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Primary Leiomyosarcoma of Bone: A Rare Case Series with Review of Literature

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Abstract

Leiomyosarcoma (LMS) is an uncommon malignant spindle cell neoplasm of smooth muscles, accounting approximately 7% of soft tissue sarcoma. Primary LMS involving bone is an exceptional entity with very few cases described in the literature. The clinical, imaging, and pathological findings were analyzed retrospectively in three confirmed cases of primary LMS of bone. Pain and swelling were the patients' clinical symptoms. On imaging, LMS was often described as a solitary ill-defined lytic lesion with cortical breach depicted on radiograph or computed tomography (CT) scan. Magnetic resonance imaging (MRI) reveals a heterogeneous intermediate-hyperintense signal lesion on T2-weighted imaging (T2WI) with postcontrast enhancement. Histopathology reveals spindle cells arranged in fascicles with nuclear atypia and smooth muscle actin (SMA) positivity on immunohistochemistry (IHC)—consistent with diagnosis of LMS. The patients underwent surgical gross total resection with curative intent, followed by adjuvant chemotherapy or radiotherapy depending upon the stage and histological grade of LMS. On follow-up, the patients were disease free with no evidence of recurrence.

Keywords
- leiomyosarcoma
- immunohistochemistry
- MRI
- PET-CT
- case series

Introduction

Leiomyosarcoma (LMS) is an uncommon malignant spindle cell neoplasm of smooth muscles. It accounts for approximately 7% of soft tissue sarcomas.[1] LMS commonly occurs in the retroperitoneum and peritoneal cavities, but it also occurs in the uterus and the gastrointestinal tract. LMS of bone is very rate, accounting for approximately 0.06% of primary bone tumors and 0.14% of malignant bone tumors.[1] LMS seldom occurs in bones, with only very few cases described in the literature.

Case Reports

Case 1

A 25-year-old man presented with complaints of pain in the right thigh for the past 6 months. A radiograph (►**Fig. 1**) revealed a lytic lesion involving the diaphysis region in the mid-distal right femur with a pathological fracture. Whole-body fluorine-18 fluorodeoxyglucose (^{18}F-FDG) position emission tomography–computed tomography (PET-CT; ►**Fig. 1**) scan showed an intramedullary lytic lesion in the mid-distal right femur with cortical breach and adjacent metabolically active soft tissue component with maximum standard uptake value (SUVmax) of approximately 6.8. Contrast-enhanced magnetic resonance imaging (MRI; ►**Fig. 1**) revealed a heterogeneous intermediate-hyperintense lesion on short tau inversion recovery (STIR)/T2 images in the mid-distal right femur. There was an associated cortical breach with enhancing soft tissue noted. CT-guided biopsy was performed through a percutaneous route. Histopathology (►**Fig. 2**) showed malignant spindle cell tumor in the fascicles in the background of a dense hyalinized stroma exhibiting high-grade nuclear atypia, brisk mitosis, and necrosis. On immunohistochemistry (IHC), the tumor cells showed

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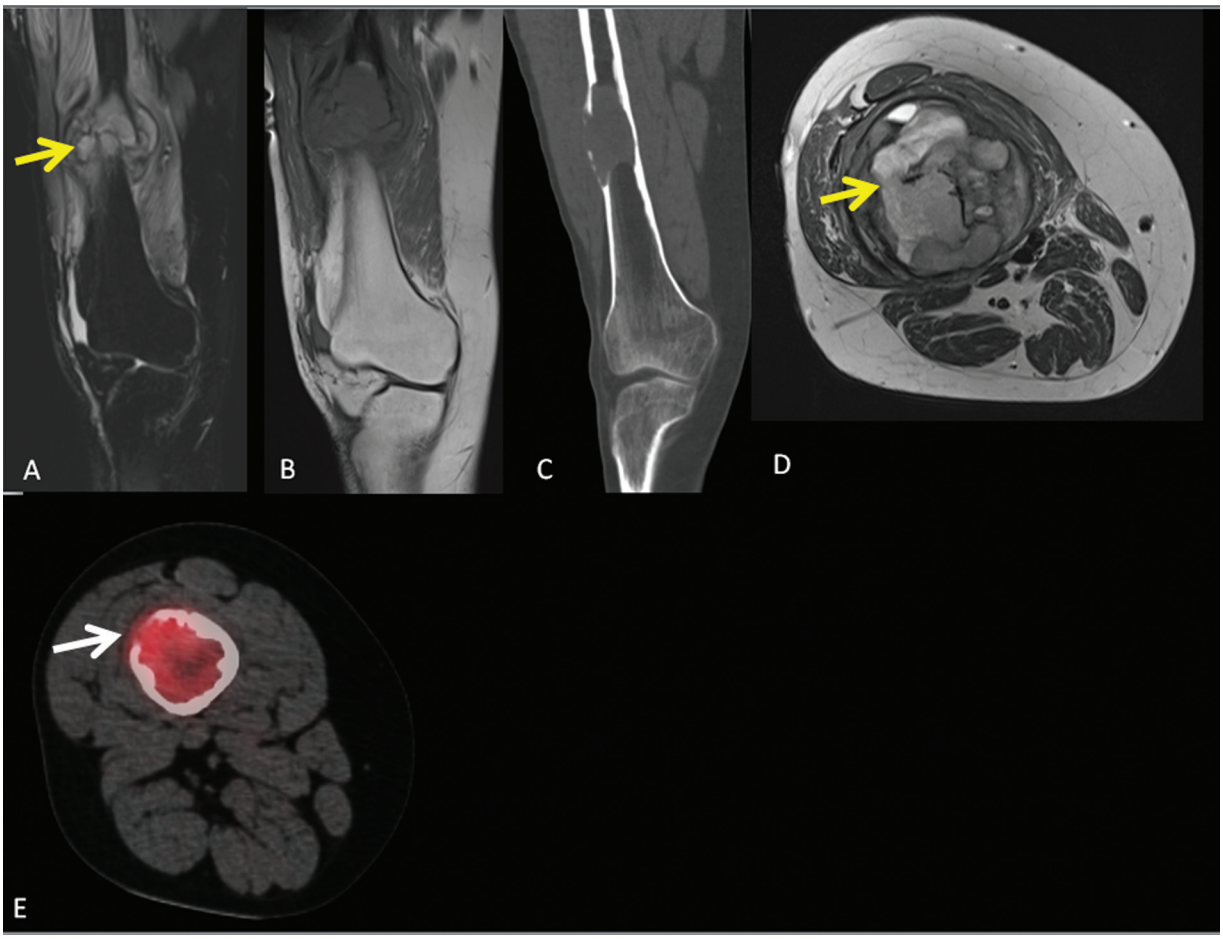

Fig. 1 Coronal STIR MRI (**A**), T1 MRI images (**B**), Coronal CT (**C**) and axial T2 MRI(**D**) images reveals heterogeneous hyperintense lesion (yellow arrows) involving the mid-shaft of the right femur with associated cortical erosions and breech with adjacent metabolically active soft tissue component with SUVmax-6.8 on PET-CT (white arrows-E) images. Abbreviations- Magnetic resonance imaging (MRI), Position emission tomography–computed tomography (PET-CT), short tau inversion recovery (STIR), maximum standard uptake value (SUVmax).

positivity for smooth muscle actin (SMA) and h-caldesmon (►**Fig. 2**) and negativity for Smooth muscle myosin heavy chain (SMMH), desmin, MyoD1, myogenin, CD68, S-100. The final diagnosis of LMS (Fédération Nationale des Centres de Lutte Contre le Cancer grade 3) was made. The patient underwent surgical intervention in the form of diaphyseal resection and reconstruction with an intramedullary nail and bone cement, followed by adjuvant chemotherapy.

Case 2

A 13-year-old adolescent boy presented with pain and progressive swelling in the left leg around the knee joint for the past 4 months. There was no history of trauma. The frontal radiograph (►**Fig. 3**) showed an ill-defined lytic lesion in the metaphysis of the proximal left tibia. Whole-body ^{18}F-FDG PET-CT (►**Fig. 3**) showed an irregular lytic lesion with cortical breach and adjacent metabolically active soft tissue component in the epi-metaphysis region of the left proximal tibia. MRI (►**Fig. 3**) revealed altered signal intensity intramedullary lesion in the proximal tibia with wide zone of transition associated with a cortical breach and heterogeneous enhancing soft tissue extending into the intramuscular compartment and showing diffusion restriction on diffusion-weighted imaging (DWI). A skip lesion was also seen in the right medial femoral condyle. A CT-guided biopsy was performed through the percutaneous route. Histopathology (►**Fig. 2**) revealed diffuse proliferation of neoplastic spindle cells organized in the fascicles exhibiting moderate nuclear atypia with increased mitosis and areas of necrosis. On IHC, tumor cells were positive for SMA and negative for CK, S100, TLE1, S100, ERG1, STAT6, SMMH, SATB2, desmin, myogenin, and MyoD1, and led to the final diagnosis of LMS. The patient underwent surgical intervention in the form of left proximal tibial resection with mega-prosthesis and flap reconstruction, followed by adjuvant chemotherapy.

Case 3

A 34-year-old man presented with complaints of pain in the left knee for the past 1 year. CT of the left knee revealed ill-defined lytic areas in the medial condyle and the intercondylar region. An MRI (►**Fig. 4**) showed left medial femoral condyle/epicondyle altered marrow signal intensity lesion with perilesional edema and mildly thickened adjacent soft tissue with irregularity of the articular surface. A CT-guided biopsy was performed through the percutaneous route.

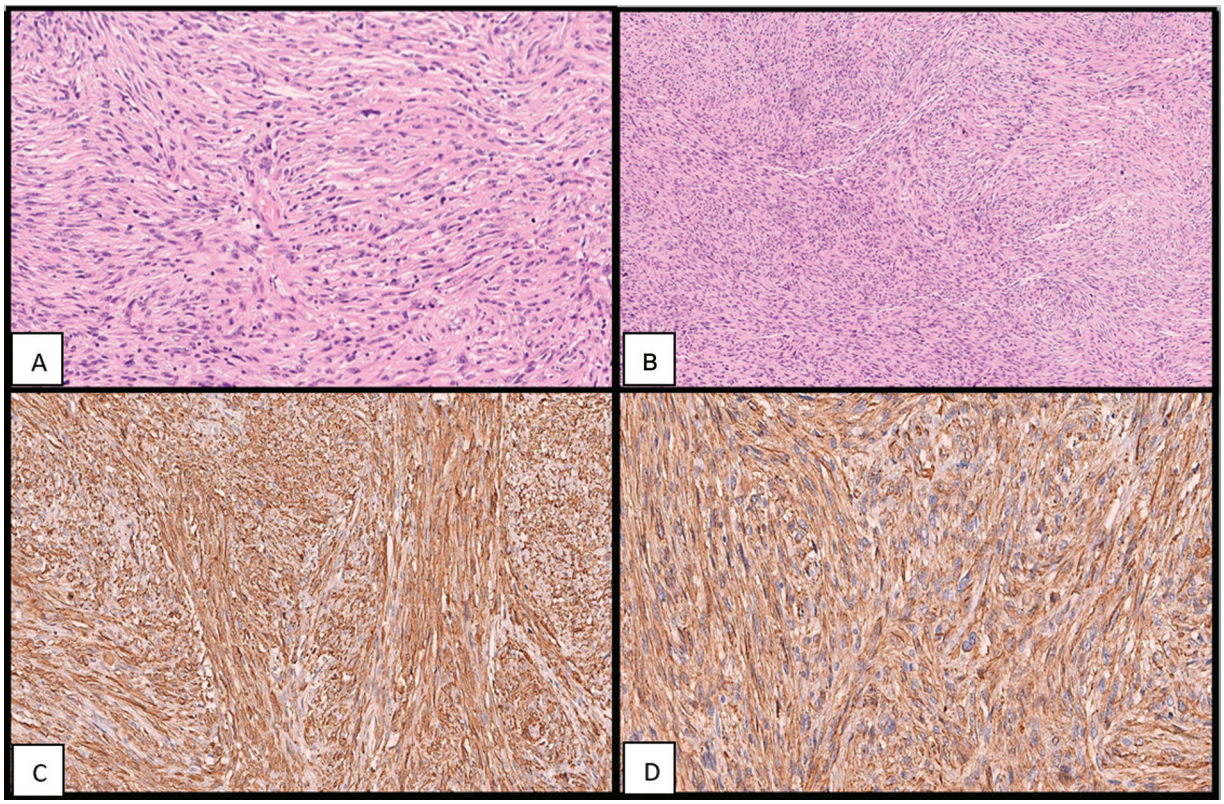

Fig. 2 (**A**, **B**) Histopathology image (in low- and high-power view) reveals spindle-shaped cells arranged in the fascicles in the background of a dense hyalinized stroma exhibiting high-grade nuclear atypia and brisk mitosis. On immunohistochemistry (IHC), the tumor cells are immunopositive for (**C**) smooth muscle actin (SMA) and (**D**) caldesmon.

Histopathology (►**Fig. 2**) revealed neoplastic spindle cells arranged in the fascicles and sheets entrapping the native bony tissue exhibiting mild nuclear atypia with low mitosis. On IHC, the tumor cells were positive for SMA and SMMH and negative for SATB2, CDK4, MDM2, desmin, and B-catenin. The final diagnosis of LMS, grade 1, was made. The patient underwent wide local excision of the left distal femur with a megaprosthesis reconstruction.

Discussion

Primary bone LMS is an uncommon sarcoma type first reported in 1965, comprising only less than 0.7% of all primary malignant bone tumors.[1] Regarding the origin of LMS, studies suggest that the tumors may arise from smooth muscle cells in the bone marrow cavity or mesenchymal stem cells that can differentiate into smooth muscle cells that can form the connective tissue matrix.[1,2]

LMS mainly presents in the middle age. There is no gender predilection, with males and females equally affected. The presenting complaints are mainly bone pain, pathological fractures, and swelling in the affected limb. Long bones, mainly the femur, tibia (around the knee joint), and humerus, are the commonly involved sites with primarily involvement of metaphysis with extension into the epiphysis and diaphysis.[1–3] Plain radiography usually reveals ill-defined lytic lesions with indistinct margins, cortical breach, and associated soft tissue component with no evidence of any osteoid or chondroid bone matrix.[1,3,4] CT helps describe alterations in the bone structure such as a cortical breach/destruction. MRI better delineates adjacent soft tissue component, skip lesions, and involvement of adjacent neurovascular bundles. ^{18}F-FDG PET-CT is useful for local evaluation of the primary lesion, detection of systemic metastasis to the lung, bone, or liver, and response evaluation after chemotherapy. Definitive diagnosis is made by biopsy under imaging guidance, usually CT or ultrasonography.[1,3,4]

As primary LMS of the bone is extremely rare, histopathology examination is the gold standard, and the histopathological features of LMS are similar to the LMS seen in other body sites showing smooth muscle differentiation. The characteristic histological features are spindle-shaped cells arranged in the fascicles with elongated, blunt-ended nuclei showing nuclear hyperchromatism, pleomorphism, abundant eosinophilic and fibrillary cytoplasm, and variable grade of nuclear atypia, mitosis, and necrosis depending on grade. On IHC, cells show positivity for SMA, desmin, and h-caldesmon in most of LMSs. SMA is the most sensitive and relatively specific marker.[1–4]

The mainstay of management is surgery with wide local excision of the lesion with curative intent. Amputation is performed for the cases where there is extensive soft tissue

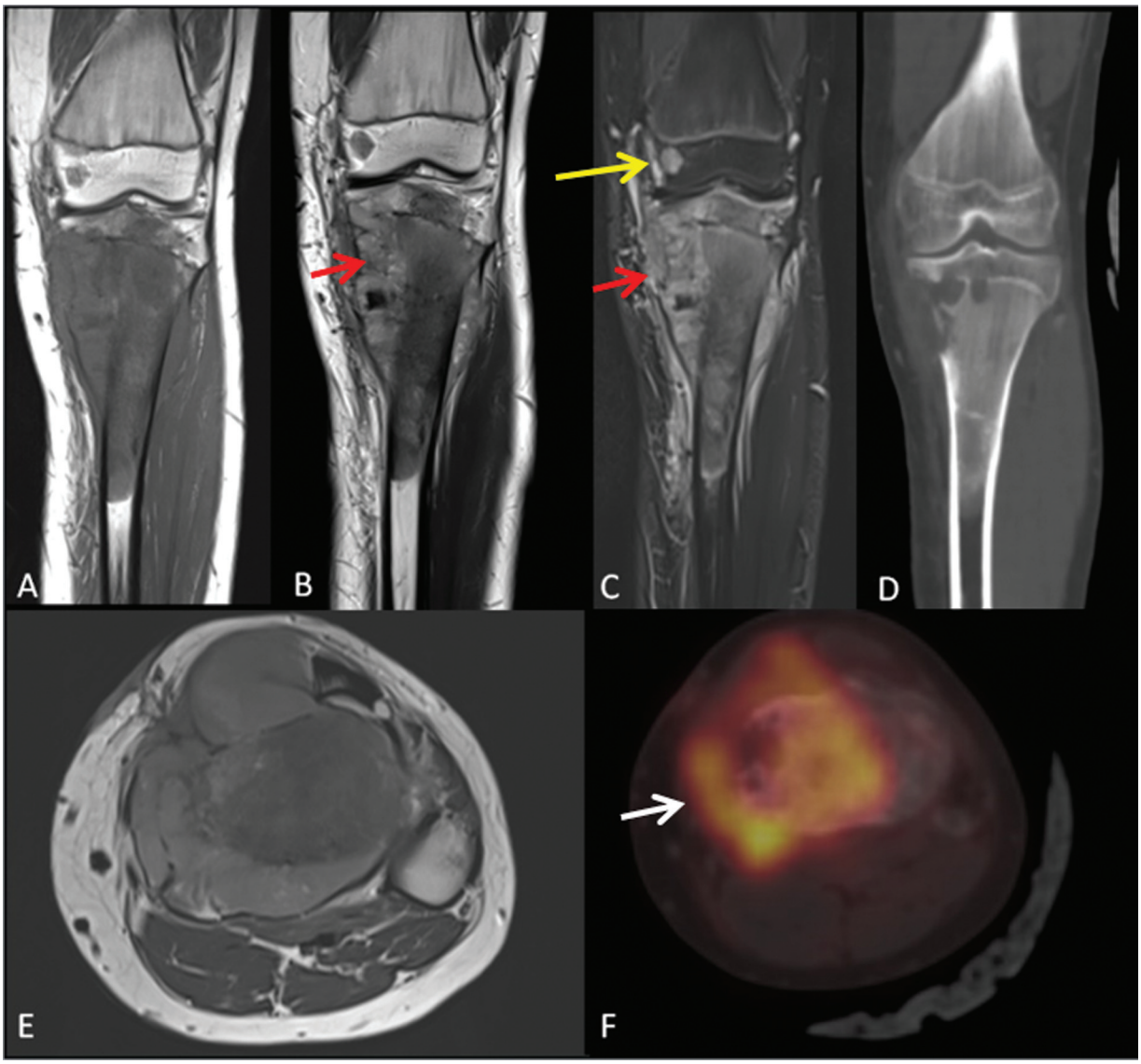

Fig. 3 Coronal T1 MRI (**A**), T2 MRI images (**B**), Coronal STIR (**C**) Coronal CT (**D**) and axial T2 MRI (**E**) images reveals heterogeneous hyperintense lytic lesion (red arrows) involving the epi-metaphysis region with cortical erosions (**D**) and adjacent metabolically active soft tissue component on (PET-CT) images(white arrows). STIR hyperintense skip lesion (yellow arrows in C)–was also seen in the right medial femoral condyle. Abbreviations- Magnetic resonance imaging (MRI), Position emission tomography–computed tomography (PET-CT), short tau inversion recovery (STIR).

involvement or adjacent to the neurovascular bundle.[5] In cases of metastatic LMS, chemotherapy is the main approach, with the most effective chemotherapeutic agents as first-line therapy being doxorubicin-based chemotherapy, cisplatin, dacarbazine, and ifosfamide.[1,6]

In our cases, the patients underwent radical surgery, followed by adjuvant chemotherapy in the first two cases, and in third case, surgery was the only definitive treatment. The patients were kept on follow-up with postoperative radiographs (►**Fig. 5**), ultrasonography of the local region, and PET-CT imaging every 6 months with no evidence of disease recurrence/metastases.

The main differential diagnoses of primary bone LMS are osteosarcoma, chondrosarcoma, fibrosarcoma, synovial sarcoma, undifferentiated pleomorphic sarcoma, and metastases.[7]

Osteosarcoma is ruled out by lack of osteoid matrix, and lack of cartilage production/chondroid matrix rules out chondrosarcoma.[7] Fibrosarcoma and undifferentiated pleomorphic sarcoma are diagnoses of exclusion due to lack of specific immunohistochemical and genetic markers.[7,8] Synovial sarcoma have monotonous spindled cells with scanty cytoplasm and specific chromosomal translocation t(X; 18) (p11; q11) with expression of TLE1, epithelial membrane antigen, and keratins.[9] Metastases lack myogenic markers like SMA and desmin.

Conclusion

LMS of bone is an exceptional occurrence. MRI and PET-CT imaging play an important role in local staging and for metastatic workup, respectively. Histopathology and

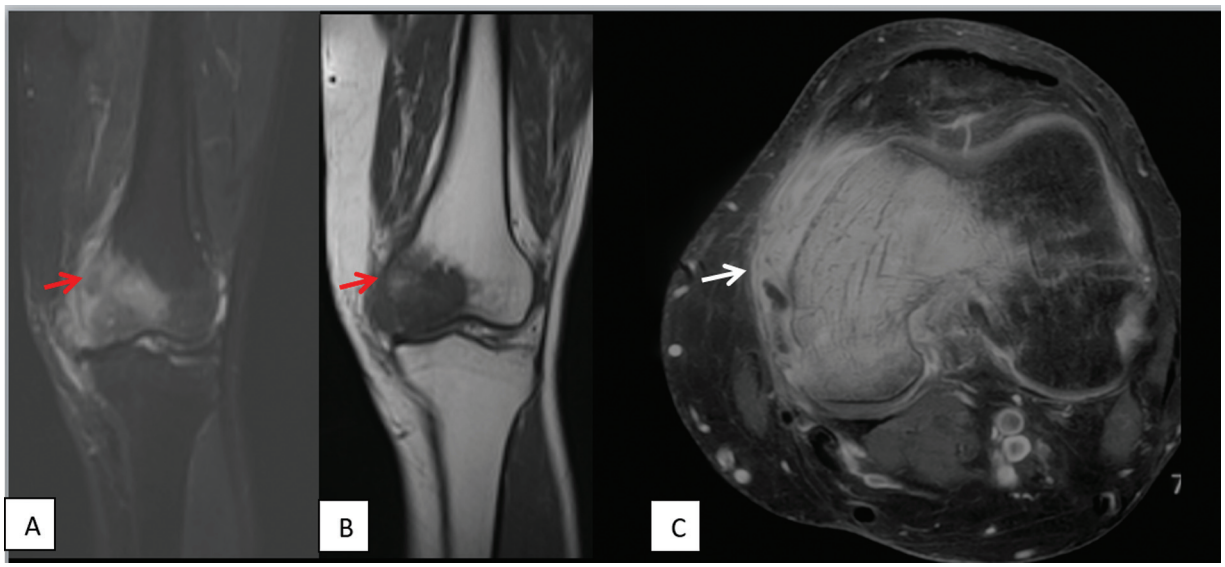

Fig. 4 (A) Heterogeneous hyperintense lesion on short tau inversion recovery (STIR) coronal image (*red arrow*), (B) hypointense on T1 coronal image of magnetic resonance imaging (MRI; *red arrow*) involving the (C) left medial femoral condyle with adjacent soft tissue component showing enhancement (*white arrow*) on axial postcontrast T1 images.

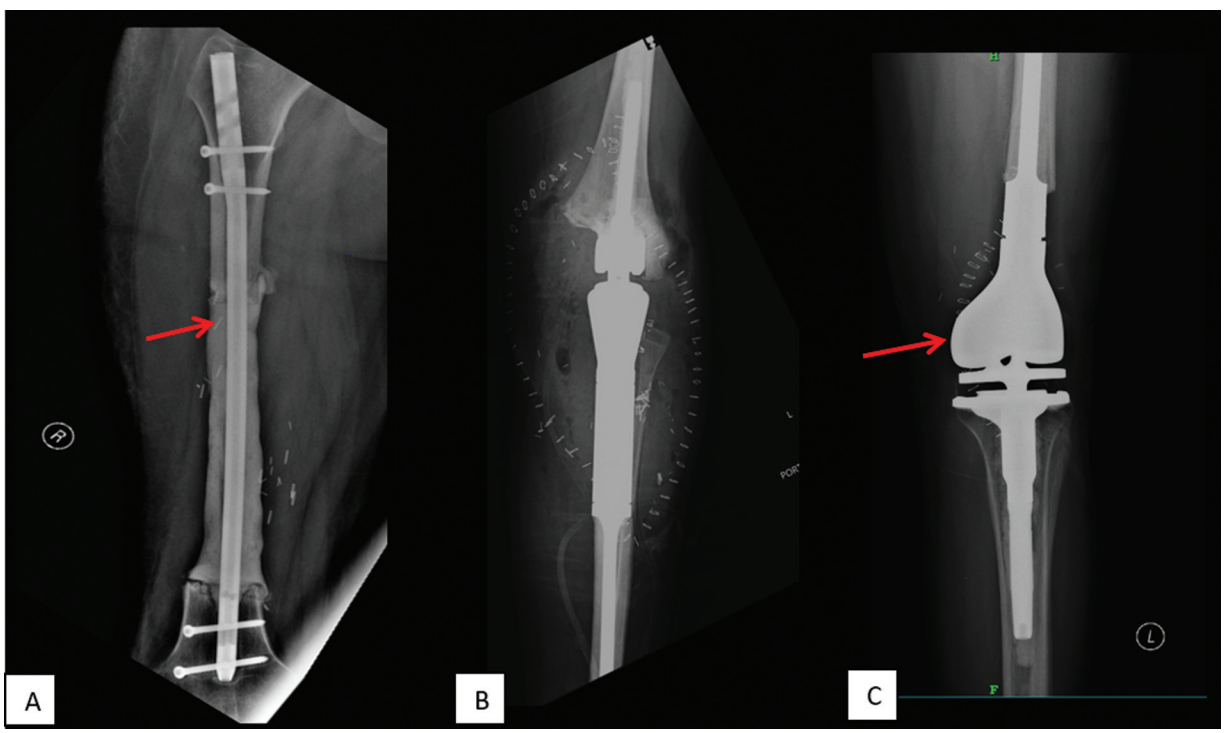

Fig. 5 (A–C) Postoperative radiographs of all three patients showing the postoperative status after resection, with the reconstruction prosthesis in situ (*red arrows*).

immunohistochemical examination remain the gold standard. Early diagnosis and treatment are essential for a favorable outcome as metastatic disease carries a worse prognosis.

Ethical Approval

This study was conducted following the Declaration of Helsinki. The Institutional Review Board of our hospital approved the study protocol, and all regulations were followed. The requirement for informed consent was waived by the board due to the retrospective nature of the study.

Patient Consent

Informed consent is waived by the IRB due to retrospective nature of study.

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None.

Conflict of Interest
None declared.

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