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Chapter 1

PRIMARY TUMORS OF THE AXIAL SPINE

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ABSTRACT

Primary tumors of the spinal column include a variety of pathologies with variable symptoms, outcomes, and treatment. Knowledge of the lesion's pathology is necessary for proper treatment of any patient presenting with a mass in the bony spinal column. Malignant tumors, such as chordomas, plasmacytomas, osteosarcomas and chondrosarcomas require aggressive surgical resection if the goal is curative intent. Adjuvant chemotherapy and radiation may be needed if the margins of the lesion are compromised, and patients should be followed for several years to monitor for tumor recurrence. In contrast , tumors of benign pathology, such as giant cell tumors and aneurismal bone cysts, may present in younger patients. In all patients, pain is the most common symptom. This chapter will review the symptoms, diagnosis and treatment for primary spinal column tumors, with a focus on the current treatment strategies to optimize patient outcomes.

INTRODUCTION

The axial skeleton is a common site for metastatic disease. However, many primary bony tumors are seen to grow and flourish within the spinal axis. Depending on location, size, and histology, these tumors may produce a variety of neurological symptoms and deficits and may affect patient quality of life and survival. It is well documented that the majority of primary spinal tumors are malignant, adding to the complexity of management. In this chapter we discuss a variety of primary bony tumors of the spine. They each display unique pathophysiological and histologic properties that help determine current diagnostic and treatment modalities. We present these tumors and describe typical presentation, imaging characteristics, diagnostic modalities, histopathological characteristics, and treatment options for each tumor.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of primary bony tumors of the spine is diverse. It includes pathology such as: multiple myeloma, chordomas, giant cell tumors, hemangiomas, osteosarcomas, chondrosarcomas, aneurysmal bone cysts, hemangiomas, eosinophilic granulomas, osteoid osteomas, and osteoblastomas.

MULTIPLE MYELOMA

Multiple myeloma accounts for over 40 % of primary spinal tumors. Myeloma cells are malignant plasma cells that arise from an overexpansion of a single clone of cells within the bone marrow [1]. Patients are typically in their mid-50s and commonly present with focal pain. Additionally, patients may develop an acute pathological fracture due to the tumor that may cause acute onset pain, as well as radiculopathy if neural foramina are compromised [1]. Patients may have other lesions throughout the body, resulting in focal pain at those sites as well. Finally, patients may present with symptoms related to associated anemia, thrombocytopenia and renal failure from involvement of the bone marrow and kidneys [1]. Infection is common in these patients.

Radiographically, multiple myeloma has a unique appearance. Myeloma tumors demonstrate a classic ‘punched-out’ lesion on xray without surrounding osteoblastic activity [1]. Computed tomography (CT) scans and magnetic resonance imaging (MRI) scans may demonstrate pathological fracture of the spine with associated foraminal compromise and/or spinal cord compression [1]. Others lesions may be noted throughout the spinal axis, as demonstrated on technetium bone scans showing increased radioactive uptake. Skeletal survey remains a recommended study to identify multiple areas of myeloma involvement throughout the entire skeleton [1].

Diagnostic modalities include bone marrow aspiration, CT-guided biopsy of lesions, serum and urine electrophoresis and a CBC. Bone marrow architecture will yield abnormal plasma cell distribution that often provides the diagnosis immediately [1]. CT guided biopsy of the spinal lesion is rarely indicated, unless diagnosis is still unclear. Hypercalcemia may be noted on the blood work in 40% of patients [1]. Histopathologically, multiple myeloma contains an overabundance of plasma cells, with the quantitative extent of plasma cells determining probability of myeloma. Immunohistochemistry is important to identify lambda and kappa heavy chain and light chain distributions, critical to the specific myeloma diagnosis [1].

Treatment for multiple myeloma is diverse. Patients with stable spinal disease without deformity or spinal cord compromise may be managed non-operatively [1]. Non-operative treatment would consist of radiotherapy for focal disease and chemotherapy for systemic disease [1]. Patients with severe spinal instability, spinal deformity, and spinal cord compromise will require surgical intervention [1]. Surgery would depend on the location, but generally involves affected vertebral body resection through an anterior or posterolateral approach with or without associated posterior decompression and fusion [1]. Despite the above treatment modalities, prognosis remains poor. The 5 year survival remains less than 30% [1].

CHORDOMAS

Chordomas are the most common primary malignant tumors of the spine in adults [2]. They are seen in middle-aged adults and frequently occur in the clivus and sacrum. However, other locations of involvement may include cervical, thoracic, or lumbar spine [3]. Chordomas are derived from notochordal rest cells that undergo transformation. Despite chordomas being classified as benign tumors, they are functionally malignant through their high recurrence rate and propensity to grow indolently into tumors of massive proportions [2, 3]. For example, tumors in the pre-sacral and sacrococcygeal region may reach such significant growth that they may distort surrounding neural structures, causing weakness, perineal numbness, or bowel/bladder dysfunction. Chordomas within the cervical or thoracic spine may present with radiculopathy and/or spinal cord compression causing myelopathy. Lumbar chordomas may present with focal back pain or if larger may present with radicular symptoms and associated weakness/numbness or cauda equina syndrome [2, 3].

Diagnostic modalities include CT and MRI that demonstrate a heterogeneously enhancing and sometimes calcified mass of varying size with possible distortion of surrounding tissues if extensive. Classically, chordomas may remodel the existing bony architecture due to their slow growth, rather than invasion and destruction of bone. Often times, a CT-guided biopsy is needed to make the diagnosis [2].

Histologically, chordomas display their pathognomonic physaliferous cells, which have an unusually vacuolated cytoplasm. Microscopically, chordoma cells react intensely for S-100 and other epithelial markers such as cytokeratins and epithelial membrane [4, 5].

The treatment of spinal chordomas has changed over the last few decades in favor of more aggressive surgical management. Surgical management involves attempted en bloc resection without violation of the tumor capsule. This offers the patient an extended progression free survival of over 60% at 5 years while minimizing local recurrence [6, 7]. Subtotal resection provides a local recurrence rate at 8 months as opposed to over 2 years with en bloc resection [11].

En bloc resection without violation of tumor capsule allows for a decrease two-fold in local recurrence [10]. If en bloc resection is not feasible, pre-operative radiation may be performed to reduce viable tumor at the margins and improve patient outcomes. When performing sacrectomies, recent evidence suggests that salvaging the sacral 2 nerve root is key to restoring a 50% chance of normal bowel and bladder function post-operatively [8, 40]. Sacral 3 root preservation will provide additional guarantee of bowel and bladder function. It has been shown that bilateral sacral 2 nerve root sparing along with unilateral sacral 3 root sparing is associated with normal bowel and bladder function [8, 40].

Cervical chordomas are classified into high cervical, mid cervical and cervicothoracic, with location influencing surgical strategy [7, 8]. Thoracic and lumbar chordomas are managed in multiple staged posterior and anterior instrumentation and fusion procedures with en bloc resection of tumor [6, 7, 8]. Sacro-coccygeal chordomas may be resected with total or partial sacrectomy, through the posterior or combined approach. Preservation of the sacro-iliac joint obviates the need for hardware fixation. Adjunctive treatment for chordomas generally involves post-operative proton beam radiotherapy, as these tumors are classified as radio-resistant [9].

GIANT CELL TUMORS

Giant cell tumors of the spine are benign expansile lesions affecting predominantly female patients between 20-50 years of age [13]. Due to the lytic and locally aggressive qualities of this benign tumor, giant cell tumors functionally act in a malignant manner. Patients may present with focal back pain, or larger lesions may cause pathological fracture with associated radiculopathy or spinal cord compression causing myelopathy [13].

Radiographically, Xrays and CT scans are helpful to define the extent of bony destruction associated with the vertebral body. MRI is useful to identify extent of tumor along the spinal column, along with any foraminal or spinal canal compromise. A radionuclide bone scan may be used and will show decreased uptake in the center of the lytic process and increased uptake along the surrounding [12]. A CT-guided biopsy is often recommended to look for the classic mononuclear stromal cells with giant cells throughout [12]. Based on histology, giant cell tumors are classified under 3 stages with stage 1 most benign and stage 3 highly aggressive [12]. Treatment for giant cell tumor varies based on tumor grade. For localized disease without neurological symptoms, some studies have demonstrated efficacy with radiotherapy [16]. For large lesions with neural compromise, en bloc spondylectomy is recommended, with studies demonstrating more effective local control and lower recurrence [14-16]. However, some studies have demonstrated an unacceptable complication rate post-operatively [14-15]. En bloc resection generally will involve a multiple staged posterior then anterior reconstruction with instrumentation and fusion, depending on site of tumor within the spinal column [15, 41]. The role of post-operative radiotherapy is currently unclear, as malignant transformation of the giant cell tumor has been reported [15, 41]. Local recurrence rates are noted to be at 41%-66.7% within the mobile spine [12-13]. 5%-13% of patients with have pulmonary metastases, which may require surgical resection [12] and whose histology will determine a benign versus malignant diagnosis [12].

HEMANGIOMA

Hemangiomas are very common benign lesions that can be found in the spinal column, typically the vertebral bodies of the thoracic spine. They are often asymptomatic lesions found incidentally on routine imaging [17]. Related symptoms are typically due to the large size or pathological fracture associated with the hemangiomas [17]. Larger lesions may encroach upon the neural foramina and spinal cord causing myelopathy. Focal kyphotic deformity with instability may result from pathological fracture [17]. Radiographically, xrays will show the classic vertical striations of the hemangioma, while CT scans will demonstrate the ‘spikes of bone’ appearance within the vertebral body. MRI will show an enhancing tumor with hemorrhage and thrombosis on T1 imaging [17]. Histologically, hemangiomas are a collection of thin-walled capillaries with an endothelial lining and surrounding capsule [17]. They may have thrombosed lumens with occasional hemosiderin deposition from vessel rupture [18]. Treatment options will depend on the clinical presentation. Asymptomatic patients only require observation of the lesion and conservative treatment [19]. If the patient has persistent pain associated with the spinal hemangioma, radiation therapy may be offered for symptomatic control with adequate results [19]. For lesions with hypertrophy or

ballooning of the posterior cortex of the vertebral body into the spinal canal causing neurologic compromise or intractable pain from deformity, studies have demonstrated acceptable results from either an anterior approach, posterolateral approach, or posterior approach [19] for corpectomy and posterior fusion. Preoperative embolization reduces the risk of intra-operative hemorrhage and should be performed when angiography identifies the arterial blood supply [19].

EOSINOPHILIC GRANULOMA

Eosinophilic granulomas of the spine are benign lesions typically of the thoracic spine that are the localized form of Langerhans Histiocytosis X. Vertebral location is noted to be around 8-25% [20]. Granulomas are typically found incidentally but acute presentations may include pain or deformity from pathological fracture, as well as radiculopathy and myelopathy from spinal cord compression [21]. Radiographically, CT and MRI scans may demonstrate vertebral flattening which precedes eventual vertebral collapse with additional lesions elsewhere within the spinal axis [21]. If patient has not been diagnosed prior with histiocytosis X, then biopsy is indicated to confirm the diagnosis [21]. Histologically, granulomas demonstrate mononuclear histiocytic cells with oval nuclei and Birbeck granules on electron microscopy. Additionally, lipid-laden foam cells and lack of nuclear atypia characterize this tumor [22-23]. Eosinophilic granulomas are usually self-limiting. Chemotherapy is recommended for the systemic form of Langerhans Histiocytosis X. Low dose conventional radiotherapy is recommended for symptomatic lesions without neurological compromise and/or patients who are not operative candidates. If lesions are causing progressively worse intractable pain and instability and/or deformity with neurological compromise, then surgical intervention is warranted [21]. Surgical approach would depend on the level along the spine, with either an anterior corpectomy with fusion or posterior or posterolateral approach for corpectomy with instrumentation [23].

ANEURYSMAL BONE CYST

Aneurysmal bone cysts (ABC) are benign expansile lesions of bone composed of blood filled cavities separated by septa of osteoclastic cells [24]. Typically, patients are in their 20's and most are incidentally discovered. Acute presentations may include severe back pain from pathological fracture and/or radiculopathy or myelopathy from spinal cord compression and kyphotic instability [24]. Radiographicallly, CT and/or MRI are the studies of choice. They will demonstrate a lytic lesion surrounded by a thin shell of cortical bone with areas of cortical disruption causing a blown-out appearance [25]. Lobulated appearance, septations, and fluid-fluid levels are very suggestive. CT scan is helpful to determine the bony anatomy and invasion of bone by tumor in order to decide on required stabilization procedures. MRI is helpful to determine the relationship of the tumor from the adjacent neural structures [25].

On histologic analysis, ABC display cavernous spaces with blood filled centers without endothelial lining separated by fibrous septa composed of fibroblasts and osteoclasts [25].

The literature describes a combination of treatments, ranging from curettage, subtotal excision, en bloc resection, embolization, intralesional injection, and radiation [25]. For lesions that are asymptomatic, conservative treatment with or without bracing is indicated. For larger lesions with neurological compromise, surgical treatment is recommended. Pre-operative embolization may play a role in management [26]. Indolent lesions may resolve spontaneously over months [24]. Overall recurrence rate is 28% and they generally occurs within the first 2 years [25].

OSTEOBLASTOMA

Osteoblastomas are rare benign tumors of the spine in young adults that are similar to osteoid osteomas, but are larger than 2 cm in size. In contrast to osteoid osteoma patients, patients with osteoblastomas are less likely to present with severe attacks of night pain, and focal pain is typically not relieved with anti-inflammatory medications such as aspirin [27].

Xrays and CT scans demonstrate the predilection for the posterior elements and show a radiolucent lesion with surrounding reactive bone with or without expansion. Bone scans will show intense isotope uptake at the site of tumor [27]. Biopsy may be performed if diagnosis is unclear. Histologically, osteoblastomas demonstrate significant production of surrounding osteoid and primitive woven bone, with areas of fibrovascular connective tissue nearby. Osteoblasts are seen in great numbers [27].

Treatment will vary depending on symptoms and size of tumor. For tumors that are small, conservative treatment and observation is warranted. For tumors that increase in size, cause mass effect upon nearby neural structures, or cause progressive spinal instability and deformity, surgical treatment is recommended. Some studies advocate intralesional excision while others recommend en bloc resection [29]. For larger lesions and en bloc resections, a staged procedure is performed with both an anterior and posterior approach, along with instrumentation and fusion [28, 29]. For patients with intralesional resection, radiation therapy can be used as an adjunct for local control [29] with good results, though osteoblastomas are not classified as radiosensitive. Malignant transformation has been reported in 12-25% of patients [29].

CHONDROSARCOMA/OSTEOSARCOMA

Osteosarcomas are malignant mesenchymally-derived tumors of the bone seen in adolescents. They rarely affect the spine [30]. Chondrosarcomas are malignant tumors of the cartilage that are seen in patients between ages 30-70 [31]. They are locally aggressive with a high recurrence rate [31]. Both of these tumors are most commonly seen in the thoracic spine [31]. Patients with both tumors may present with focal pain throughout the day [30]. Lesions may grow large enough to cause neurological symptoms such as radicular pain or myelopathy [30]. Radiographically, xrays and CT scans for osteosarcomas demonstrate a destructive lytic lesion with evidence of new bony formation and periosteal reaction, with or without an associated soft tissue mass [30].

Xrays and CT scans for chondrosarcomas demonstrate irregularly mottled calcification with bony destruction and invasion. MRI will demonstrate a heterogeneously enhancing mass with hypointensity on T1 and hyperintensity on T2 imaging. A biopsy may be performed when diagnosis is unclear. Histologically, osteosarcomas have pleomorphic giant and atypical cells with mitotic figures. They produce osteoid with eosinophilic trabecula with occasional areas of calcification. The tumor cells are within the osteoid matrix. Chondrosarcomas demonstrate undifferentiated cartilaginous cells with mitotic figures and atypia [30, 31]. Sarcomas of the spine are quite complex but in cases of neurological compromise from compression and/or instability, surgical treatment is warranted. Recent evidence for chondrosarcomas has emerged showing an increased progression-free survival after en bloc resection without violation of tumor capsule.

This typically involves a multi-stage anterior and posterior reconstruction with instrumentation and fusion [31, 32]. Outcome for chondrosarcomas is based on histology, patient age, and en bloc resection [31, 32]. Metastatic disease is the most important factor for survival in patients with osteosarcoma. With adjunctive therapy such as chemotherapy, osteosarcoma survival is 50% over 5 years. Osteosarcomas are radioresistant and thus surgical resection for appropriate tumors will require aggressive multi-stage approaches [332].

OSTEOID OSTEOMA

Osteoid osteomas are benign tumors typically in males aged 4-30 of the posterior elements of the spine that are less than 2 cm in size. As previously described, osteoblastomas are lesions greater than 2 cm [33]. Patients may present with severe focal night pain that is relieved with aspirin [33]. Radiographically, xrays and CT scans will demonstrate areas of reactive bony formation with a low attenuation nidus and sclerotic border [34]. Technetium bone scans may demonstrate intense uptake at the site of the lesion [33, 34]. MRI demonstrates a T1 nidus with intermediate signal intensity and T2 hypointensity with heterogenous enhancement [34].

Rarely is biopsy needed for the diagnosis. Histologically, osteomas have yellowish to red areas of osteoid and woven bone with interconnected trabeculae, amidst a background of vascularized, fibrous connective tissue [33].

Osteomas are typically self-limiting. Small lesions can be treated conservatively with non-steroidal anti-inflammatory medications such as aspirin. Pain from these lesions typically responds to non-steroidal anti-inflammatory drugs such as aspirin [33, 35]. When pain is intractable or patient’s tumor is causing instability or neural compromise, surgery is indicated. Surgical treatment generally involves instrumentation and fusion for tumors that are large and near neural structures [35].

FIBROUS DYSPLASIA

Fibrous dysplasia is a predominantly osteolytic disorder that affects young children and adolescents. It affects males and females equally [36]. Most of the time, patients are

asymptomatic [37] but symptomatic patients may present with focal pain or radiculopathy from foraminal compromise.

Radiographically, xrays, CT, and MRI demonstrate a ground-glass appearance with definite sclerotic margins. CT may show an expansile lesion with a blown-out cortical rim. McCune-Albright syndrome is a severe form of polyostotic fibrous dysplasia combined with an endocrinopathy and café-au-lait spots, and should be suspected in patients with severe dysplasia [37]. Histologically, fibrous dysplasia demonstrates curvilinear trabecular woven bone with a background of fibroblasts. Foamy macrophages may also be seen [37].

Patients should undergo metabolic and endocrinological evaluation to treat an underlying vitamin D deficiency, phosphate wasting, and/or hyperparathyroidism. Oral bisphosphonates are effective for relief of pain in fibrous dysplasia [38]. Surgery is indicated in cases of neural compromise and/or instability. Surgical approach would depend on the location along the spinal axis but may require multi-stage corpectomy with instrumentation and fusion [39].

CONCLUSION

The primary bony tumors of the spine are a diverse and heterogenous group of tumors. They each exhibit unique structural and pathophysiological mechanisms that then determine specific diagnosis and treatment modalities. Recent advances such as en bloc resection without violation of tumor capsule in patients with spinal chordomas and chondrosarcomas has significantly advanced progression free survival. Ongoing research continues to establish optimal diagnosis and treatment options for each of these primary spinal tumors.

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