

# Cytological Classification of Soft Tissue Tumours Based on the Principal Pattern

The majority of soft tissue tumours can be classified into one of the following five groups.

## Pleomorphic Pattern

The typical features are a marked variation in cellular and nuclear size and shape and in case of sarcoma marked nuclear pleomorphism including atypical multinucleated tumour cells and prominent nucleoli.

Benign soft tissue tumours in this category are nodular fasciitis and pleomorphic lipoma.

Typical examples of sarcomas are pleomorphic sarcoma of the MFH type, pleomorphic leiomyosarcoma, pleomorphic liposarcoma and the less common pleomorphic MPNST and pleomorphic rhabdomyosarcoma.

Diagnostic pitfalls in this group are the pleomorphic malignant melanoma, anaplastic large cell carcinoma and ALCL (table 7).

## Spindle Cell Pattern

The spindle cell pattern is characterized by a predominance of more or less atypical spindle cells with fusiform or ovoid nuclei and elongated uni- or bipolar cytoplasm. The cells are mostly arranged in sheets or fascicles, but dissociated cells are often present. A small population of larger rounded, polygonal or triangular cells with relatively abundant cytoplasm and nuclei of variable size and shape may be present in some sarcomas. Common examples of benign tumours are neurilemoma and desmoid fibromatosis, rare examples are deep-seated leiomyoma, spindle cell lipoma with a predominance of spindle cells and solitary fibrous tumour. Typical spindle cell sarcomas include

the leiomyosarcoma, a subset of monophasic synovial sarcoma, MPNST and dermatofibrosarcoma protuberans and infrequently spindle cell GIST and fibrosarcoma (infantile and adult) (table 7).

## Myxoid Pattern

The myxoid character is often noted already when the sample is smeared on the glass slides: a thick and viscous, more or less haemorrhagic fluid. Aspirates of myxoid tumours often look like droplets of glue. Under low power magnification there is an evident myxoid background matrix, blue or blue-violet, more or less fibrillary in MGG and faintly pink in HE and faintly green in Pap. The cellular pattern is variable: pleomorphic, spindly or round cells.

A myxoid pattern is common to several soft tissue tumours. Examples of benign tumours are intramuscular myxoma, many cases of nodular fasciitis, and the rare entities of OFMT, perineurioma, parachordoma and mixed tumour of soft tissue. The most common sarcomas are myxofibrosarcoma and myxoid liposarcoma, less common are low-grade fibromyxoid sarcoma and extraskeletal myxoid chondrosarcoma (table 8).

## Small Round/Ovoid Cell Pattern

Smears are typically cellular and composed of small to medium-sized cells with rounded or ovoid nuclei and a variable amount of cytoplasm. The shape of the cells is variable: rounded, ovoid, fusiform or triangular. Nuclei are often bland and nucleoli small.

This pattern is shown mainly by sarcomas: extraskeletal ES/PNET, rhabdomyosarcoma (especially alveolar),

**Table 7.** Cytological evaluation of soft tissue tumours based on pleomorphic and spindle cell pattern

Tumour	Diagnostically important features	Ancillary tests	Notes
<i>Pleomorphic pattern</i>			
Nodular fasciitis	Marked pleomorphism in proliferating fibroblasts/myofibroblasts; ganglion cell-like cells; uniform chromatin structure	DNA ploidy analysis	Painful, tender, rapidly growing; most often spontaneous regression
MFH-type sarcoma	Marked pleomorphism, multinucleated (bizarre) tumour giant cells; mitoses (atypical); necrosis		
Pleomorphic leiomyosarcoma	Atypical cells with blunted/segmented nuclei; nuclei in tandem position	IC: desmin, SMA, caldesmon	
Pleomorphic MPNST	Atypical spindle cells with wavy, thin nuclei with pointed ends, comma-like nuclei	IC: S-100	
Pleomorphic rhabdomyosarcoma	Atypical rhabdomyoblast-like cells, triangular, rounded with eccentric nuclei and eosinophilic cytoplasm	IC: desmin, MyoD1, myoglobin	
<i>Pitfalls</i>			
Anaplastic carcinoma	Moulded clusters; 'owl's eye'	IC: cytokeratin	
Sarcomatous melanoma	Macronucleoli	IC: S-100, HMB45, Melan A	
Sarcomatous anaplastic large cell lymphoma	Reed-Sternberg-like cells; deep blue cytoplasm (MGG); presence of plasma cells, lymphocytes and histiocytes	IC: CD30, EMA, Alk1 Cytogenetic analysis	
<i>Spindle cell pattern</i>			
Neurilemoma	Predominantly tumour tissue fragments; indistinct cytoplasmic borders; fibrillary background; thin, wavy (comma-shaped) tapered nuclei; few dispersed cells	IC: S-100	Often sharp, radiating pain at needling; neurilemmomas in extremities often fusiform at palpation and movable laterally but not craniocaudal
Desmoid	Runs, sheets or small groups of fibroblasts and fragments of cell-poor collagenous matrix; moderate pleomorphism in fibroblasts; occasionally muscle giant cells		Desmoid with prominent collagenous stroma firm to the needle and difficult to aspirate
Solitary fibrous tumour	Cell-tight irregular, three-dimensional tissue fragments mixed with dispersed cells; bland spindle cells	IC: CD34, CD99	
Deep leiomyoma	Tumour cells with cigar-shaped/blunted nuclei; segmented nuclei; moderate anisokaryosis; no mitoses	IC: desmin, SMA	
Leiomyosarcoma	Fascicles of more or less atypical spindle cells; cigar-shaped/blunted nuclei; segmented nuclei; nuclei in tandem position; scattered large atypical cells (stripped nuclei outside fascicles)	IC: desmin, SMA, caldesmon EM	

**Table 7** (continued)

Tumour	Diagnostically important features	Ancillary tests	Notes
MPNST	Fascicles of atypical spindle cells with elongated, wavy nuclei with pointed ends; fibrillary background; comma-shaped nuclei; variable amount of dispersed cells	IC: S-100	
Monophasic synovial sarcoma	Mixture of cell-tight irregular, three-dimensional tissue fragment and dispersed cells with many stripped nuclei; often vascular network in fragments; bland nuclei but mitoses in fragments; mast cells	IC: EMA, cytokeratin, CD99 EM Cytogenetic analysis	Calcifications may be observed at radiographic investigation
Dermatofibrosarcoma protuberans	Mixture of cell-tight tissue, three-dimensional fragments and dispersed cells; moderate nuclear atypia; Touton-type giant cells and foam cells not present	IC: CD34	Cutaneous-subcutaneous tumour; often multinodular
Spindle cell GIST	No specific features; may mimick smooth muscle cells	IC: CD117, CD34	Abdominal tumour
Adult fibrosarcoma	Sheets, fascicles of atypical spindle cells		Diagnosis of exclusion
<i>Pitfalls</i>			
Squamous cell carcinoma, spindle cell type		IC: cytokeratins	
Spindle cell malignant melanoma		IC: HMB45, Melan A	

**Table 8.** Cytological evaluation of soft tissue tumours based on pattern: myxoid pattern

Tumour	Diagnostically important features	Ancillary tests	Notes
Intramuscular myxoma	Poor cellularity; small cell clusters and dispersed cells; cells with long thin bipolar cytoplasmic processes and ovoid or elongated bland nuclei; occasionally individual vessel fragments and 'muscle giant cells'		
OFMT	Mixture of dissociated cells and cell clusters; occasionally acinar-like structures; rounded nuclei in cytoplasm-rich cells	IC: S-100, SMA	Subcutaneous tumour Thick fibrous capsula often with bone trabeculae
Perineurioma	Elongated cells with thin cytoplasmic processes; rounded, ovoid or fusiform nuclei; moderate anisokaryosis; stripped nuclei	IC: EMA	Extremely rare
Parachordoma	Variable cellular morphology: rounded, elongated, polygonal cells; rounded or ovoid nuclei; cytoplasmic vacuolation; moderate anisokaryosis (chordoma-like cytology)	IC: S-100, cytokeratin	Extremely rare
Mixed tumour of soft tissue	Salivary pleomorphic adenoma-like cytology	IC: cytokeratin, S-100, SMA, GFAP	Site important for diagnosis; subcutaneous tumours difficult to distinguish from chondroid syringoma

**Table 8** (continued)

Tumour	Diagnostically important features	Ancillary tests	Notes
Myxofibrosarcoma	Curved vessel fragments in myxoid background; low-grade tumours predominantly spindly with moderate atypia; high grade tumours pleomorphic		
Low-grade fibromyxoid sarcoma	Slight to moderate atypia in constitutional spindle cells; occasional vessel fragments in myxoid background		Difficult to distinguish from low-grade myxofibrosarcoma
EMC	Variable arrangement of cells: cell balls, branching strands, clusters; chondroblastoma-like nuclei (coffee bean nuclei); almost never cartilage-like fragments	IC: S-100 Cytogenetic analysis	
<i>Pitfalls</i> Myxoid malignant melanoma		IC: HMB45, Melan A	

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

Tumour	Diagnostically important features	Ancillary tests	Notes
Glomus tumour	Presence of myxoid background matrix; lesional cells with rounded, ovoid, bland nuclei; presence of spindle cells	IC: SMA	Intensive pain at needling
Neuroblastoma	Dispersed cells and clusters; stripped nuclei; neuropil background; small moulded clusters, occasional rosettes; in preserved cells long thin cytoplasmic processes connecting cells; dark irregular nuclei	IC: NSE, chromogranin, synaptophysin EM	
ES/PNET family; classic ES	Double cell population large light and small dark cells; large cells with abundant cytoplasm with vacuoles and clear spaces; bland nuclear morphology, inconspicuous nucleoli	IC: CD99 EM Cytogenetic analysis	
ES/PNET family; PNET	Occasional rosettes; small unipolar cytoplasmic processes; moderate pleomorphism	IC: CD99, NSE, chromogranin EM Cytogenetic analysis	
Alveolar rhabdomyosarcoma	Rounded, pear-shaped or triangular myoblast-like cells; eosinophilic cytoplasm; occasionally multinucleated giant cells with numerous small nuclei	IC: desmin, MyoD1 EM Cytogenetic analysis	
Desmoplastic small round cell tumour	Dispersed cells and loosely cohesive clusters; scant cytoplasm; inconspicuous nucleoli; occasionally stromal fibroblasts	IC: cytokeratin, desmin, NSE Cytogenetic analysis	Predominantly abdominal tumour
Poorly differentiated areas in synovial sarcoma	Mixture of cell-tight irregular, three-dimensional tissue fragments and dispersed cells with stripped nuclei; vessel network in fragments; preserved cells small with rounded ES-like nuclei	IC: EMA, cytokeratin, CD99 EM Cytogenetic analysis	
<i>Pitfalls</i> Small cell carcinoma		IC: cytokeratin	
Lymphoblastic lymphoma		IC: CD3, CD79a; CD10, Tdt	
Small cell melanoma		IC: S-100, HMB45, Melan A	

**Table 10.** Cytological evaluation of soft tissue tumours based on pattern: epithelioid cell pattern

Tumour	Diagnostically important features	Ancillary tests	Notes
Granular cell tumour	Stripped nuclei and granular background; abundant cytoplasm, indistinct cytoplasmic borders; granulated cytoplasm; predominantly small nuclei	IC: S-100, NSE EM	
Adult rhabdomyoma	Abundant eosinophilic, granulated cytoplasm; cytoplasmic vacuolation; small nuclei with prominent nucleoli	IC: desmin, myoglobin	
Paraganglioma	Acinar/follicle-like structures; moderate pleomorphism; red-granulated cytoplasm	IC: NSE, chromogranin EM	
Epithelioid sarcoma	Rounded, polygonal, spindly tumour cells; large nucleoli; admixture of lymphocytes, plasma cells, histiocytes, granuloma-like structures; necrosis	IC: cytokeratin, EMA, CD34	Ulceration may be seen in subcutaneous tumours; inflammatory cells may predominate
Clear cell sarcoma	Predominantly dispersed cells; round, polygonal tumour cells; rounded nuclei with prominent nucleoli	IC: S-100, HMB45, Melan A	
Alveolar soft part sarcoma	Moderately abundant granular cytoplasm; binucleated, multinucleated cells; rounded nuclei with prominent nucleoli; stripped nuclei	IC: muscle specific actin, SMA, desmin EM	
Malignant extrarenal rhabdoid tumour	Variable cellular shape; eccentric nuclei; prominent nucleoli; cytoplasmic paranuclear inclusions	IC: cytokeratin, NSE	
<i>Pitfalls</i> Malignant melanoma		IC: HMB45, Melan A	Site of tumour important versus clear cell sarcoma
Carcinoma		IC: cytokeratins EM	

neuroblastoma, pure round cell liposarcoma, most monophasic synovial sarcoma and desmoplastic small round cell malignant tumour. The main diagnostic pitfalls are small cell carcinoma, non-Hodgkin's lymphoma and small cell malignant melanoma (table 9).

### Epithelioid Cell Pattern

The epithelioid cell pattern is created by cells with epithelioid features: rounded or polygonal cells with distinct cytoplasmic borders, rather abundant cytoplasm, and rounded, ovoid or irregular nuclei. Nucleoli are often prominent. The tumour cells are arranged in groups, tight clusters or are

dissociated. Stripped nuclei are a common finding. Most tumours in this group are rare and infrequent targets for needling. Typical examples of benign tumours are granular cell tumour, adult rhabdomyoma and paraganglioma and among the sarcomas epithelioid sarcoma, clear cell sarcoma, alveolar soft part sarcoma, malignant rhabdoid tumour and epithelioid cell GIST. Diagnostic pitfalls include carcinoma and malignant melanoma (table 10).

It is not possible to classify all soft tissue tumours into these five groups. In most benign adipose tumours large fat cells predominate and vascular tumours may appear as examples of either the pleomorphic pattern, the spindle cell pattern or the epithelioid cell pattern.