

**Original contribution** 

# Human PATHOLOGY

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# Paraspinal pseudoneoplasms: a series of 58 consultation cases emphasizing the importance of pathology-radiology correlation<sup>☆</sup>

John M. Gross MD<sup>a</sup>, Stephen M. Broski MD<sup>b</sup>, Benjamin M. Howe MD<sup>b</sup>, Andrew L. Folpe MD<sup>a,\*</sup>

<sup>a</sup> Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, 99505, USA <sup>b</sup> Department of Radiology, Mayo Clinic, Rochester, MN, 99505, USA

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#### **Keywords:**

Herniated disc; Intervertebral disc histology; Paraspinal pseudoneoplasm; Synovial cyst; Compression fracture; Pathology—radiology correlation Summary A variety of non-neoplastic diseases of the spine, including herniated/sequestered intervertebral discs, synovial cysts, and degenerative or post-traumatic changes, may present as mass lesions. Over the past several years, we have seen a large number of such paraspinal pseudoneoplasms in consultation, referred out of concern for malignancy on the part of the clinician, pathologist, or both. Herein, we report our experience with these specimens, emphasizing the clinical, radiologic, and histopathological features that allow their confident distinction from various mesenchymal tumors. Fiftyeight cases were identified within our consultation archives, referred in consultation to exclude malignancy and diagnosed as non-neoplastic disease involving the intervertebral disc, ligamentum flavum, or paraspinal soft tissues (2006–2019). Available radiologic studies were reviewed by 2 musculoskeletal radiologists. The histologic features of all cases were re-evaluated. Available clinical records were reviewed. The masses occurred in adults (median age 62 years, range 20-86 years) with a male predominance (35 males and 23 females). Sites included lumbar spine (N = 33), thoracic spine (N = 15), cervical spine (N = 6), paraspinal region (N = 3), and sacral spine (N = 1). In 44 cases (76%), the referring pathologist regarded the specimen as representing a benign or malignant neoplasm, either primary or metastatic. Fifteen cases (26%) were sent for second opinion at the request of the treating clinician, following an initial malignant diagnosis. Advanced imaging studies were available for rereview in 37 cases (64%) and showed herniated/extruded disc (N = 17), compression fracture (N = 9), synovial cyst (N = 8), and degenerative joint disease (N = 7). Multiple radiologic findings were seen in 9 patients. Histologically, the specimens showed a spectrum of often florid reactive changes involving degenerating disc material, ligamentum flavum, and bone. Awareness that nonneoplastic spinal processes may form pseudoneoplastic mass lesions, and careful clinical-radiologicpathologic correlation should allow their confident distinction from potential morphologic mimics. © 2020 Elsevier Inc. All rights reserved.

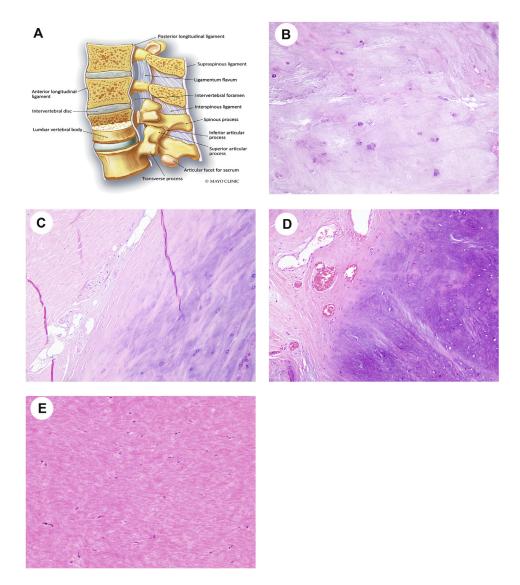
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\* Corresponding author. Division of Laboratory Medicine, Mayo Clinic, 200 1st St, Rochester, MN, USA. *E-mail address:* folpe.andrew@mayo.edu (A.L. Folpe).

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# 1. Introduction

Non-neoplastic disorders of the spine and paraspinal soft tissues are common, especially in older adults, and include changes related to degenerative arthritis, intervertebral disc-related problems such as herniated or sequestered discs, post-traumatic lesions including fracture, and facet joint-associated conditions such as synovial cyst. In most instances, these various spinal and paraspinal conditions are readily recognized by the astute clinician and radiologist and thus do not come to the attention of surgical pathologists. However, on occasion, these disorders may present as mass lesions mimicking neoplasms and undergo biopsy or excision with pathological evaluation. Over the past several years, we have seen in consultation a considerable number of such paraspinal pseudoneoplasms, referred out of concern for malignancy on the part of the clinician, pathologist, or both. Anecdotally, our impression has been that a significant percentage of these cases were sent in consultation either because of a lack of clinical-radiologic-pathologic correlation at the referring institution, lack of familiarity by pathologists with the normal histology of the intervertebral discs and paraspinal ligaments, or both (Fig. 1). Although most pathologists are well aware of the importance of pathologic-radiologic correlation in the diagnosis of bone tumors, this seems to be less emphasized for paraspinal lesions. Furthermore, although the orthopedic and radiology literature is replete



**Fig. 1** The anatomy of the vertebral column is complex. Tissues from this region that may come to the attention of the surgical pathologist include the intervertebral disk, the facet joint, bone, and various ligaments, including the ligamentum flavum (A). Normal components of the intervertebral disc include the nucleus pulposus (B), the annulus fibrosum (C), and the cartilaginous end-plate (D). The ligamentum flavum is notably hypocellular and has a distinctive, somewhat lamellar architecture (E).

Table

Case number Sex       Age/ Site suggested diagnosis       Contributors' suggested cartilaginous proliferation"       Final diagnosis after radiology- pathology correlation       Case number         1       72 F Lumbar       "Atypical cartilaginous proliferation"       Disc with reactive changes       21         2       53 M Thoracic       "Epidural tumor"       Spinal ligament and disc with reactive changes       22         3       83 F Lumbar       Not given       Compression fracture       23         4       86 M Thoracic       "Spindl cell meoplasm"       Disc with reactive changes       24         5       57 M Lumbar       Chondrosarcoma meoplasm"       Herniated disc with fracture       24         6       56 M Lumbar       Chondrosarcoma meoplasm"       Compression fracture       25         8       47 M Lumbar       Chondrosarcoma meoplasm"       Compression fracture       27         9       73 F Lumbar       "Chondroid meoplasm"       Ternited disc meoplasm"       28         10       51 M Thoracic       "Chondroid meoplasm"       Spinal ligament and disc with reactive changes       29         11       51 M Thoracic       "Chondroid meoplasm"       Spinal ligament and disc with reactive changes       30         12       41 F Cervical       Metastatic meoplasm"       Spinal ligamen	Table	Studi	ed cases, v	with referral and fin	nal diagnoses.	Table	(ca
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<ul> <li>47 M Lumbar Chondrosarcoma Compression fracture 27</li> <li>73 F Lumbar "Chondroid neoplasm" with florid reactive changes</li> <li>51 M Cervical "Chondroid spinal ligament and disc with neoplasm" and disc with reactive changes</li> <li>51 M Thoracic "Chondroid Herniated disc neoplasm" 30</li> <li>12 41 F Cervical Metastatic carcinoma and disc with reactive changes</li> <li>13 55 F Lumbar "Chondroid Herniated disc 32</li> <li>14 62 F Thoracic "Chondroid neoplasm" into compression fracture</li> <li>15 59 F Lumbar Chondroid Herniated disc 33</li> <li>14 62 F Thoracic "Chondroid Herniated disc 34</li> <li>15 59 F Lumbar Chondroid Herniated disc 34</li> <li>16 20 M Lumbar Osteoblastoma vs with florid reactive changes</li> <li>16 20 M Lumbar Osteoblastoma vs Facet joint metastasis</li> <li>17 59 F Lumbar "Sarcoma" Herniated disc 36</li> <li>17 59 F Lumbar "Chondro- osseous lesion; rule out malignancy"</li> <li>19 74 F Lumbar Discitis vs osteonyelitis vs Disc with reactive changes</li> <li>30</li> </ul>				osseous lesion"	ligament with	25	8
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Table (	contini	ued)		
Case number	Age/ Sex	Site	Contributors' suggested diagnosis	Final diagnosis after radiology- pathology correlation
21	73 F	Lumbar	and fracture; rule out malignancy" Chondrosarcoma	into compression fracture Synovial cyst, spinal ligament, and disc with reactive changes
22	67 M	Thoracic	Pigmented villonodular synovitis vs meningioma vs vascular tumor	Synovial cyst, spinal ligament, and disc with reactive changes
23	86 M	Thoracic	Not given	Compression fracture
24	69 F	Cervical	"Spindle cell neoplasm"	Spinal ligament and disc with reactive changes
25	84 M	Thoracic	Chondrosarcoma	Compression
26	69 F	Lumbar	"Chondroid neoplasm"	Compression fracture
27	47 M	Thoracic	Osteoid osteoma vs osteoblastoma	Bone, spinal ligament, and disc with reactive changes
28	70 M	Lumbar	"Epidural mass"	Disc with reactive
29	69 F	Paraspinal	"Chondroid neoplasm"	changes Herniated disc
30 31		Paraspinal Paraspinal	Chordoma Myxoma vs myxoid chondroma	Herniated disc Herniated disc
32	62 M	Lumbar	Chordoma vs chondroma	Herniated disc
33	83 M	Thoracic	"Spindle cell neoplasm"	Compression fracture
34	31 M	Cervical	Phosphaturic mesenchymal tumor	Compression fracture
35	46 M	Thoracic	Fibrosarcoma vs fibromatosis	Spinal ligament and disc with reactive changes
36	46 F	Lumbar	"Benign degenerative fibrocartilage"	Disc with reactive changes
37	60 F	Lumbar	"Extradural mass"	Herniated disc
38	47 M	Lumbar	"Giant cell rich neoplasm within synovial cyst"	Pseudocyst involving spinal ligament and disc with reactive changes
39	51 M	Thoracic	Not given	Herniated disc and synovial cyst

41 42 43	72 F 75 M 63 F	Lumbar Lumbar Cervical Thoracic Lumbar	Chordoma Osteomyelitis vs fracture Hemangioma vs aneurysmal bone cyst "Epidural mass" Chordoma vs extraskeletal	Herniated disc with florid reactive changes Discitis Discitis Herniated disc Herniated disc
42 ·	75 M 63 F	Cervical Thoracic	fracture Hemangioma vs aneurysmal bone cyst "Epidural mass" Chordoma vs	Discitis Discitis Herniated disc
43	63 F	Thoracic	aneurysmal bone cyst "Epidural mass" Chordoma vs	Herniated disc
			Chordoma vs	
44 ·	44 M	Lumbar	Chordoma vs	Herniated disc
			myxoid chondrosarcoma vs chondrosarcoma	with reactive changes including cyst formation
45	54 M	Lumbar	"Atypical cartilaginous proliferation"	Herniated disc
46	52 F	Lumbar	Not given	Synovial cyst
47	72 M	Thoracic	Chondrosarcoma	Disc with reactive changes
		Cervical	"Cannot exclude neoplasm"	Disc with reactive changes
49	60 M	Lumbar	"Nerve sheath tumor"	Herniated and sequestered disc with florid reactive changes
50	38 F	Lumbar	Giant cell tumor of bone	Disc with reactive changes
51	78 F	Thoracic	Metastatic carcinoma	Compression fracture
52	51 F	Lumbar	"Intraspinal extradural mass"	Herniated disc and synovial cyst
53	65 M	Lumbar	"Benign cystic lesion"	Herniated disc and synovial cyst with florid reactive changes
54	76 M	Lumbar	"Atypical myxoid lesion with giant cells"	Herniated disc
55	80 M	Lumbar	"Cannot exclude neoplasm"	Herniated disc
56	73 M	Lumbar	Chondrosarcoma	Herniated disc into compression fracture
57	70 M	Lumbar	Chondrosarcoma	
58	75 M	Lumbar	Not given	Herniated disc

with reports of non-neoplastic paraspinal lesions mimicking tumors, information on this subject in the pathology literature is quite sparse.

Herein, we review our experience with paraspinal pseudoneoplasms sent in consultation, emphasizing the critical importance of careful clinical-radiologic-pathologic correlation, and familiarity with the morphology of this region, in their distinction from potentially more ominous mesenchymal neoplasms.

# 2. Materials and methods

The approval for this study was granted by the Mayo Clinic Institutional Review Board. The consultation archives of the senior author (A.L.F.) were searched for nonneoplastic cases coded as "herniated intervertebral disc", "spinal", or "paraspinal" for the period 2006-2019, yielding 83 cases. These cases comprised approximately 17% of the roughly 500 vertebral or paraspinal consultation cases seen during this time period. On re-review, 25 cases were excluded either for insufficient material or because pathologic-radiologic correlation strongly suggested a nondiagnostic biopsy or sampling error, leaving a final study population of 58 cases. Demographic and clinical information was obtained from the contributing pathologist or clinician. All available slides were re-reviewed (J.M.G, A.L.F) and relevant radiologic imaging studies were rereviewed by two experienced musculoskeletal radiologists (B.M.H, S.M.B). Contributors' suggested diagnoses were recorded, when available.

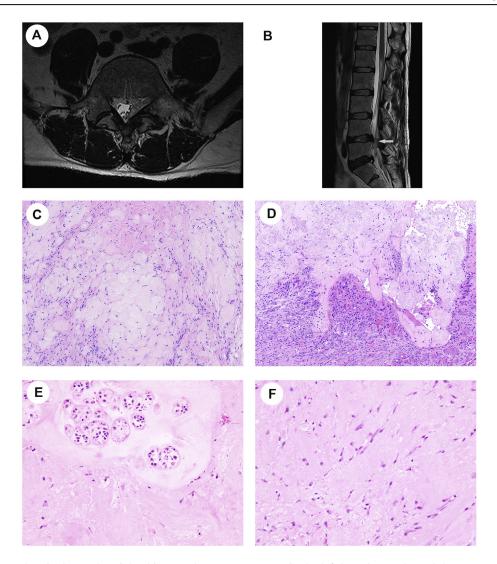
# 3. Results

Table summarizes the clinicopathologic and radiologic findings and submitting diagnoses for the 58 studied cases.

### 3.1. Clinical features and suggested diagnoses

The masses occurred in 35 males and 23 females (M: F = 3:2), ranging from 20 to 86 years of age (median: 62 years of age; males 60 years, females 63 years). Sites included lumbar spine (N = 38), thoracic spine (N = 11), cervical spine (N = 6), psoas region (N = 2), and sacral spine (N = 1). Thoracic lesions were more common in males (M:F = 12 cases:3 cases); no differences were noted in cervical (M:F = 3 cases:3 cases), lumbar (M:F = 18 cases: 15 cases), sacral (M:F = 1 case: 0 cases), or "paraspinal" (M:F = 1 case: 2 cases) locations.

In 44 cases (76%), the specimens had been submitted to the original pathologist with a clinical impression of "neoplasm", "tumor", "mass", or "lesion". Fifty-three cases (91%) were submitted with a contributor diagnosis or impression, including cartilaginous tumor (N = 20), "spindle cell neoplasm" (N = 4), giant cell tumor of bone (N = 4), chordoma (N = 5), myxoid neoplasm (N = 3),



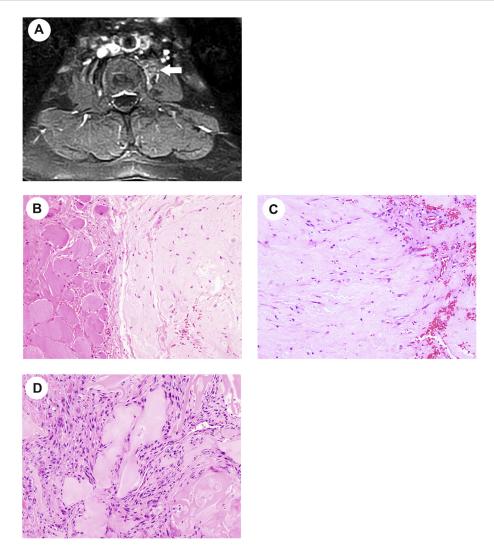
**Fig. 2** Axial (A) and sagittal (B) T2-weighted images demonstrate a mass in the left lateral central canal that causes mass effect on the thecal sac (arrows). There is an L5-S1 disc annular tear (B, arrowhead) with decrease in the nucleus pulposus signal. Findings are consistent with a posteriorly extruded disc fragment. Herniated intervertebral disc, consisting of small islands of hyalinized, degenerating nucleus pulposus, scattered viable chondrocytes within lacunae, and proliferating small capillaries (C). At the periphery, degenerating disc fragments may evoke a highly cellular capillary and myofibroblastic proliferation, simulating chondromyxoid fibroma or even dedifferentiated chondrosarcoma (D). Reactive cartilage within degenerating disc showing chondrocyte clustering and containing many chondrocytes within individual lacunae, a feature easily misinterpreted as representing the hypercellularity and bi-nucleation seen in chondrosarcoma (E). Myxoid change within a degenerating disc may simulate the "cord and chain" patterns of myxoid chondrosarcoma or chordoma (F).

vascular neoplasm (N = 2), metastatic carcinoma (N = 2), osteogenic neoplasm (N = 2), and others. In 15 instances (26%), the specimen was sent for second opinion at the request of the treating clinician, after a malignant diagnosis had been rendered by the original pathologist.

Immunohistochemical studies for various markers, including keratins, S100 protein, glial fibrillary acidic protein, smooth muscle actins, epithelial membrane antigen, CD31, and CD34 had been performed in an ad-hoc fashion at the referring institutions in 17 (30%) cases; in some cases, numerous immunostains were performed.

#### 3.2. Radiologic findings

In almost all instances, available radiologic studies had been previously reviewed by Mayo Clinic musculoskeletal radiologists as part of the original consultation, although a detailed description of the radiologic findings was generally not included in the final pathology report. Advanced imaging studies (magnetic resonance imaging [MRI] and computed tomography) were available for re-review in 37 cases (64%). Imaging findings were consistent with a herniated/extruded disc (N = 15), compression fracture



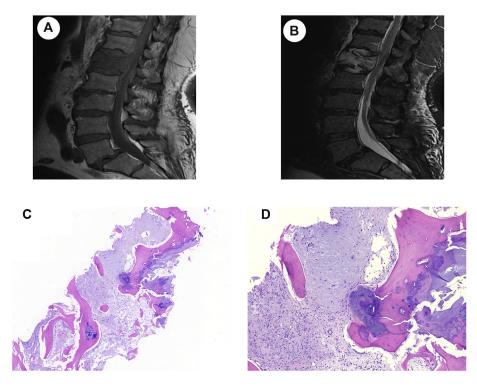
**Fig. 3** Axial T1-weighted, postcontrast MRI (A) demonstrates a heterogeneously enhancing left paraspinal mass associated with the psoas muscle (arrow), found to be a lateral disc herniation. Extreme lateral disc herniation, with extrusion of disc material into adjacent skeletal muscle, simulating chondrosarcoma (B). Florid capillary ingrowth into herniated discs may simulate angiosarcoma, although close inspection discloses well-formed vessels without endothelial atypia (C). "End-stage" herniated disc, with minute islands of hyalinized nucleus pulposus surrounded by capillaries and myofibroblasts (D). MRI, magnetic resonance imaging.

(N = 10), synovial cyst (N = 8), intervertebral disc "bulge" (N = 5), and degenerative facet joint disease (N = 4). Multiple findings were present for 9 patients (eg herniated disc with associated fracture). The imaging features of posterior disc herniation, lateral disc herniation, disc material extruded into a vertebral body, synovial cyst, and compression fracture are illustrated in Figs. 2A and B, 3A, 4A and B, 5A, and 6A, respectively.

## 3.3. Pathologic findings

The great majority of submitted cases (53/58, 91%) consisted at least in part of intervertebral disc material, typically showing a variety of reactive changes, including capillary proliferation (sometime florid), "fasciitis-like"

zones of mitotically active myofibroblastic ingrowth, myxoid stromal change, chondrocyte clustering, chondrocyte nuclear enlargement, and the presence of lacunae containing more than a single chondrocyte (often misinterpreted as representing bi-nucleated chondrocytes) (Figs. 2C-F, 3B-D, 4C and D). As noted in Table, these vascular, myofibroblastic, and cartilaginous reactive changes often raised concern for an endothelial, spindle cell, or cartilaginous tumor, respectively. In some instances, relatively normal intervertebral disc was misinterpreted as representing a myxoid or cartilaginous neoplasm, presumably reflecting lack of familiarity with the normal histology of this tissue. Three cases of herniated disc showed "extreme" lateral herniation, with extension of disc material into the psoas muscle and



**Fig. 4** Sagittal T1 (A) and STIR (B) images of the lumbar spine demonstrate a fracture of the L1 vertebra. Intervertebral disc material can be seen extruding through the fracture into the vertebral body. When herniated disc material is extruded into vertebral bone, it can closely simulate the permeative growth pattern seen in chondrosarcoma (C). Higher-power magnification, however, shows typical features of herniated disc, with areas of relatively normal, myxoid nucleus pulposus juxtaposed to hyalinized islands of degenerating disc material and reactive stromal cells (D).

paraspinal musculature, simulating muscle invasion by a cartilaginous neoplasm (Fig. 3B). The presence of extruded disc material within bone was typically misinterpreted as representing permeative growth of a chondrosarcoma (Fig. 4C and D).

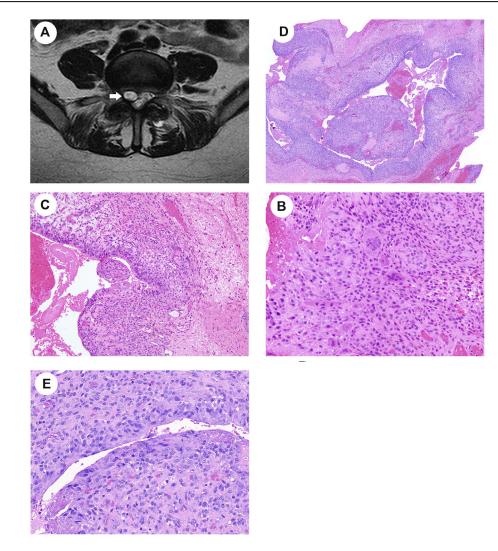
The morphologic features of 8 cases radiologically interpreted as representing "synovial cysts" included exuberant myofibroblastic and capillary proliferation, osteoclastic giant cells, dystrophic calcification, and rarely pseudocyst formation with synovial metaplasia of the lining (Fig. 5B-E). In cases of disc disease and/or synovial cyst with associated compression fracture, cellular and mitotically active osteocartilaginous matrix (fracture callus) was usually present, raising the possineoplasms bility of various matrix-producing (Fig. 6B-D). Close inspection of these foci, however, revealed reassuring features, such as "maturation" and absent hyperchromatism or atypical mitotic activity. Finally, in some instances, tissue derived from the ligamentum flavum was confused with a necrotic spindle cell malignancy, owing to its unusual hypocellular, lamellar, collagenous appearance, or with some sort of calcifying neoplasm (Fig. 7A and B).

As none of the studied cases contained a discrete neoplastic population, all of the submitted immunohistochemical studies were considered to be noncontributory.

# 4. Discussion

The results of the present study suggest that the diagnosis of paraspinal pseudoneoplasms represents an ongoing challenge for many pathologists. We believe that these difficulties are largely because of (1) lack of familiarity with the normal histology and histopathology of this anatomical region, (2) limited appreciation of the necessity for pathology-radiology correlation in the diagnosis of paraspinal masses, with poor interdisciplinary communication, and (3) general unease with the distinction of reactive processes involving paraspinal tissues from potential neoplastic mimics.

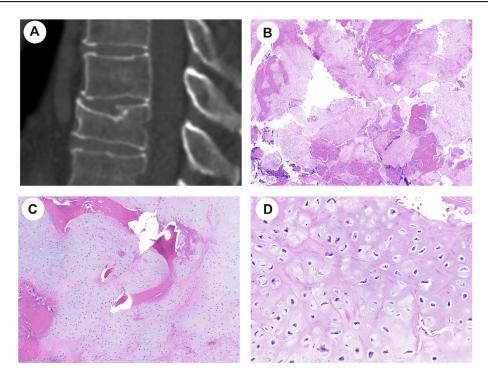
The spine and paraspinal region is remarkably complex and is composed of various bones, joints, intervertebral discs, articular surfaces, spinal ligaments, and surrounding soft tissues, including fat, fibrous tissue, nerves, and vessels. The microanatomy of the intervertebral discs is similarly complex, with 3 distinct, interdependent specialized structures: the central viscous nucleus pulposus, the outer fibrillar annulus fibrosus, and the cartilaginous end plates, a 1-mm-thick layer of cartilage that anchors the disc to the adjacent vertebral bodies superiorly and inferiorly. The nucleus pulposus, the cushioning core of the adult intervertebral disc, is derived from the notochord, whereas the annulus fibrosis, which provides the structural



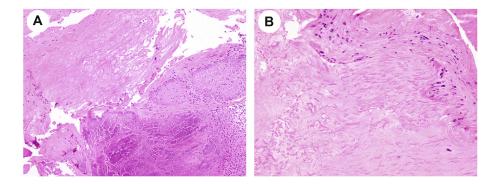
**Fig. 5** Axial T2-weighted image of the lumbar spine (A) demonstrates an extradural mass along the right lateral central canal with a peripheral T2 hypointense rim immediately adjacent to the right L4-L5 facet joint (arrow), consistent with a facet joint synovial cyst. Low-power view of facet joint synovial cyst (B). This particular example contains a well-defined layer of synovial cells, overlying a granulation tissue stroma. A synovial lining is not typically present in tissues removed from radiologic ally classical synovial cysts (C). Cellular, osteoclast-rich areas within synovial cysts may simulate giant cell tumor of bone or aneurysmal bone cyst (D). Mitotic activity is frequently present, as well (E).

properties of the disc, is derived from ventral sclerotome, which also gives rise to the vertebral bodies [1]. The annulus fibrosus firmly binds the vertebral bodies together and also keeps the nucleus pulposus under constant pressure [2]. In humans, the adult intervertebral disc is the largest avascular tissue in the body and therefore dependent on the cartilaginous end-plate for nutrient exchange via passive diffusion from the highly vascularized vertebral bodies [3]. With advancing age, the cartilaginous end-plate becomes calcified, and the bony interface becomes sclerotic, leading to decreased nutrient delivery, weakness, and degeneration of the disc [4,5]. In this setting, small tears in the annulus fibrosus or cartilaginous end-plate may develop with subsequent extrusion of disc material, neovascularization, granulation tissue formation, and myofibroblastic proliferation, all of which contribute to formation of a pseudoneoplastic, clinically appreciable mass [6-9].

Disc herniation is generally defined as displacement of a still-attached disc beyond its normal anatomic confines, whereas disc sequestration refers to complete separation of the disc and migration into surrounding tissues [6]. Most herniated/sequestered discs extrude through small defects in the annulus fibrosis in lateral or posterolateral directions (because of the strength of the anterior longitudinal ligament) or cranial-caudally through the endplates [6,10,11]. So-called "Schmorl nodes", which may mimic a cartilaginous neoplasm, represent herniation of



**Fig. 6** Sagittal-reformatted CT image of the lower thoracic spine (A) demonstrates a moderate compression fracture of the T10 vertebral body. Fracture callus, removed during repair of a vertebral compression fracture. In the absence of clinical history and radiologic correlation, the cellular osteocartilaginous proliferation that characterizes fracture callus in any location may raise concern for osteosarcoma (B). Fracture callus may also extend within pre-existing bone, simulating chondrosarcoma (C). Out of context, the relatively high cellularity and nuclear enlargement seen in fracture callus may be alarming (D). CT, computed tomography.



**Fig. 7** Tissue from the ligamentum flavum is often present in surgical specimens received for disc disease, compression fractures, or synovial cysts. The unusual pattern of dystrophic calcification seen in this example suggested the possibility of a phosphaturic mesenchymal tumor to the referring pathologist (A). The hypocellular, lamellar appearance of the ligamentum flavum is sometimes confused with a spindle cell neoplasm showing "bland necrosis", particularly when more cellular, reactive foci are present at the periphery (B).

the nucleus pulposus through the cartilaginous end-plate into the body of the vertebra [12,13]. Herniated/sequestered discs may extend for a considerable distance laterally, as exemplified by the 3 cases in this series that presented as masses in the psoas muscle and paraspinal musculature. "Extreme" lateral disc herniations most often involve the L3/4 and L4/5 interspaces, have been estimated to represent roughly 10% of all lumbar disc herniations [14], and are often confused clinically with a paraspinal nerve sheath tumor or retroperitoneal sarcoma [14,15].

Synovial cysts are also relatively common paraspinal pseudoneoplasms, as evidenced by the 8 cases included in this series. Lumbar intraspinal synovial cysts originate from the zygoapophaseal joint capsule and most commonly occur at the L4/5 level and to a lesser extent at L3/L4 and L5/S1 [16]. These lesions most likely arise secondary to facet joint degeneration, typically in a

background of more generalized osteoarthritis [17]. In our experience, histologic evaluation of lumbar synovial cysts with classic radiologic features seldom discloses true synovium, showing instead a variety of florid nonspecific stromal changes, most notably myofibroblastic and capillary proliferation. Occasional cases show pseudocyst formation, sometimes with what seems to represent synovial metaplasia, rather than residual preexisting synovium. Both synovial cysts and disc herniation/extrusion can occur in association with compression fractures, which show features similar to repairing fractures at other sites, with exuberant endochondral ossification and a fasciitis-like myofibroblastic/vascular proliferation.

Although we strongly suspect that most (if not all) pathologists appreciate the critical importance of pathology-radiology correlation in the diagnosis of neoplastic and non-neoplastic disease of bone, this does not seem to be the case for paraspinal lesions, many of which are referred in consultation without radiologic studies or without evidence of multidisciplinary interaction. As hope, the present we study indicates communication between the clinician, radiologist, and pathologist is at least as crucial in the evaluation of paraspinal masses as it is in lesions of bone.

MRI is generally felt to be the best imaging modality for evaluation of the spine and its contents. Migrated disc fragments typically show low signal intensity on T1weighted and high signal on T2-weighted images [18]; contrast-enhanced MRI scans are useful to differentiate a herniated disc from a disc space infection or tumor, with peripheral enhancement usually seen around an otherwise nonenhancing disc fragment [18-22]. Unlike chondrosarcomas, herniated discs do not show destruction of bone [23]. MRI is also an excellent tool for the distinction of herniated/sequestered discs from metastases [18,24], epidural abscesses [18], nerve sheath tumors, and meningiomas [18]. In general, the presence of striking surrounding stromal edema on MRI points toward nonneoplastic processes. Facet joint synovial cysts are also well-evaluated by MRI. While some synovial cysts display simple fluid signal intensity, with homogenous low T1 and high T2 signal, others may have more complex signal, with high T1 signal secondary to hemorrhage and heterogeneous T2 signal if hemorrhage or calcification is present. However, close relationship with the facet joint, peripheral enhancement, and a peripheral T2 hypointense rim are key features that allow confident radiologic diagnosis [25] The histopathologic differential diagnosis of paraspinal pseudoneoplasms is broad and depends on the underlying process (eg disc disease, cyst, or fracture) and which reactive/degenerating element is most prominent. Awareness of the normal morphological features of the intervertebral disc and recognition of reactive/reparative features such as neovascularization and surrounding myofibroblastic proliferation should allow the distinction of disc disease from cartilaginous tumors in most instances. It should be kept in mind that extrusion of disc material into bone may closely mimic the permeative growth pattern of chondrosarcoma. Richly vascularized herniated disc material may resemble chondromyxoid fibroma, although the latter lesion is quite rare in the spine and has characteristic imaging features, with surrounding sclerosis. Herniated discs or synovial cysts with associated fracture may also mimic (chondroblastic) osteosarcoma to a degree but lack the clear-cut chromatin abnormalities, "lace-like" osteoid, and destructive growth that characterize osteosarcoma in most instances. Although osteoclastic giant cells may be present in paraspinal pseudoneoplasms, these lesions lack the sheet-like proliferation of osteoclasts and H3.3 G34W-positive mononuclear cells of giant cell tumor of bone [26-29] and the large, blood filled spaces, and USP6 rearrangements that characterize aneurysmal bone cyst [30].

Some paraspinal pseudoneoplasms in the present series were also confused with chordoma, angiosarcoma, and phosphaturic mesenchymal tumor. Chordomas generally occur in the sacrum and clivus but may rarely involve lumbar, thoracic, cervical, and extra-axial locations [31,32]. Microscopically, chordomas are characterized by a cord and chain-like proliferation of large, eosinophilic, vacuolated, keratin, and brachyury-positive cells, features not seen in herniated discs [33,34]. Close attention to the well-formed capillaries, absence of solid or sieve-like growth, and bland nuclear features of richly vascularized discs and synovial cysts should allow their confident distinction from angiosarcoma. Finally, phosphaturic mesenchymal tumors, while remarkably protean in appearance, usually contain areas of unusual, "grungy" calcified matrix produced by very bland, FGF23 CISHpositive spindled cells, features absent in potential nonneoplastic simulants [35]. On MRI, phosphaturic mesenchymal tumors are T1 isointense, T2 hyperintense, and solidly enhancing, often with areas of dark signal [36,37].

In conclusion, the results of this study suggest that paraspinal pseudoneoplasms are a relatively common cause of diagnostic confusion, most likely related to lack of familiarity with the histopathological features of this region and most critically to the absence of multidisciplinary communication. Arguably, inappropriate immunohistochemical workups and the need for second opinion delay diagnosis, add cost, and most importantly may result in considerable anxiety for patients incorrectly thought to have a tumor involving the spine and/or paraspinal soft tissues. Awareness of these pseudoneoplasms, better understanding of the morphological features of normal and diseased paraspinal tissues, and pathology-radiology correlation should allow for confident diagnosis in most instances.

# References

- Colombier P, Clouet J, Hamel O, Lescaudron L, Guicheux J. The lumbar intervertebral disc: from embryonic development to degeneration. Joint Bone Spine 2014;81:125–9.
- [2] Mixter WJ, Ayer JB. Herniation or rupture of the intervertebral disc into the spinal canal: report of thirty-four cases. N Engl J Med 1935; 213:385–93.
- [3] Urban JP, Smith S, Fairbank JC. Nutrition of the intervertebral disc. Spine 2004;29:2700–9 (Phila Pa 1976).
- [4] Keyes DC, Compere EL. The normal and pathological physiology of the nucleus pulposus of the intervertebral disc: an anatomic, clinical and experimental study. JBJS 1932;14:897.
- [5] Roberts S, Evans H, Trivedi J, Menage J. Histology and pathology of the human intervertebral disc. J Bone Jt Surg Am 2006;88(Suppl 2): 10-4.
- [6] Schellinger D, Manz HJ, Vidic B, et al. Disk fragment migration. Radiology 1990;175:831–6.
- [7] Abbrecht PH. The relationship between intervertebral disc degeneration and disc prolapse. Spine 2001;26:2400–3.
- [8] Peng B, Wu W, Hou S, Shang W, Wang X, Yang Y. The pathogenesis of Schmorl's nodes. J Bone Jt Surg Br 2003;85:879–82.
- [9] Ito T, Yamada M, Ikuta F, et al. Histologic evidence of absorption of sequestration-type herniated disc. Spine 1996;21:230–4.
- [10] Neugroschl C, Kehrli P, Gigaud M, et al. Posterior extradural migration of extruded thoracic and lumbar disc fragments: role of MRI. Neuroradiology 1999;41:630-5.
- [11] Aydin MV, Ozel S, Sen O, Erdogan B, Yildirim T. Intradural disc mimicking: a spinal tumor lesion. Spinal Cord 2004;42:52–4.
- [12] Vernon-Roberts B, Christian Georg Schmorl. Pioneer of spinal pathology and radiology. Spine 1994;19:2724–7 (Phila Pa 1976).
- [13] Kyere KA, Than KD, Wang AC, et al. Schmorl's nodes. Eur Spine J 2012;21:2115–21.
- [14] Abdullah AF, Wolber PG, Warfield JR, Gunadi IK. Surgical management of extreme lateral lumbar disc herniations: review of 138 cases. Neurosurgery 1988;22:648–53.
- [15] Levene HB, Nimmagadda A, Levi AD. An unusual case of footdrop: anterior disc herniation mimicking a nerve sheath tumor. Neurosurgery 2010;66:E419–20. discussion E420.
- [16] Yarde WL, Arnold PM, Kepes JJ, O'Boynick PL, Wilkinson SB, Batnitzky S. Synovial cysts of the lumbar spine: diagnosis, surgical management, and pathogenesis. Report of eight cases. Surg Neurol 1995;43:459–64. discussion 465.
- [17] Bullough PG. Pigmented villonodular synovitis and synovial cysts of the spine [comment]. AJNR Am J Neuroradiol 1992;13:167–8.
- [18] Hoch B, Hermann G. Migrated herniated disc mimicking a neoplasm. Skeletal Radiol 2010;39:1245–9.

- [19] Suthar P, Patel R, Mehta C, Patel N. MRI evaluation of lumbar disc degenerative disease. J Clin Diagn Res 2015;9. TC04-09.
- [20] Moon SM. Challenges and advances in MR imaging of the intervertebral disc — can the cartilaginous endplate be a biomarker for the disc health? Biomed Eng Lett 2014;4:19–24.
- [21] Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 1988;166:193–9.
- [22] Stäbler A, Bellan M, Weiss M, Gärtner C, Brossmann J, Reiser MF. MR imaging of enhancing intraosseous disk herniation (Schmorl's nodes). AJR Am J Roentgenol 1997;168:933–8.
- [23] Schoenfeld AJ, Hornicek FJ, Pedlow FX, Schwab JH. Chondrosarcoma of the mobile spine: a review of 21 cases treated at a single center. Spine J 2010;10:S21–2.
- [24] Han SH, Song HJ, Hong WK, Lee HS, Choi GS, Shin JH. Rhabdomyomatous mesenchymal hamartoma of the vagina. Pediatr Dermatol 2009;26:753–5.
- [25] Liu SS, Williams KD, Drayer BP, Spetzler RF, Sonntag VK. Synovial cysts of the lumbosacral spine: diagnosis by MR imaging. AJR Am J Roentgenol 1990;154:163–6.
- [26] van der Heijden L, Dijkstra PDS, Blay J-Y, Gelderblom H. Giant cell tumour of bone in the denosumab era. Eur J Canc 2017;77:75–83.
- [27] Junming M, Cheng Y, Dong C, et al. Giant cell tumor of the cervical spine: a series of 22 cases and outcomes. Spine 2008;33:280–8.
- [28] Kamath N, Agarwal J, Gulia A. Axial giant cell tumor current standard of practice. J Clin Orthop Trauma 2019;10:1027–32.
- [29] van der Heijden L, Dijkstra PD, van de Sande MA, et al. The clinical approach toward giant cell tumor of bone. Oncol 2014;19:550–61.
- [30] Oliveira AM, Hsi BL, Weremowicz S, et al. USP6 (Tre2) fusion oncogenes in aneurysmal bone cyst. Canc Res 2004;64:1920–3.
- [31] Harsh GRIV, Vaz-Guimaraes F. Chordomas and chondrosarcomas of the skull base and spine. Academic Press; 2017.
- [32] Dahlin DC, Maccarty CS. Chordoma. Cancer 1952;5:1170-8.
- [33] Tirabosco R, Mangham DC, Rosenberg AE, et al. Brachyury expression in extra-axial skeletal and soft tissue chordomas: a marker that distinguishes chordoma from mixed tumor/myoepithelioma/parachordoma in soft tissue. Am J Surg Pathol 2008; 32:572-80.
- [34] Miettinen M, Wang Z, Lasota J, Heery C, Schlom J, Palena C. Nuclear brachyury expression is consistent in chordoma, common in germ cell tumors and small cell carcinomas, and rare in other carcinomas and sarcomas: an immunohistochemical study of 5229 cases. Am J Surg Pathol 2015;39:1305–12.
- [35] Folpe AL, Fanburg-Smith JC, Billings SD, et al. Most osteomalaciaassociated mesenchymal tumors are a single histopathologic entity: an analysis of 32 cases and a comprehensive review of the literature. Am J Surg Pathol 2004;28:1–30.
- [36] Broski SM, Folpe AL, Wenger DE. Imaging features of phosphaturic mesenchymal tumors. Skeletal Radiol 2019;48:119–27.
- [37] Folpe AL. Phosphaturic mesenchymal tumors: a review and update. Semin Diagn Pathol 2019;36:260-8.