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Henryk A. Domanski
Fine Needle Aspiration of Soft Tissue Tumours

Surgical Biopsy, Core Needle Biopsy or Fine Needle Aspiration in the Primary Diagnosis

In the majority of musculoskeletal tumour centres the definitive diagnosis of soft tissue tumours, especially suspected sarcomas, is based on the histopathological evaluation of a biopsy sample or a core needle biopsy with an outer diameter of 1.2–1.4 mm.

Although FNA with needles having an outer diameter of 0.4–0.8 mm has been a universally accepted diagnostic method in the definitive diagnosis of various tumour entities for many years, objections have been raised to FNA in the primary diagnosis of soft tissue tumours. An important objection has been the postulated inability to aspirate tumour material sufficient for reliable biotypic diagnosis with a thin needle. Due to the numerous subtypes and morphologic heterogeneity among specific entities, soft tissue tumours have been considered to pose some of the greatest diagnostic challenges in surgical pathology and routine light microscopy is often not sufficient for a diagnostic evaluation. Additional diagnostic methods such as histochemistry, immunohistochemistry, electron microscopy (EM), DNA ploidy analysis and chromosomal analysis and molecular genetics often have to be applied to reach a reliable diagnosis.

However, articles and book chapters on soft tissue tumours as a target for FNA began to appear at the beginning of the 1980s. The first case series published were often small and the diagnostic workup was not critically investigated.

In spite of a negative attitude to FNA among surgeons, oncologists and pathologists, it has been shown that the same advantages which have made FNA a first-choice diagnostic approach in breast tumours, thyroid tumours, salivary gland tumours or malignant lymphomas are also applicable in the diagnostic workup of a soft tissue tumour.

FNA of a suspected soft tissue tumour is an outpatient procedure. No anaesthesia is necessary. One exception is the needling of soft tissue masses in children in whom a brief general anaesthesia may be needed. An evaluation of the aspirate within 10–15 min after needling is possible with a rapid haematoxylin-eosin (HE) or Diff-Quik stain. The adequacy of the material can thus be checked while the patient is waiting, and a preliminary diagnosis is sometimes possible. The purpose of a preliminary evaluation is 2-fold: it might be important information on the type of ancillary diagnostic methods that should be used and the surgeon can inform the patient and suggest further investigative work-up at his/her first visit. Since the diagnosis and treatment of soft tissue sarcomas should preferably be centralized to multidisciplinary tumour centres, it is important to refer patients that the necessary information is obtained rapidly and the number of visits are as few as possible. Experience from the Musculoskeletal Tumour Centre at the University Hospital of Lund has shown that for patients referred to the centre for tumours suspicious of malignancy one visit was usually sufficient when the tumour proved to be benign at the combined evaluation of clinical examination, FNA diagnosis and radiographic examination, if any [3].

Core needle biopsy is also an outpatient procedure, but a preliminary diagnosis is less feasible than with FNA. FNA also permits sampling of different parts of large tumours to evaluate tumour heterogeneity, providing important information in, for example, lipomatous tumours.

A novel diagnostic approach, recently tested at our centre, is a combination of FNA and core needle biopsy in selected patients referred for FNA. The FNA as well as the core needle biopsy is performed by the cytopathologist at the same visit. This approach combines the advantages of both sampling methods: sampling from different parts of large tumours, a rapid preliminary report, the possibility to evaluate the tissue architecture in the core biopsy (often difficult in an FNA smear) (fig. 1a, b). In addition material sufficient for various ancillary methods such as immunohistochemistry, EM and cytogenetic/molecular genetic analyses [4] is obtained with greater certainty.
Diagnostic Accuracy of Fine Needle Aspiration Biopsy

Several reports of diagnostic accuracy (i.e. differentiation of benign vs. malignant process) have been published. Accuracy has been greater than 90% in most publications but the case series have been small and the number of sarcomas evaluated often few [5–8]. Only a few large series from multidisciplinary centres have been published. In a retrospective 20-year study of 517 tumours, 315 benign and 202 sarcoma cases of the extremities and trunk from the Musculoskeletal Tumour Centre, University Hospital of
Fig. 2. A subcutaneous sarcoma removed with the overlying skin. The insertion point is marked by the tattoo (arrow).

the same insertion point. Due to tumour tissue heterogeneity, especially in large tumours, it is important to sample tissue from different parts of the tumour.

The microscopic evaluation should be based on both wet-fixed (HE or Papanicolaou (Pap)) and air-dried (May-Grünwald-Giemsa (MGG) or Diff-Quik) smears.

The wet-fixed material is superior for evaluation of nuclear details such as chromatin structure and nucleoli, while the MGG staining gives excellent information on cytoplasmic details and the background matrix.

**Cytodiagnosis**

One common objection to FNA in the primary diagnosis of soft tissue tumours is the supposed inability to correctly and reliably diagnose the numerous different histotypes in smears. However, the necessary diagnostic level for a soft tissue tumour is determined by the primary treatment envisaged in the individual case. First of all the surgeon must know whether the tumour in question is a true soft tissue lesion/tumour or a soft tissue metastasis or a primary soft tissue lymphoma. In case of sarcoma the standard treatment in the majority of cases is primary radical surgery, sometimes followed by radiotherapy. The type of surgical intervention depends more on the site (subcutaneous or deep), size and the relation of the sarcoma to vessels, nerve bundles and periosteum than on the histotype. Thus a reliable diagnosis of sarcoma is sufficient for the surgeon in those cases where primary radical surgery is the proposed treatment.

When the treatment in phase neoadjuvant therapy (radiotherapy or chemotherapy) followed by surgery, the FNA evaluation must equal that of a histopathological evaluation as regards histotype and malignancy grade.

At this point, neoadjuvant therapy is used for rhabdomyosarcoma, neuroblastoma, the extraskeletal Ewing/PNET family of tumours and in some centres selected cases of soft tissue sarcomas.

On the other hand, in case of a benign soft tissue tumour or reactive soft tissue lesion the surgeon often wants to know the histotype in order to inform the patient of the two treatment options: observation/follow-up or local excision. Observation may be suggested in the pseudosarcomatous soft tissue lesions, especially nodular fasciitis and pseudomalignant myositids ossificans, and in case of lipoma or neurilemoma and desmoid fibromatosis. A shelling out of the tumour is sufficient treatment for most benign soft tissue tumours except desmoid fibromatosis, which requires more extensive margins due to its infiltrative growth.

**Classification of the Cytodiagnosis**

Standardized reporting is an advantage both to the surgeon and to the cytopathologist. At our Musculoskeletal Tumour Centre we have for many years used four main diagnoses: benign, sarcoma, other malignancy or inconclusive. Inconclusive means either that the material is insufficient for
Fig. 11. Examples of regenerating striated muscle fibres. a Typical ‘muscle giant cells’ with rows of nuclei and dark blue cytoplasm. MGG. High magnification. b The cytoplasm is eosinophilic in HE. High magnification.

size and shape. They are rounded, polyhedral, strap-shaped or tadpole-like. The cytoplasm is densely eosinophilic in HE and dark blue in MGG. The multiple nuclei are moderately large, uniform in size and often harbour a prominent nucleolus. The nuclei are typically arranged in rows, eccentrically located (fig. 11a–c).
**Table 4.** A summary of benign ‘pseudomalignant changes’ in aspirated material from fibrous, adipose tissue and striated muscle

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Cellular changes</th>
<th>Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroblasts/myofibroblasts</td>
<td>Variation in size, atypia, shape; elongated, multinucleated cytoplasm; plump with eosinophilic cytoplasm; variable nuclear shape and size; binucleation; prominent nucleoli</td>
<td>Benign-pseudosarcomatous soft tissue lesions, posttraumatic states</td>
</tr>
<tr>
<td>Adipose tissue</td>
<td>Increased vascularity; increased cellularity (fibroblasts, endothelial cells, histiocytes); multivacuolated cytoplasm in adipocytes; uni- or multinucleated histiocytes between fat fragments (lipophages)</td>
<td>Status after fat necrosis, posttraumatic states, adipose tissue surrounding various non-adipose tumours</td>
</tr>
<tr>
<td>Striated muscle</td>
<td>Multi- or uninucleated regenerating muscle fibres (‘muscle giant cells’); occasionally presence of tadpole-like regenerating muscle fibres; prominent; nucleoli; dense eosinophilic (HE) or dark blue (MGG) cytoplasm</td>
<td>Aspirates from tumours/lesions infiltrating striated muscle; examples: intramuscular lipoma, intramuscular myxoma, desmoid, fibromatosis coli</td>
</tr>
</tbody>
</table>

Regenerating muscle fibres are mainly found within FNA samples from tumours infiltrating striated muscle. Typical examples are infantile fibromatosis colli and desmoid fibromatosis.

A summary of the reactive cytological changes in fibrous tissue, adipose tissue and striated muscle is presented in Table 4.
Fig. 13. Intramuscular lipoma. Fragments of adipose tissue composed of mature adipocytes and fragments of striated muscle. a Overview, low magnification. b High magnification. a, b HE.

Pleomorphic lipomas may have a myxoid stroma and collagen bundles similar to those in spindle cell lipoma are often present. Transitional forms between pleomorphic and spindle cell lipoma are fairly common. The giant cells stain for CD34.

Cytological features of pleomorphic lipoma (fig. 17a, b)
Fragments of mature fat

A variable number of large cells with hyperchromatic nuclei and eosinophilic cytoplasm (HE) both in the background and in tissue fragments
A variable number of 'floret cells'
Clusters or runs of spindle cells seen in transitional forms

Differential diagnosis
Well-differentiated liposarcoma (atypical lipomatous tumour)
Comment

The most important differential diagnosis of pleomorphic lipoma is atypical lipomatous tumour/well-differentiated liposarcoma, which often displays large cells with hyperchromatic nuclei and occasional ‘floret cells’ in smears. The main differences between these two entities are the clinical presentation and the occurrence of atypical lipoblasts in liposarcoma. Pleomorphic lipomas are subcutaneous tumours whereas atypical lipomatous tumours/well-differentiated liposarcoma usually are deep-seated tumours of the limbs or the retroperitoneum. Cytogenetic findings are also helpful, since atypical lipomatous tumour/well-differentiated liposarcoma typically displays giant marker chromosomes while the pleomorphic lipoma shows involvement of chromosomes 13 and 16, similar to spindle cell lipoma.

Hibernoma

Hibernoma, derived from brown fat, is a rare lipomatous tumour, which occurs mainly in patients between 20 and 50 years of age.

Most hibernomas occur in the back but some in the thigh and in the armpit. Though usually subcutaneous, they can be intramuscular.

Histopathology

Hibernomas are usually well circumscribed and show a tan-brown cut surface. They are lobulated and composed of a variable amount of mature adipocytes mixed with large rounded cells having a finely vacuolated cytoplasm and similar cells with eosinophilic granular cytoplasm. Mature adipocytes are the most common cellular component and may dominate the microscopic picture entirely. Hibernomas are well vascularized. The cytology of hibernoma has been evaluated in case reports and small series [16–18].

Cytological features of hibernoma (fig. 18a, b)

- Fragments of mature fat tissue intermingled with ‘hibernoma’ cells (rounded cells with abundant finely vacuolated or granular cytoplasm and centrally located, small, uniform nuclei)
- The fat fragments often contain numerous capillary vessels

Differential diagnosis

Subcutaneous lipoma
Granular cell tumour
Adult rhabdomyoma
Liposarcoma

Comments

If ‘hibernoma cells’ dominate the smears, granular cell tumour as well as adult rhabdomyoma can be diagnostic pitfalls. IC is helpful since the cells of granular cell tumour show double positivity for NSA and S-100, and rhabdomyoma cells stain positive for myoglobin. Hibernoma cells have been misinterpreted as lipoblasts but nuclei are neither atypical nor scalloped.

Hibernomas with a large proportion of mature fat cells are often diagnosed as common lipoma.
Histopathology

Chondroid lipoma is a well-demarcated, at times encapsulated tumour. It has a lobular pattern and is composed of rounded cells arranged in nests or strands in a chondroid-like matrix. The tumour cells may resemble multivacuolated lipoblasts, others have an eosinophilic granular cytoplasm. Foci of mature fat cells are also present. The nuclei are often irregular with a folded nuclear membrane.

The cytological features of chondroid lipoma are described in FNA smears based on individual cases [70, 71].
Fig. 19. Lipoblastoma. a Myxoid background with fatty vacuoles and fragments of tightly packed small fat cells. MGG. Low magnification. b A thin capillary strand in a myxoid background surrounded by lipblast-like cells. MGG. High magnification.

Comments
In the few cases hitherto described, the branching capillary network seen in myxoid liposarcoma has not been present. In addition the myxoid matrix is less abundant and the nuclei of the lipoblast-like cells are more irregular compared to the rounded, slightly atypical nuclei seen in myxoid liposarcoma.

Extra-Adrenal Myelolipoma
Extra-adrenal myelolipoma, a tumour-like lesion composed of mature fat and bone marrow cells, is mainly found in the adrenals. These lesions may also arise in the pelvic region and retroperitoneum. In cytological practice myelolipoma is part of the differential diagnostic spectrum when tumour-like masses in the pelvic region or retroperitoneum are needlel [72].
Comment
The cytological diagnosis of elastofibroma is difficult. The main diagnostic feature is the presence of degenerate elastic fibres.

Malignant Tumours

Adult Fibrosarcoma
Adult fibrosarcoma is at present considered as a rare tumour and a diagnosis of exclusion. It is a deep-seated tumour of elderly adults and the limbs are the most frequent sites. The majority of sarcomas formerly diagnosed as fibrosarcoma are today classified either as monophasic synovial sarcoma or MPNST.

Histopathology
The pattern is fascicular, the fascicles of cells are often arranged in a herringbone-like pattern. The tumour cells are fibroblast-like, exhibiting variable nuclear atypia. The stroma is variably fibrous.

Cytological features of adult fibrosarcoma
Uniform population of spindle cells, both dispersed and arranged in clusters or fascicular structures
Stripped nuclei not uncommon
Spindle-shaped cells with fusiform nuclei and elongated cytoplasm
Fibrous Hamartoma of Infancy

Fibrous hamartoma of infancy is very rare after the age of 2 years and typically presents as a subcutaneous mass in the upper arm or around the shoulder.

Histopathology

This lesion has ill-defined boundaries and is composed of a mixture of mature adipose tissue, fibrous septa or bands and myxoid foci with small rounded primitive cells.

The features of fibrous hamartoma of infancy have been described in individual case reports [83].

Cytological features of fibrous hamartoma of infancy (fig. 33a, b)

- Mixture of mature adipose tissue and clusters or runs of spindly cells
- More or less abundant tufts of myxoid background substance

Differential diagnosis

Infantile fibrosarcoma

Malignant Tumours

Infantile Fibrosarcoma

Infantile fibrosarcoma may be congenital and is generally seen before the age of 2. Most infantile fibrosarcomas arise in the arms or legs and present as a large, non-tender mass.

Histopathology

Fascicles of tightly packed fibroblasts with slight nuclear atypia and often numerous mitoses. Myxoid stroma and areas of round cells as well as a haemangiopericytoma-like vascular pattern may be seen. Lymphocytic infiltrates and haemorrhages and foci of necrosis may be found.
Fig. 34. Infantile fibrosarcoma. a In our only case there was an abundant yield of three-dimensional fascicular fragments composed of tightly packed spindle cells. HE. Low magnification. b The cell population is uniform and has bland, slightly atypical spindly nuclei. HE. High magnification.

Fibrohistiocytic Tumours

Some of the variants of fibrohistiocytic tumours are the most common objects of FNA. Myxofibrosarcoma and ‘malignant fibrous histiocytoma’ are the most frequent sarcomas referred for FNA, localized giant cell tumour of tendon sheath is part of the soft tissue tumour spectrum in every FNA clinic and some cases of dermatofibrosarcoma protuberans are also biopsied.
Fig. 38. Myxofibrosarcoma, low and high grade. a Cell clusters and dispersed cells in a myxoid background. MGG. Low magnification. b Mildly atypical spindle cells from a low-grade tumour. MGG. High magnification. c Cellular atypia is obvious in this high-grade tumour. HE. High magnification. d, e Irrespective of grade, curved vessel fragments in the myxoid background are an important diagnostic sign. HE. High magnification.
Fig. 51. Perineurioma. a Dispersed and clustered tumour cells in a myxoid background matrix. Perineurioma shares this appearance in smears at lower magnification with several other 'myxoid' soft tissue tumours. MGG. Low magnification. b The elongated intact tumour cells have long cytoplasmic processes and bland nuclei. HE. Medium magnification. c A group of perineurioma cells. The myxoid matrix is more obvious in MGG-stained smears. MGG. Medium magnification.

The cytological features of perineurioma have been described in a single case [96]; the microscopic features listed below are collected from that case report and our individual cases.

Cytological features of perineurioma (fig. 51a–c)
- Abundant myxoid background matrix
- Variable cellularity
- Elongated cells with ovoid, fusiform or rounded nuclei
- Many stripped nuclei
- Intact cells have long, thin bipolar cytoplasmic processes
- Moderate anisokaryosis
- Uniform chromatin structure
- Scattered vessel fragments in the background matrix

Differential diagnosis
- Neurolipoma with predominant Antoni B areas with abundant myxoid background matrix
- Neurofibroma
- Intramuscular myxoma
- Low-grade myxofibrosarcoma
- Fibromyxoid low-grade sarcoma

Comment
Aspirates from perineurioma are most commonly diagnosed as 'benign myxoid soft tissue tumours' although the cellularity and anisokaryosis might be misinterpreted as indicating a low-grade myxoid sarcoma. A specific diagnosis of perineurioma is most probably not possible without the help of IC and/or EM.

Malignant Tumours

Malignant Peripheral Nerve Sheath Tumour
MPNST include those malignant tumours which arise from the different cells of the nerve sheath (Schwann cells, perineural cells, fibroblasts). It is estimated that MPNST
Fig. 62. ES/PNET family of tumours. Conventional ES. a A cell-rich smear of uniform small rounded cells with rounded nuclei. HE. Low magnification. b The two diagnostically important cell types are shown in this field: large light cells (long arrow) and small dark cells (short arrow), best visualized in MGG. MGG. High magnification.

The presence of a double cell population has also been described in histological sections. Although the 'small dark cells' are regarded as degenerate cells by most investigators, this feature is an important diagnostic sign in cytological material.

IC and EM are both valuable adjunctive diagnostic methods (fig. 4a, b, 65). CD99 should not be used as a single antibody as it is not specific for the ES/PNET family (table 2).

The cytogenetic/molecular genetic analysis is, in our opinion, the most important ancillary method. The presence of t(11;22)(q24;q12) and/or the fusion transcript between the EWS/FLI1 genes indicate that the tumour in question belongs to the ES/PNET family. FISH of the common EWS breakpoints is another method, well suited for FNA material [66]. It has to be remembered, however, that rearrangements of the EWS gene also occur in desmoplastic small round cell tumour (DSRCT), clear cell sarcoma and myxoid liposarcoma. The two latter tumours present no differential diagnostic problems as their cytology is quite different from that of ES/PNET, but DSRCT may be a diagnostic pitfall in retroperitoneal tumours, especially when the yield is poor and the typical double cell population is absent.

FISH should be supplemented with IC in the differential diagnosis between ES/PNET and DSRCT. Due to the polyphenotypic immunexpression in DSRCT cytokeratins,
Fig. 65. One criterion common to tumours in the ES/PNET family is positive staining with CD99. CD99 immunostaining on cell block preparation.

Fig. 66. Extraskeletal osteosarcoma. a Large, often rounded, pleomorphic tumour cells with rounded nuclei. MGG. Medium magnification. b Intercellular strands of osteoid (arrow). MGG. High magnification. c Mitotic figures (arrow) are observed in most cases if smears are rich in cells. MGG. Medium magnification.

EMA, desmin and NSE should be part of the antibody panel besides CD99. CD99 has been reported to be focally positive in DSRCT.

In our experience the combined use of electron-microscopic examination and molecular genetic analysis gives the optimal diagnostic information. FNA samples are more suitable for PCR and FISH than for conventional karyotyping [64, 66].

**Osseous Tumours**

**Osteosarcoma of Soft Tissue**

Extraskeletal osteosarcoma is a rare sarcoma in middle-aged and old adults. It is extremely rare in children and adolescents. The most frequent site is the legs, less frequently the pelvis, retroperitoneum and arms. Most tumours are deep-seated. Radiographic examination may reveal calcified areas.

**Histopathology**

Extraskeletal osteosarcoma is a pleomorphic sarcoma resembling the pleomorphic sarcoma of the MFH type. The clue to the diagnosis is the presence of osteoid produced by the tumour cells. The osteoid is usually seen as narrow bands in a lace-like pattern encircling the tumour cells. Extraskeletal osteosarcoma may contain areas of neoplastic cartilage or the tumour cells may be mainly spindle-shaped resembling fibroblastic conventional osteosarcoma.
have been demonstrated in 20–75% of cases in different series. Staining is often focal.

EMA is positive in up to 25% and neuroendocrine differentiation (NSE and synaptophyisin) has been described in a number of cases. Staining for cytokeratin is negative in the majority of tumours and SMA and desmin are negative.

Ultrastructurally, cells of classic EMC are enclosed in a fibrillary matrix. The cytoplasm has short projections and typically exhibits prominent Golgi zones and dilated rough reticulum, often filled with granular material associated with numerous mitochondria. Neuroendocrine differentiation in the form of neurosecretory granules is present in a small number of cases.

The cytogenetic analysis has revealed a characteristic translocation t(9;22)(q22;q12). This translocation involves the EWS gene at 22q12 and the CHN gene at 9q22. The cytological features of EMC have been described in a small series and in case reports [132–134].

The published cases are all examples of classic EMC. One case in our files showed signs of neuroendocrine differentiation [134].

**Cytological features of EMC (fig. 76a–d)**

- Abundant myxoid background
- Variable arrangement of tumour cells, clusters, branching strands, cell balls and dispersed cells
- Often a central core of branching capillaries in the clusters
- Cells are variably rounded, elongated, or fusiform
- Nuclei are rounded, ovoid or thin, spindle-shaped
- Chondroblastoma-like nuclei with nuclear folds or indentations (coffee bean nuclei) are often observed

**Differential diagnosis**

- Classic EMC
  - Intramuscular myxoma
  - Mixed tumour of soft tissue
  - Myxoid liposarcoma
  - Low-grade myxofibrosarcoma
  - Low-grade fibromyxoid sarcoma
  - Parachordoma
- Solid, hypercellular EMC
  - ES/PNET
  - Poorly differentiated synovial sarcoma

**Comment**

IC is of limited value as S-100 protein positivity is present in less than 50% of tumours. A broad panel of antibodies is, however, helpful to exclude epithelial, neuroectodermal and schwannian differentiation.

Electron-microscopic examination is a useful diagnostic cytological examination [68].

**Synovial Sarcoma**

Synovial sarcoma accounts for 5–10% of soft tissue sarcomas. It can occur at any age including childhood, but is most common in young and middle-aged adults. The majority arises in the extremities and trunk, and more than 96% are deep-seated.

**Histopathology**

There are four main histological types: monophasic fibrous, biphasic, monophasic epithelial and poorly differentiated (focally or entirely) [135]. The monophasic fibrous and biphasic subtypes are the most common ones, the monophasic epithelial subtype is uncommon.

Most of the cells are either spindle-shaped, uniform with scanty cytoplasm and ovoid bland nuclei or fibrosarcoma-like with fusiform nuclei. Three morphological variants of the poorly differentiated subtype have been described. One has high-grade malignant spindle cells with hyperchromatic nuclei and enlarged nucleoli, this subtype is composed of large epithelioid cells that fuse with rhabdoid features, with rounded nucleoli and prominent nucleoli. Finally there is a small cell variant with scanty cytoplasm and rounded bland nuclei resembling the cells of the ES/PNET family of tumours.

**Immunohistochemically, most synovial sarcomas stain positively for cytokeratins (CK7 and CK19) and EMA. The staining may be focal, and both cytokeratins and EMA should be used as some tumours stain only for EMA and vice versa. More than half are positive for CD99 and Bcl-2 protein positivity has been reported in 70–90% of tumours. Up to a third stain for S-100 protein.**

Important ultrastructural features include junctions or desmosome-like structures, and small pseudoglandular spaces bordered by short microvilli.

The majority of synovial sarcomas, including poorly differentiated tumours, share a distinct chromosomal aberration, t(X;18)(p11;q11.2). The translocation involves the SYT gene on chromosome 18 and the SSX gene family on the X chromosome. There are two major gene fusions, SYT/SSX1 and SYT/SSX2. According to two reported series of tumours, the SYT/SSX2 variant is biologically more aggressive than the SYT/SSX1 variant [136, 137].

The cytological features of synovial sarcoma have been evaluated in some series of tumours and in numerous case reports. Above all the monophasic fibrous and biphasic variants have been investigated [35–38]. Individual case reports describing the cytological features of poorly differentiated synovial sarcoma have been published [138]. Recently we
**Table 8** (continued)

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Diagnostically important features</th>
<th>Ancillary tests</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxofibrosarcoma</td>
<td>Curved vessel fragments in myxoid background; low-grade tumours predominantly spindly with moderate atypia; high grade tumours pleomorphic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-grade fibromyxoid sarcoma</td>
<td>Slight to moderate atypia in constitutional spindle cells; occasional vessel fragments in myxoid background</td>
<td></td>
<td>Difficult to distinguish from low-grade myxofibrosarcoma</td>
</tr>
<tr>
<td>EMC</td>
<td>Variable arrangement of cells: cell balls, branching strands, clusters; chondroblastoma-like nuclei (coffee bean nuclei); almost never cartilage-like fragments</td>
<td>IC: S-100</td>
<td>Cytogenetic analysis</td>
</tr>
</tbody>
</table>

**Pitfalls**

- Myxoid malignant melanoma
  - IC: HMB45, Melan A

---

**Table 9.** Cytological evaluation of soft tissue tumours based on pattern: small round ovoid cell pattern

<table>
<thead>
<tr>
<th>Tumour</th>
<th>Diagnostically important features</th>
<th>Ancillary tests</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomus tumour</td>
<td>Presence of myxoid background matrix; lesional cells with rounded, ovoid, bland nuclei; presence of spindle cells</td>
<td>IC: SMA</td>
<td>Intensive pain at needling</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>Dispersed cells and clusters; stripped nuclei; neuropil background; small moulded cells; occasional rosettes; in preserved cells thin cytoplasmic processes connecting cells; dark irregular nuclei</td>
<td>IC: CD99, S-100, chromogranin, synaptophysin, EM</td>
<td>Cytogenetic analysis</td>
</tr>
<tr>
<td>ES/PNET family, classic ES</td>
<td>Dark cells; large cells; abundant cytoplasm with vacuole-like spaces; bland nuclear morphology; inconspicuous nucleoli</td>
<td>IC: CD99, NSE, chromogranin, EM</td>
<td>Cytogenetic analysis</td>
</tr>
<tr>
<td>ES/PNET family, PNET</td>
<td>Occasional rosettes; small unipolar cytoplasmic processes; moderate pleomorphism</td>
<td>IC: CD99, NSE, chromogranin, EM</td>
<td>Cytogenetic analysis</td>
</tr>
<tr>
<td>Alveolar rhabdomyosarcoma</td>
<td>Rounded, pear-shaped or triangular myoblast-like cells; eosinophilic cytoplasm; occasionally multinucleated giant cells with numerous small nuclei</td>
<td>IC: desmin, MyoD1, EM</td>
<td>Cytogenetic analysis</td>
</tr>
<tr>
<td>Desmoplastic small round cell tumour</td>
<td>Dispersed cells and loosely cohesive clusters; scant cytoplasm; inconspicuous nucleoli; occasionally stromal fibroblasts</td>
<td>IC: cytokeratin, desmin, NSE, CD99, EM</td>
<td>Cytogenetic analysis, Predominantly abdominal tumour</td>
</tr>
<tr>
<td>Poorly differentiated areas in synovial sarcoma</td>
<td>Mixture of cell-right irregular, three-dimensional tissue fragments and dispersed cells with stripped nuclei; vessel network in fragments; preserved cells small with rounded ES-like nuclei</td>
<td>IC: EMA, cytokeratin, CD99, EM</td>
<td>Cytogenetic analysis</td>
</tr>
</tbody>
</table>

**Pitfalls**

- Small cell carcinoma
  - IC: cytokeratin
- Lymphoblastic lymphoma
  - IC: CD3, CD79a, CD10, Tdt
- Small cell melanoma
  - IC: S-100, HMB45, Melan A


