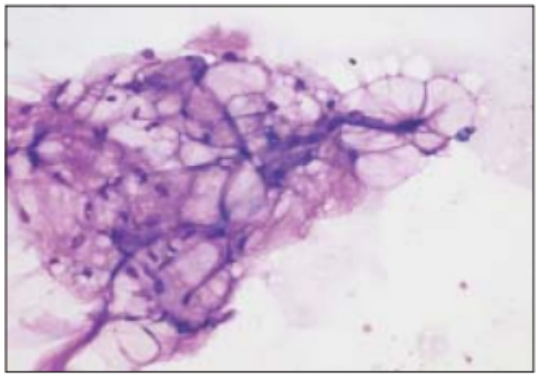

Figure 1: Aspirate from lipoma showing normal looking adipose tissue with many capillary sized blood vessels.

***Address for Correspondence:** Dr. Venkateswaran K Iyer, Department of Pathology, AIIMS, New Delhi, India.*

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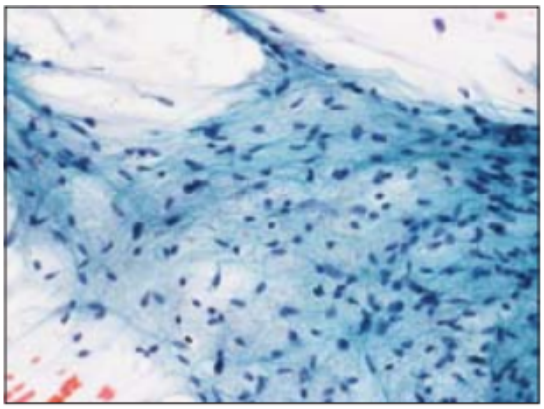

Figure 2: Aspirate from benign nerve sheath tumor showing fibrillary background and sparse cellularity of spindle cells.

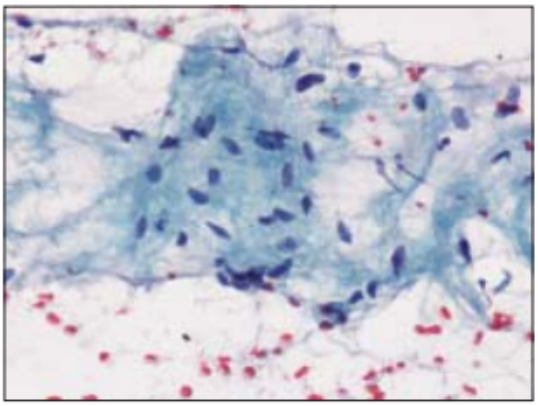

Figure 3: Aspirate from fibromatosis showing sparse cellularity and collagenous stroma.

Aspirates from aggressive fibromatosis are more cellular although mitoses are rare to absent. [12] Collagen matrix is more difficult to identify in aspirates (Figure 3). Such tumors are difficult to differentiate from low-grade spindle cell sarcomas and hence, an inconclusive report on cytology and a subsequent histological examination is needed for diagnosis. **(Figure 3,4)**

Leiomyoma: Leiomyomas are much less common in the subcutaneous region as compared to lipomas, nerve sheath tumors, and fibromatosis. Leiomyoma is differentiated from leiomyosarcoma based on the mitotic counts done as part of the histological examination. As such, FNAC has a limited role in diagnosis. The main objective is the identification of smooth muscle differentiation on FNAC which may be difficult to accomplish. A diagnosis of a nonspecific, benign spindle cell tumor is usually returned. Aspirates from leiomyoma are usually sparsely cellular, although some aspirates may be cellular. The tumor cells may have clear-cut, spindle-shaped cytoplasmic processes on either side that stain pale blue in Giemsa stain. Bare nuclei may predominate in some aspirates and if necrosis is found, a differential diagnosis with a leiomyosarcoma would require a biopsy.

Benign fibrous histiocytoma group: This is a group of neoplasms which on aspiration, show an admixture of spindle-shaped fibroblastic cells and polygonal histiocytic cells. A number of tumors such as dermatofibroma, tendon sheath fibroma, and proliferative fasciitis among others, have a similar appearance on aspiration, and hence, a definite diagnosis of benign fibrous histiocytoma cannot be made. Aspirates from benign fibrous histiocytomas show spindleshaped fibroblasts with collagenised stroma and polygonal cells with a moderate amount of foamy cytoplasm. Giant cells may be seen including Touton giant cells. May-Gr¸nwald-Giemsa (MGG) staining may show polygonal cells with blue cytoplasm; mitotic figures are absent. Pleomorphism may be seen in the giant cells.

Giant cell tumor of the tendon sheath: This tumor usually occurs in the fingers and toes and may be associated with trauma. It is still uncertain whether it represents a true neoplasm or a reactive proliferation in response to trauma. It is mostly considered to belong to the benign fibrous histiocytoma group. However, as its typical clinical and cytological features permit diagnosis, it requires separate mention. Location is classical and radiological demonstration of the lack of bone involvement is useful in diagnosis. Aspirates show multinucleated giant cells of osteoclastic cell type and two kinds of stromal cells: spindle-shaped cells and polygonal cells with cytoplasm. Nuclear grooves are frequent in the stromal cells; binucleated cells are seen.

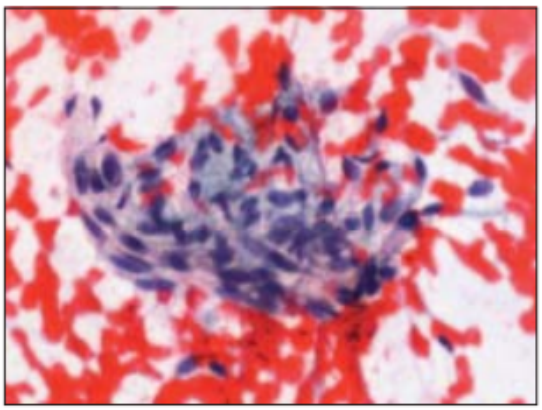

Figure 4: Aspirate from aggressive fibromatosis showing cellular spindle cell lesion without collagen.

Benign tumor-like and reactive conditions of soft tissues: A number of conditions with unclear etiology are grouped together under the general category of tumor-like conditions of the soft tissue. It is now clear that a majority of these are actually neoplastic and hence, the term, ìtumor-likeî is inappropriate. Although these are grouped under neoplasms in the WHO classification, they are still regarded by tradition as being tumor-like or reactive conditions. Of these, the most important are nodular fasciitis, proliferative fasciitis, proliferative myositis, myositis ossificans, and inflammatory pseudotumor. Aspirates from inflammatory pseudotumors usually have an inflammatory background with a predominance of acute or chronic inflammatory cells in different cases; plasma cells are frequent. However, the most striking feature is the presence of pleomorphic spindle cells and these aspirates are usually suspected to be malignant.

Atypical fibroxanthoma: This is another tumor which can be misdiagnosed as being malignant on aspiration. This tumor typically occurs as a small skin nodule on the sun-exposed skin of elderly individuals. On aspiration, highly pleomorphic cells are seen and a myxoid background may be present. It is important not to misdiagnose this as a malignancy but to give an inconclusive report asking for a biopsy diagnosis.

Nodular fasciitis, proliferative fasciitis, and proliferative myositis: Nodular fasciitis presents as a rapidly enlarging, tender skin nodule in the upper limbs of young adults. Aspirates tend to be cellular with cohesive cell groups having a feathery edge. Most tumor cells appear stellate with long cytoplasmic processes. Nuclei are finely granular with inconspicuous nucleoli. Ganglion-like cells and inflammatory cells including foamy macrophages may be found. Proliferative fasciitis is similar to nodular fasciitis, occurring in the lower limbs in an older age group than nodular fasciitis.

Proliferative myositis also affects older individuals in the shoulder and scapular regions. Aspiration cytology findings are similar to nodular fasciitis with a more frequent presence of ganglion-like cells. Atypical spindle cells can also be seen in myositis ossificans and must not be misdiagnosed as a malignancy. Classical locations and correlation with radiography findings are essential for proper diagnosis of these lesions.

Benign spindle cell tumors: Approach to diagnosis: Aspirates from swellings may not show the typical findings detailed above and in many instances, it is enough to make a distinction from malignancy on FNAC rather than give a precise histological diagnosis. In any aspirate from a spindle cell lesion, the main criteria to be assessed are cellularity, nuclear

pleomorphism, mitosis, and necrosis. In aspirates from any tumor showing spindle cell fragments with high cellularity and/or nuclear pleomorphism in the form of hyperchromasia or anisonucleosis and/or mitotic figures and/or presence of necrosis, any one feature should prompt an inconclusive report making histological examination mandatory. Aspirates not showing definite necrosis or any mitosis or clearly pleomorphic nuclei or very high cellularity should be carefully evaluated to distinguish a low-grade sarcoma from a benign spindle cell lesion. Even the slightest increase of cellularity or nuclear chromatin abnormality in the absence of specific features for one of the above tumors, should mandate a histological examination.

To conclude, the purpose of FNAC in benign soft tissue lesions is to be an initial screening test to differentiate from infective lesions and it should be used to triage patients requiring early biopsy. The specific diagnosis is almost always made on histopathology and FNAC should not be used as a replacement for an excision biopsy. Immunocytochemistry on aspirates has little role in the evaluation of benign mesenchymal lesions and will anyway not help to distinguish between benign and malignant lesions.

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