Paraspinal mesenchymal tumors: the overlap between neuropathology and soft tissue pathology

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Abstract

Mesenchymal/soft tissue tumours represent a broad spectrum of lesions, ranging from benign processes to malignant sarcomas. Presenting at virtually any anatomic site, they are encountered in the surgical pathology workload of all histopathologists. The diagnosis can be substantially challenging, especially in small biopsy specimen, and require integration of morphology, clinical data, and ancillary studies. Herein, we review the most common mesenchymal/soft tissue tumours encountered in the central nervous system with particular focus on the paraspinal region, highlighting key points to help the general pathologists approaching such cases, and describing how to distinguish these lesions from potential mimics. In this article we broadly divide the discussed entities into four major categories, primarily based on their morphologic patterns: small round blue cell tumours, non-neural spindle cell tumours, vascular lesions and other (to include chordomas and chondrosarcoma).

Keywords alveolar; anastomosing haemangioma; angiosarcoma; chondrosarcoma; chordoma; desmoplastic small round cell tumour; embryonal; Ewing sarcoma; hemangioendothelioma; neuroblastic tumours; paraspinal tumours; rhabdomyosarcoma; solitary fibrous tumour; synovial sarcoma

Introduction

Spinal tumours are a diverse collection of neoplasms that often cross the subspeciality comfort zones of neuropathology and soft tissue pathology. A paraspinal tumour includes any soft tissue mass involving the paraspinal space, defined anatomically as the zone extending from the intraspinal region to the paravertebral soft tissue. Primary spinal tumours may arise from the spinal cord, the surrounding leptomeninges, or the extradural soft tissues and bony structures. Primary tumours of the spine are uncommon and represent <5% of all bone neoplasms when compared with secondary metastatic disease, multiple myeloma, and lymphoma.[1] Often involving major nerve roots, these lesions can present acutely with neurologic symptoms and even cord compression. Pathologists often see these lesions at the time of intraoperative frozen section, making familiarity with the differential diagnoses and morphologic characteristics of the wide array of lesions that present in the region of utmost importance. In a review of spinal cord compression due to malignancy in the paediatric population, the majority of tumours were extradural (71%); 54% of which were soft tissue sarcomas and neuroblastoma.[2] The majority of intradural tumours were outside the spinal cord (75% representing metastatic medulloblastoma). In contrast, epithelial tumours (i.e. metastatic carcinoma) far outnumber mesenchymal tumours as the most frequent malignant paraspinal tumours in the adult population.

Practical approach to mesenchymal tumours: primary mesenchymal tumours of the central nervous system (CNS) are rare and most commonly arise in the meninges or secondarily involve the CNS through direct extension, rather than involve CNS parenchyma. Other than lipomatous lesions and vascular lesions, the radiographic appearance of these lesions is non-specific, further underscoring the importance of recognizing the entities histologically. Establishing a diagnosis of a mesenchymal tumour is challenging; while many lesions represent true neoplasms, a bewildering array of pseudoneoplastic proliferations are frequently encountered as well. Adding to the challenge, a variety of different non-mesenchymal neoplasms may mimic sarcoma, in particular sarcomatoid carcinoma and melanoma. With the exception of tumours encountered in children, the most common malignancy involving the paraspinal region in the >40 year age group will represent metastatic carcinoma. Therefore, it is prudent to exclude epithelial neoplasms before making a diagnosis of a mesenchymal tumour. Essential clinical information for the pathologist includes the patient's age, sex, and site, size and duration of the tumour, as well as knowledge of previous therapy. Ancillary studies are often essential in diagnosis and triaging fresh tissue at the time of biopsy or resection is highly recommended. Current practice at many institutions includes submitting a portion of tumour fresh for cytogenetic analysis, snap freezing a portion for molecular studies and preparing unstained touch imprints for possible fluorescence *in situ* hybridization (FISH) analysis.

A systematic, histologic pattern approach to mesenchymal tumours is best. We recommend initial review of the lesion to determine its growth pattern(s), cellular composition and the presence or absence of matrix. When possible, it is helpful to morphologically classify the lesion based on cellular morphology into four major categories: round cell, spindle cell (to include some pleomorphic patterns), vascular and other (Table 1). A panel of immunohistochemical stains such as CD99, FLI-1, keratin, neuroendocrine markers chromogranin and synaptophysin, S100, desmin, smooth muscle actin (SMA), epithelial membrane antigen (EMA), and leucocyte common antigen (LCA) can be helpful as an initial immunohistochemical approach to determine lineage of differentiation (Table 2).

As with primary tumours of the CNS, many mesenchymal tumours are defined according to their characteristic cytogenetic or molecular alterations, so ancillary studies such as FISH or RT-PCR analysis, performed on fresh or paraffin-embedded, formalin-fixed tissue, are necessary to confirm diagnoses in many instances.

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Morphologic approach to paraspinal soft tissue tumours

Category	Entities discussed
Small round blue cell tumours	Ewing Family of tumours, rhabomyosarcoma, neuroblastic tumours, desmoplastic small round cell tumour, angiomatoid fibrous histiocytoma
Non-neural spindle cell tumours[a]	Solitary fibrous tumour/hemangiopericytoma, synovial sarcoma, peripheral nerve sheath tumours
Vascular lesions	Haemangioma, anastomosing haemangioma, epithelioid hemangioendothelioma, angiosarcoma
Other	Chordoma, chondrosarcoma

[a] Peripheral nerve sheath tumours discussed in a separate review.

Table 1

Small round blue tumours

Small round blue cell tumours encompass a group of tumours with overlapping morphologic and immunohistochemical features. Distinguishing different sarcoma types requires clinical correlation along with ancillary diagnostic tests, most often immunohistochemistry and FISH. This article reviews the most commonly encountered in the central nervous system and paraspinal region.

Ewing Family of tumours

Ewing Family of tumours (EFT) is a distinctive round cell sarcoma that occurs in bone as well as in soft tissue.[3] They typically affect children and young adults, with a male predilection. They are driven by a chimeric fusion gene involving *EWSR1* and *ETS* gene family (Table 3). Ewing Sarcoma-like (ES-like) is a term that has been used to describe two groups of tumours: 1) with *EWSR1* rearrangement and a fusion partner other than an *ETS* family. 2) morphologically resembling Ewing Sarcoma (ES) but without *EWRS1* gene rearrangement.[3]

Pathologic features: typically, ES has a lobulated gross appearance (Figure 1a), with a variable degree of necrosis. Regional areas of cystic changes and haemorrhage may be present. On histologic examination, ES is characterized by monotonous cells with uniform, round nuclei, fine chromatin, inconspicuous nucleoli, scant clear to eosinophilic cytoplasm and indistinct cell borders (Figure 1b). The cytoplasm of tumour cells often contains PAS-positive glycogen. Mitosis, necrosis and apoptotic bodies are frequently seen. Rosettes, lobular architecture, metaplastic bone and cartilage may be present. Typically tumour cells are diffusely and strongly positive for CD99, with distinctive membranous expression (Figure 1c). Other immunohistochemical stains such as FLI-1, epithelial markers (20%), occasional desmin, S100, and synaptophysin can be positive. ES-like sarcomas share morphological features of ES and can express diffuse CD99 membranous staining, but exhibit atypical nuclear morphology, including prominent nucleoli. NKX2-2 immunostaining can be helpful to distinguish ES from its mimics.[4] The definitive feature of ES is the presence of *EWSR1* gene fusion and FISH for *EWRS1* on touch imprint or paraffin-fixed tissue is important to confirm the diagnosis. Importantly, *EWRS1* gene rearrangement is not specific for ES and can be seen in other tumours; therefore, it is important to interpret the tumours in context of clinical, morphological and immunohistochemical features as a whole.

Prognosis: the prognosis of ES has improved with developing therapeutic options. The key prognostic factor in ES is the presence or absence of metastases. The approximate five-year survival rate for patients with localized disease is 70%, while they average 33% for those who have overt metastases at diagnosis. Patients presenting with primary axial tumours (i.e., pelvis, rib,

Molecular abnormalities in classical Ewing sarcoma

Chromosomal rearrangement	Fusion gene	Frequency
EWS-ETS fusions		
t(11;22)(q24;q12)	EWSR1-FLI1	85
t(21;22)(q12;q12)	EWSR1-ERG	10
t(7;22)(p22;q12)	EWRS1-ETV1	<1
t(17;22)(q12;q12)	EWRS1-ETV4	<1
t(2;22)(q23;q12)	EWRS1-FEV	<1
TET-ETS fusion		
t(16;21)(p11;q22)	FUS-ERG	<1
t(2;6)(q35;p11)	FUS-FEV	<1

Table 3

Small round blue cell tumour immunohistochemical screening panel

Antibody	ES	RMS	DSRCT	Neuroblastoma	AFH	Lymphoma
CD99	+	Variable	Variable	−	Variable	Variable
Keratin	Variable	−	+	−	−	−
Desmin	Variable	+	+	−	Variable	−
CD45/TdT	−	−	−	−	−	+/−
Synaptophysin	Variable	−	−	+	−	−

Table 2

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