Bone Tumors

This edition of *FP Essentials™* will update family physicians on bone tumors and will cover four sections: benign bone tumors, primary bone cancers, multiple myeloma, and secondary bone cancer (metastatic bone disease).

This edition of *FP Essentials* should be approximately 10,000 words in length, divided into four sections of approximately 2,500 words each (each with an abstract of 200 words or less) plus key practice recommendations, a maximum of 15 tables and figures, recommended reading, and approximately 100 references. This edition should focus on what is new in each topic and should answer the key questions listed for each section. Each section should begin with an illustrative case, similar to the examples provided, with modifications to emphasize key points; each case should have a conclusion that demonstrates resolution of the clinical situation. The references here include information that should be considered in preparation of this *FP Essentials*. However, these references are only a useful starting point that should be used to identify additional information to review.

**Needs assessment:** Secondary bone cancer (metastatic bone disease) is the most common form of bone cancer and is a condition that family physicians regularly encounter. Primary benign bone tumors, however, are uncommon and the true incidence of these lesions is unknown as many are asymptomatic and go undetected unless incidentally discovered. Primary bone cancers also are uncommon, but they are associated with significant morbidity and mortality, so clinicians should be familiar with their presentation and the approach to diagnosis. Multiple myeloma, on the other hand, is relatively common and accounts for approximately 10% of hematologic malignancies in the United States. Family physicians have an important role in the initial evaluation of patients experiencing these diseases. Because most patients may present late in the course of the disease, a high degree of suspicion is necessary to diagnose these conditions. Bone pain that awakens the patient at night should concern family physicians, and imaging should be obtained promptly. Furthermore, family physicians may have an important role in managing comorbid issues such as pain, nutrition, psychological support, and end-of-life care.
Section 1: Benign Bone Tumors

Example case: Emily, a 21-year-old woman, comes to your office with a mildly painful enlargement on the outside of her right knee that has been present for several months. She recalls sustaining a twisting injury to the knee while playing soccer approximately one year ago, but those symptoms resolved a few weeks after the injury. She has no other medical conditions and reports no systemic symptoms. Her physical examination is remarkable only for mild tenderness and swelling over the proximal fibula. X-ray findings of her knee show a lesion of the head of the fibula. There is a rim of calcification indicating the periosteum is intact. Internal trabeculations also are seen within the lesion.

Key questions to consider:

Address the questions below, as applicable, for each of the most common benign bone tumors: osteochondroma, giant cell tumor, enchondroma, osteoid osteoma, and osteoblastoma:

- Which populations and ages are most commonly affected?
- What are the presenting signs and symptoms? What are the physical findings?
- What are the most common location(s) at which they occur?
- What are the x-ray findings?
- Can any of these benign bone tumors metastasize?
- Are bone biopsies necessary for the diagnosis? What other evaluations are necessary for diagnosis?
- After diagnosis, what are the common management strategies? When is observation and follow-up recommended rather than active therapy? What adjunctive therapies are used?
- What are the complications if left untreated? What is the risk of fracture?
- Can these benign bone tumors progress to malignant bone cancer?
- What is the recurrence rate after therapy?

Initial references to consider:


Section 2: Primary Bone Cancers

Example case: Darius, a 12-year-old male, is brought to your office by his mother, Carla, because he has been experiencing right upper extremity pain for the last 2 weeks. The pain started insidiously and there is no history of injury. Carla says she has noticed some general malaise, and Darius has been feverish and awakened at night because of pain. Though right hand dominant, Carla says he has been avoiding using his right upper extremity. On examination there is no swelling, tenderness, warmth, or redness in the area of discomfort. Laboratory findings show an elevated erythrocyte sedimentation rate and C-reactive protein. Initial x-ray results of the humerus show no bony abnormalities, but a magnetic resonance imaging study showed an abnormal bone marrow signal within the humeral shaft; a lesion with irregular cortical borders and periosteal reaction. A biopsy and culture of the lesion is performed. Gram stain and culture findings are negative for bacteria, but pathologic examination of the biopsy specimen reveals a malignant, small blue cell tumor consistent with Ewing sarcoma.

Key questions to consider:

Address the questions below, as applicable, for each of the most common primary bone cancers: osteosarcoma, Ewing sarcoma, chondrosarcoma, and malignant giant cell tumor:

- What is the pathophysiology or etiology?
- Which populations are most commonly affected?
- Which risk factors are associated with the development of the cancer?
- What are the history, symptoms, and physical examination findings? How is the cancer most commonly detected and diagnosed?
- What are the most common locations for the primary lesion and metastases?
- What is the x-ray finding? What other evaluations are needed to diagnose these cancers? Are biopsies necessary for diagnosis? What are the common associated signs and symptoms?
- After diagnosis, what are the common management strategies? What adjunctive therapies are used in the management of these cancers?
- What are the cure rates and prognosis? What is the recurrence rate?

Initial references to consider:


Section 3: Multiple Myeloma

Example case: Angela is a 61-year-old woman who has had recurrent severe respiratory infections during the past year. Recently, she presented with gradual onset of generalized weakness, fatigue, myalgia, and anorexia. Initial laboratory findings were remarkable for anemia and acute kidney injury. She was hospitalized and further evaluation revealed an elevated erythrocyte sedimentation rate. A peripheral blood test showed rouleaux of red blood cells and urinalysis indicated proteinuria. A skeletal survey is obtained and shows lytic punched-out lesions in the skull and pelvis.

Key questions to consider:

- What is the incidence and prevalence of multiple myeloma? What is the underlying etiology of multiple myeloma? What is the pathophysiology?
- Which risk factors are associated with the development of multiple myeloma?
- How common is monoclonal gammopathy of undetermined significance (MGUS) and how often does it progress to multiple myeloma? What are risk factors for progression, and what monitoring is needed for patients with MGUS to allow early detection of myeloma?
- What are the history, symptoms, and physical examination findings associated with multiple myeloma? What are the common systemic complications of multiple myeloma?
- What are the typical x-ray findings of multiple myeloma? What are the causes of these findings? What other x-ray studies can be helpful in the diagnosis of this disease?
- What other studies are needed in the diagnostic evaluation of multiple myeloma? Discuss bone marrow aspiration, urinalysis findings, complete blood count, peripheral blood testing, erythrocyte sedimentation rate, chemistry panel, serum and urine protein electrophoresis (M-protein, Bence Jones protein). Are there other tests that should be obtained?
- What diagnostic criteria differentiate multiple myeloma from other malignancies? How should monoclonal gammopathies be monitored?
- What is the International Staging System for multiple myeloma?
- After diagnosis, what are the common management strategies for multiple myeloma? Consider interventions such as chemotherapy, radiation, corticosteroids, immunomodulatory drugs, monoclonal antibodies, stem cell transplantation, bisphosphonates, and the management of complications. Discuss the CRAB (calcium, renal impairment, anemia, and bone involvement) mnemonic. Is aerobic exercise beneficial to patients with multiple myeloma?
- What should family physicians monitor in patients who received treatment for myeloma?
- Which immunizations are recommended for patients with multiple myeloma?
- What is the prognosis of patients diagnosed with multiple myeloma?
- What are the recommended strategies for pain management in patients with multiple myeloma?
Initial references to consider:

- Smith D, Yong K. Multiple myeloma. *BMJ.* 2013;346:f3863.
Section 4: Secondary Bone Cancer (Metastatic Bone Disease)

Example case: Jasmine, a 59-year-old woman with a 5-year history of breast cancer, comes to your office because of right-sided chest pain that began 2 weeks ago. She underwent a mastectomy with axillary node dissection and received hormone-based chemotherapy. The pain is dull and not related to activity or exertion. She denies trauma. She has taken nonprescription analgesics without relief. Her physical examination reveals mild tenderness over the right rib cage without swelling, warmth, or redness. X-rays of her chest show a bony lesion in the right fourth rib. A suspicious lesion on one of her thoracic vertebrae also is seen. A bone scan shows hot spots in the fourth thoracic vertebra, left sixth rib, right fourth rib, and third lumbar vertebra.

Key questions to consider:

Address the questions below, as applicable, for each of the most common secondary bone cancers: breast, prostate, lung, thyroid, and kidney:

- Which bones are most commonly affected by metastatic disease?
- What are the symptoms and physical examination findings associated with secondary bone cancers? Can symptoms of metastasis precede symptoms of the primary tumor?
- What are the x-ray findings of these cancers? Which cancers are mostly osteolytic versus osteoblastic? How do they differ on x-ray?
- What other diagnostic studies are useful in the diagnosis of these cancers? When are magnetic resonance imaging, computed tomography (CT), positron emission tomography-CT, and bone scans indicated?
- When is biopsy indicated?
- What is the management strategy for common secondary bone cancers? Discuss chemotherapy, radiation, bisphosphonates, hormone therapy, receptor activator of nuclear factor kappa B ligand (receptor activator of nuclear factor kappa B ligand [RANKL] inhibitors). When is surgery indicated?
- Is management different when bone metastases appear long after initial (apparently successful) therapy and resection of the primary cancer?
- What is the prognosis of patients diagnosed with secondary bone cancer?

Initial references to consider:


