Chapter 5

Surgical Management of Metastatic Bone Disease: General Considerations

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BACKGROUND

- The skeleton is the third most common site of metastatic disease, after the lungs and liver.[4,11] Prostate, breast, lung, kidney, and thyroid cancers account for 80% of skeletal metastases.[4,11] The prolonged survival with disease of increasing numbers of cancer patients has led to growing numbers of patients with metastatic bone disease (MBD). The exact incidence of bone metastasis is unknown, but it is estimated that in the United States alone 350,000 people annually die with bone metastases.[13]
- MBD is a major factor contributing to deterioration of quality of life in patients with cancer. These patients may require surgical intervention for the management of impending or current pathological fractures or for the alleviation of intractable pain associated with a locally progressive lesion.
- Those skeletal crises are associated with a considerable loss of function, pain, and the associated impairment of quality of life. Surgery also may be performed to remove a solitary bone metastasis with the intent of improving long-term survival in selected patients, [1,10] but other than this rare exception, these surgical interventions are primarily palliative and are aimed at achieving local tumor control, structural stability of the surgically treated site, and restoration of normal function as quickly as possible. Failure to achieve one of these goals usually necessitates a second surgical intervention, and this is associated with additional impairment of an already compromised quality of life.
- Reports show failure rates of surgeries performed for MBD as high as 40%, occurring as the result of a poor initial fixation, improper implant selection, or progression of disease in the operative field.[3,8,14,15]
- An attempt to treat a pathological fracture as one would treat a traumatic fracture will fail, in most cases, because the underlying disease impedes the fracture healing process. The prognosis for union of a pathological fracture also is determined to some extent by the tumor type: fractures associated with metastatic adenocarcinomas of breast and prostate, multiple myeloma, and lymphoma are much more likely to unite successfully than are those associated with malignancies of the lung, kidney, and gastrointestinal tract.[5–7]
- Furthermore, even when healing does occur, it does so after an unreasonably long period of time and is of less than satisfactory quality. Reduction and immobilization used in the management of traumatic fractures are, therefore, not applicable in the management of pathological fractures due to MBD.
- Gainor and Buchert[5] analyzed 129 pathological fractures and found that the long bone fractures that healed most predictably were those that had been internally fixed and irradiated and were in patients who survived for more than 6 months postoperatively.
- Similar observations were made by Harrington et al.[7] Cemented hardware or prostheses are used preferentially for fixation to achieve immediate stability, and reconstruction techniques that rely on a biologic process of bone healing (eg, autologous bone grafts, allografts, or allograft–prosthetic composites) are inappropriate for the surgical management of MBD.[2,6,7,9]

INDICATIONS

- Existing pathological fracture
- Impending pathological fracture
- Intractable pain associated with locally progressive disease that had shown inadequate response to narcotics and preoperative radiation therapy
- Solitary bone metastasis in selected tumor types
- Surgical intervention for MBD is appropriate for patients who are expected to survive for more than 3 months. Patients who are expected to survive for less than 3 months are less likely to benefit from an operation, because they usually do not have the physical strength required for rehabilitation or the time needed for its completion. Those patients are treated with nonoperative approaches, such as sling and arm brace for the upper extremities or protected weight-bearing for the lower extremities.

IMAGING AND OTHER STAGING STUDIES

Plain Radiography

- Plain radiographs and CT scans of the affected site should be done, as well as plain radiographs of any additional site in which the patient reports joint or bone pain. The combined results of these studies will define the extent of bone destruction and soft tissue extension (**FIG 1A,B**).
- If the investigated metastasis is located in a long bone, plain radiographs of reasonable quality of its entire extent should also be obtained to exclude additional metastases, because these data are crucial for surgical planning. Missed metastases could cause pathological fractures on postoperative weight bearing and require an extensive surgery for their repair (**FIG 1C–F**).
- Chest radiographs also should be done routinely as a screening study to rule out lung metastases, considering that the lungs may be involved in most common cancers. Table 1 summarizes the list of recommended studies for patients with bone metastasis whose primary site of disease is unknown.

Bone Scan

- A total body bone scintigraphic evaluation using technetium Tc 99m (^{99m}Tc)-MDP should be done prior to any surgical intervention. This examination provides information for staging of the entire skeleton in the case of additional metastases and also can detect metastases that may require simultaneous surgery. Bone scanning is highly sensitive for bone pathology. Tracer uptake, however, is not specific for MBD and may display spuriously a large variety of inflammatory, infectious, posttraumatic, and other benign conditions. Therefore, plain radiography also should be done of any positive site on bone scan.

FIG 1 • **A.** Plain radiograph showing a metastatic tumor of the right acetabulum in a 72-year-old man with a known history of thyroid carcinoma. **B.** CT scan shows extensive bone destruction and soft tissue extension. Attempt at resection based on the radiographic findings alone probably would result in intralesional debulking and potential exsanguination due to the extensive vascularity of this tumor. Given these radiologic findings, this patient underwent preoperative angiographic embolization, which diminished blood loss in surgery and allowed successful resection. **C.** Plain radiograph showing a pathological hip fracture in a 69-year-old woman with a known history of breast cancer. **D,E.** Hip hemiarthroplasty was performed within 24 hours of fracture occurrence, but postoperative radiographs showed an additional metastasis just below the tip of the prosthetic stem that was missed because of the poor quality of the preoperative radiographs and because whole-bone radiographs were not done before surgery. **F.** While the patient was still in the hospital, she suffered a pathological fracture through that lesion as she was being shifted from her bed to a reclining chair.

■ Bone scanning is not a substitute for plain radiographs of the entire affected bone or other sites with bone pain, because some tumors (eg, multiple myeloma, metastatic melanoma, thyroid carcinoma) may not show up on a bone scan (**FIG 2**).

Laboratory Studies

■ A complete blood count and blood chemistries should be ordered. The calcium level is of specific concern in those studies, because hypercalcemia may be a life-threatening complication of MBD. An ionized calcium level is helpful in the diagnosis of hypercalcemia, because low albumin levels may lower total calcium levels. Hypercalcemia should be treated before any surgical intervention is undertaken. Levels of specific tumor markers should be evaluated, if applicable to the specific tumor type.

Biopsy

■ The mere presence of a bone lesion with a presumed diagnosis of metastasis does not mandate a biopsy. Such a lesion in a

Table 1 **Studies Required for the Preliminary Evaluation of a Patient With a Metastatic Disease With an Undetermined Primary Site of Disease**

Physical examination	Focus on evaluation of skin, presence of lymphadenopathy, breast, thyroid, prostate, rectal examination
Laboratory studies	Complete blood count, blood chemistries, liver function tests, erythrocyte sedimentation rate, serum and urine protein electrophoresis, prostate-specific antigen, urinalysis, stool guaiac study
Imaging studies	CT of chest, abdomen, pelvis

patient with an established history of malignancy and with radiologic evidence of other bone metastases does not require a biopsy prior to surgical intervention.

- On the other hand, biopsy must be performed on a solitary bone metastasis in a patient with a known history of malignancy or a lesion with atypical radiologic or clinical manifestations, even in the presence of other bone metastases prior to any intervention.

PREOPERATIVE PLANNING AND CONCERNS

- Although planned surgery for patients with MBD should not be delayed, preoperative evaluation and staging must not be compromised but, rather, thoroughly mapped out. This evaluation makes it possible to understand the morphology of the lesion and its relation to adjacent structures, determine the

FIG 2 • **A.** Plain radiograph showing a pathological fracture of the proximal femur in a 59-year-old woman with multiple myeloma. **B.** Bone scintigraphy revealed no additional bone lesion, and she was treated with open reduction (without tumor removal) and uncemented internal fixation. She reported unrelenting ipsilateral knee pain and was clinically diagnosed as having degenerative joint disease and associated pain. Two weeks after the reduction surgery, she reported an acute onset of severe knee pain and swelling on weight bearing. **C,D.** A pathological fracture of the distal femur was demonstrated on plain radiographs. **E.** This patient underwent total femur resection with endoprosthetic reconstruction.

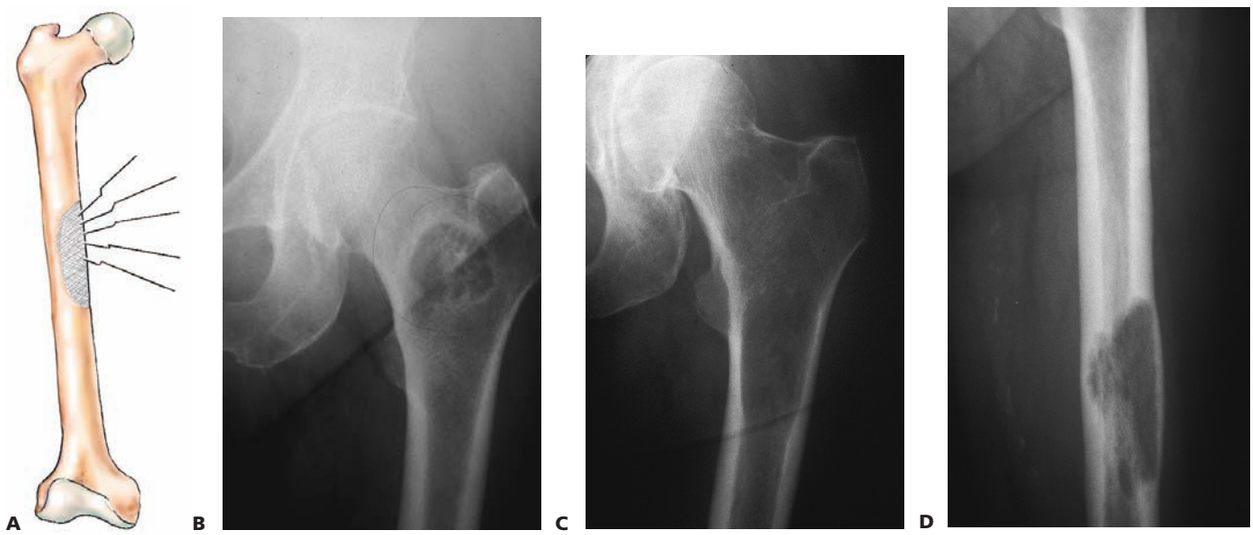

FIG 3 • **A.** A bone lesion measuring more than 2.5 cm, occupying over 50% of the cortical diameter, and associated with pain on weight bearing is considered to be an impending pathological fracture. **B.** Metastatic breast carcinoma of the proximal femur in a 59-year-old woman. The lesion was asymptomatic and had been noted on a follow-up bone scan that showed increased uptake at that site. The lesion was larger than 2.5 cm. However, because it had a sclerotic rim, occupied less than 50% of the cortical diameter at that region, and did not reach the cortices to violate their integrity, surgical intervention was not required, and the patient was treated successfully with radiation therapy and bisphosphonates. **C.** Subtrochanteric femoral metastatic breast carcinoma in a 62-year-old woman. **D.** Metastatic lung carcinoma of the femoral diaphysis in a 70-year-old man. Both were symptomatic on weight-bearing, and both evidenced a large lytic lesion occupying over 50% of the cortical diameter with cortical destruction ranging from endosteal scalloping to frank breakthrough. Both lesions required prophylactic surgical intervention.

overall skeletal staging of the patient, and detect any other metastases that may require simultaneous surgery. Because most patients who present with skeletal metastases have an established diagnosis of cancer, clinical and radiologic evaluations usually are aimed at evaluating the extent of the disease and the presence of any complications rather than at identifying its site of origin.

History and Physical Examination

- Medical history should include current oncologic status and related treatments and medications. It is crucial to question the patient or family members about his or her overall functional status and, specifically, about the status of the affected extremity prior to the occurrence of the metastatic lesion. For example, a surgeon would be justifiably reluctant to perform major surgery on a lower extremity in a patient who was bedridden or wheelchair-bound, because stabilization of the extremity for greater ease in maintaining pain-free personal hygiene in that patient would require a less extensive procedure.
- The orthopaedic surgeon also should inform the medical oncologist of the impending operation, verify the oncologic information he or she has received, and be provided with the patient's estimated life expectancy. The physical examination should include evaluation of the principal symptomatic area as well as other symptomatic sites. Examination should focus on the degree of soft tissue tumor extension and its relation to the neurovascular bundle of the extremity, muscle strength and range-of-motion of the adjacent joints, neurovascular status of the affected extremity, and limb edema.

Impending Pathologic Fractures

- Patients with MBD who have a pathological fracture experience a sudden onset of debilitating pain and loss of function. They require urgent hospitalization, which may interrupt the course of ongoing oncologic treatment. Furthermore, surgery for these fractures often is complicated by the presence of a substantial hematoma, soft tissue edema, and difficulties in obtaining appropriate reduction and alignment because of extensive bone destruction. For these reasons, it is important to identify those metastatic bone lesions that are likely to cause a pathological fracture (ie, "impending" pathological fractures) and to stabilize them prophylactically.
- Although the consensus is that impending fractures require prophylactic fixation, numerous reports have described varying concepts and methods of evaluation of these lesions as well as criteria for defining them. The agreed-to and most commonly used criteria include a lytic bone lesion that measures 2.5 cm, causes circumferential destruction of 50% or more of the adjacent cortical bone, and is associated with increasing pain on weight bearing that has not responded to treatment with radiation therapy (**FIG 3**).[6,7,12]

PRINCIPLES OF SURGERY

- The primary goals of surgery for MBD are to achieve local tumor control and structural stability of the surgically treated site. Surgery has no effect on the overall progression of disease or on patient survival. Most failures of these surgeries are attributed to inadequate tumor removal and improper reconstruction. Radiation therapy is most effective when applied to

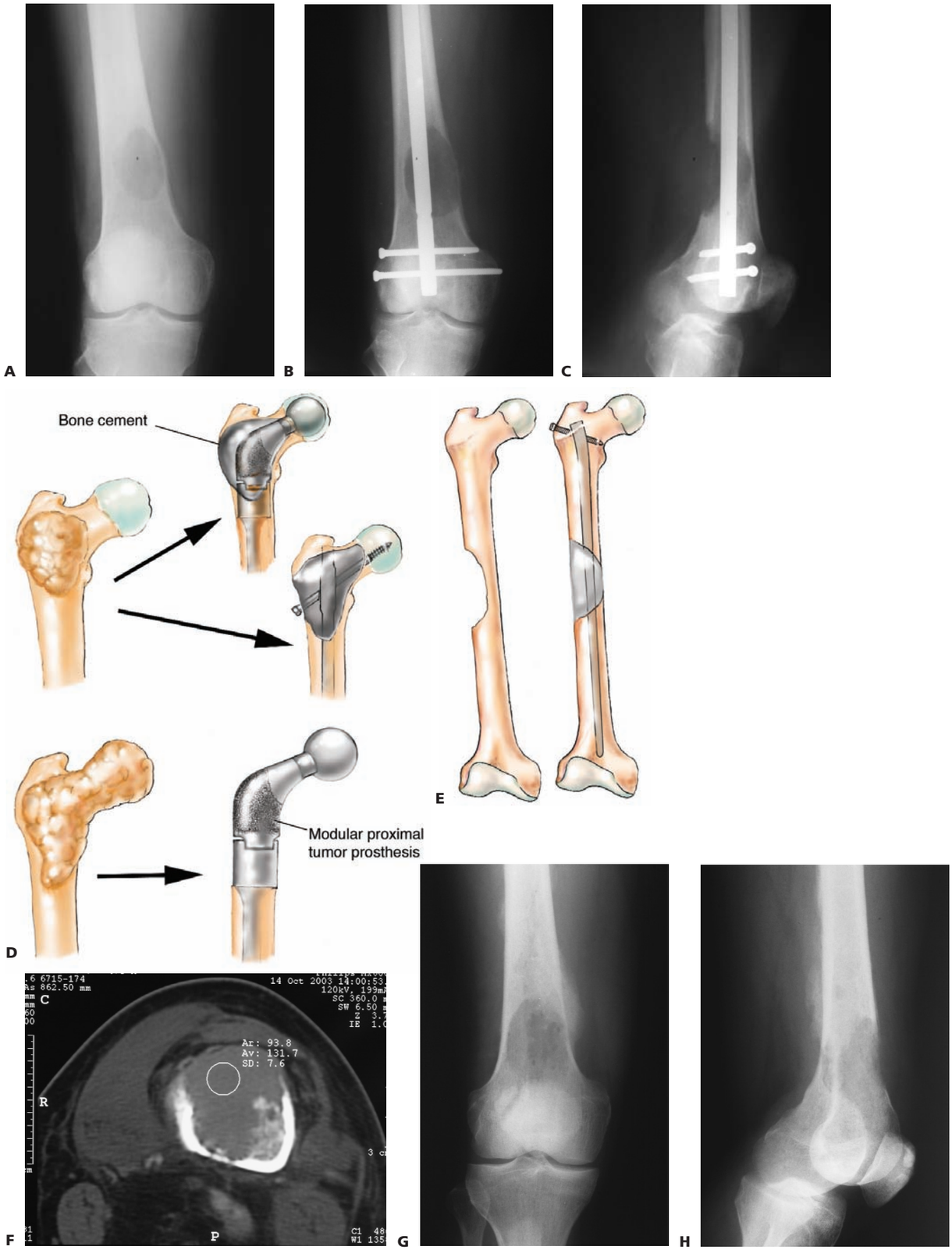

FIG 4 • *(continued)*

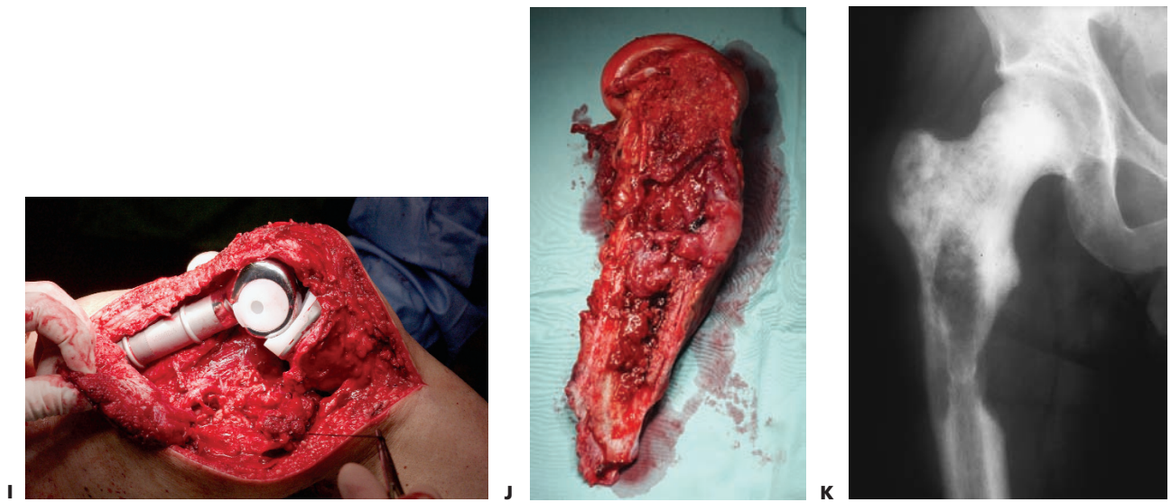

FIG 4 • **A.** Plain radiograph showing metastatic renal cell carcinoma of the distal femoral diaphysis. This patient was treated with closed (ie, without tumor exposure and removal) retrograde intramedullary nailing and referred for postoperative radiation therapy. **B,C.** Radiographs taken 3 months after surgery show considerable local tumor progression, which required additional, extensive surgical intervention. **D.** A metastatic lesion of the proximal femur. Lesions such as this that do not extend to the femoral head may be treated with intralesional tumor removal and reconstruction with cemented intramedullary nailing. Lesions that cause extensive destruction of the femoral head, on the other hand, may require proximal femur resection and reconstruction with a cemented prosthetic implant. **E.** A metastatic lesion of the diaphysis. Lesions such as this that have enough residual cortex to allow continuity may be treated with intralesional tumor removal and reconstruction with cemented intramedullary nailing. Lesions that have caused extensive destruction and violated that continuity, however, require intercalary resection of the humeral diaphysis. CT scan (**F**) and plain radiographs (**G,H**) showing multiple myeloma involving the distal femur with extensive bone destruction. **I.** Most of the cortical diameter was destroyed, and even the remaining posterior cortex had been infiltrated and thinned by the disease, so distal femur resection with endoprosthetic reconstruction was carried out. **J.** The surgical specimen. **K.** Extensive and destructive metastasis of proximal femur, which leaves no option but resection of the proximal femur and reconstruction with prosthesis.

microscopic disease and is considerably less effective when applied to large tumor volume.

- Surgeries done for impending or current pathological fractures should, therefore, follow the same steps: first, removal of the tumor, and only then reconstruction (**FIG 4A–C**). The decision to perform intralesional tumor removal or proceed with a resection of the affected bone segment depends on the local extent of bone loss and proximity to the adjacent joint (**FIG 4D–K**).
- Because bone metastases usually have less soft tissue extension than do primary sarcomas of bone, resection of bone metastases usually does not require en bloc removal of the surrounding soft tissues (**FIG 5A,B**).
- Reconstruction must provide immediate stability that must not rely on biologic healing processes. Therefore, the use of autologous bone grafts, allografts, or allograft-prosthetic composites is inappropriate in surgery for MBD. Similarly, cementless prosthetic implants have no place in this setting.
- Reconstruction should include the combined use of hardware or prosthetic implants and bone cement (ie, polymethylmethacrylate). The latter is used to reinforce the hardware by increasing the diameter of the construct through which the mechanical load is transmitted and improving its attachment to the neighboring bone, thereby allowing the construct to withstand the mechanical stresses of immediate weight bearing and function.
- Stiffness and strength are related to the diameter of the intramedullary construct: the amount of stiffness in the act of bending is proportional to the diameter raised to the fourth power, and the strength in bending varies with the third power of the diameter (**FIG 5C–H**).

POSTOPERATIVE CARE

Rehabilitation

- Full weight bearing and passive and active range-of-motion exercises of the adjacent joints should be practiced as soon as possible, depending on wound healing and patient ability.

Adjuvant Radiation Therapy

- Postoperative external-beam radiation therapy of 3000 to 3500 Gy routinely is administered to the entire surgical field to control remaining microscopic disease. That dose of radiation does not impede callus formation if it is feasible, as determined by underlying fracture characteristics and the patient's overall status.[5–7] Radiation treatment is given to patients once the surgical wound has healed, usually 3 to 4 weeks after surgery.

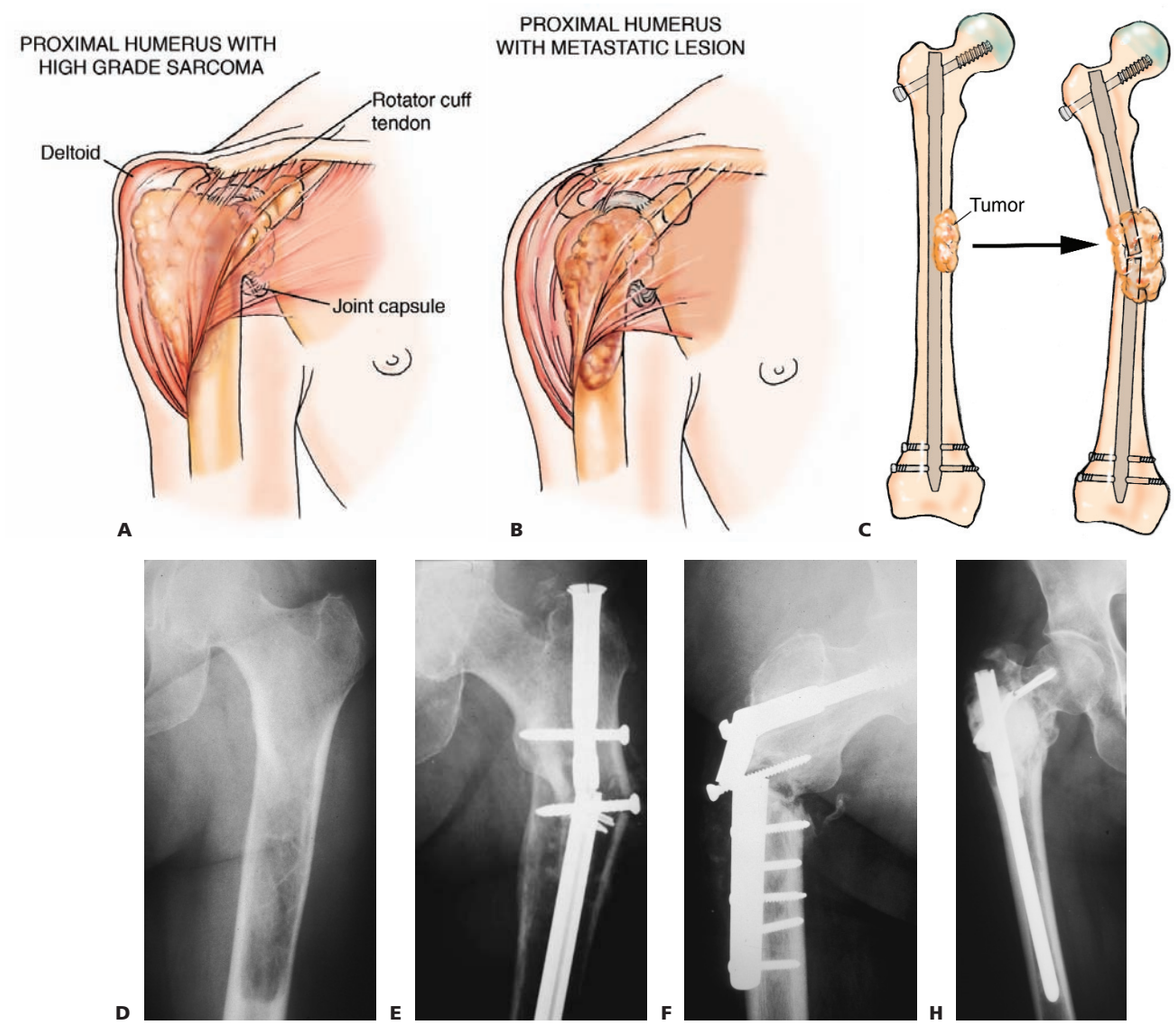

FIG 5 • A,B. Primary bone sarcomas usually have considerable extension into the soft tissues. Resection of such tumors at the proximal humerus would require en bloc removal of the overlying deltoid muscle, the rotator cuff tendons, and the joint capsule. Bone metastases, however, usually present with less extensive soft tissue involvement, and their resection involves removal of bony elements with only a thin layer of surrounding soft tissues. **C.** A metastatic bone lesion treated by closed nailing. This procedure is simple to perform, but it may fail, because tumor progression leaves the nail as the only load-transmitting component of the lower extremity, ultimately resulting in hardware failure and breakage. **D.** Plain radiograph showing an impending fracture of the femoral diaphysis due to multiple myeloma. Tumor removal, cemented nailing, and postoperative radiation most likely would have resulted in local tumor control and durable reconstruction. **E.** Closed nailing was done in this patient, however, and tumor progression (despite radiation) resulted in unavoidable hardware breakage. **F.** Similar outcome with uncemented fixation of metastatic renal cell carcinoma of the subtrochanteric region. **G.** Surgery should include meticulous tumor removal and filling of the entire tumor cavity with bone cement. **H.** Plain radiograph showing renal cell carcinoma (RCC) metastasis to the proximal femur treated with partial removal and cemented intramedullary fixation. RCCs usually are unresponsive to radiation therapy; the remaining tumor in this patient progressed and resulted in hardware failure at the hardware–cement interface.

PEARLS AND PITFALLS

Preoperative	■ Acquisition of data regarding patient's functional status pre-MBD ■ Consultation with patient's medical oncologist for current oncologic status and estimated survival ■ General assessment; rule out hypercalcemia ■ Plain radiographs of the entire affected bone ■ Total body bone scan before surgical intervention ■ Evidence of painful lytic long bone metastasis more than 2.5 cm in diameter, occupying over 50% of the cortical diameter, defines an impending fracture that requires prophylactic surgical intervention.
Intraoperative	■ Tumor resection is done first ■ Reconstruction should include cemented internal fixation—biologic reconstruction is inappropriate
Postoperative	■ Immediate weight bearing and range-of-motion exercises ■ External-beam radiation therapy

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