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Giant Cell-Rich Osteosarcoma and Osteopoikilosis: A Case Report

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Abstract

Osteopoikilosis is a rare, usually asymptomatic sclerosing bone dysplasia characterized by multiple small, well-defined sclerotic bone islands. In patients with a primary bone malignancy, these lesions may mimic osteoblastic metastases and complicate staging. A 20-year-old man presented with a four-month history of progressive right foot pain, including rest and nocturnal pain, an antalgic gait, and a palpable lateral calcaneal mass. There was no family history of malignant diseases or inherited musculoskeletal conditions. Radiographs and magnetic resonance imaging demonstrated an aggressive osteolytic lesion of the calcaneus with cortical destruction and soft-tissue extension. Histopathological examination of an open biopsy demonstrated a giant cell-rich osteosarcoma. Staging computed tomography showed multiple small sclerotic lesions throughout the skeleton. These lesions had the characteristic distribution of osteopoikilosis and showed no abnormal radiotracer uptake on bone scintigraphy, supporting a diagnosis of osteopoikilosis rather than osteoblastic metastatic disease. This case illustrates the diagnostic challenge created by the coexistence of osteopoikilosis and a primary malignant bone tumor. In patients with osteosarcoma and multiple sclerotic skeletal lesions, recognition of the characteristic imaging pattern of osteopoikilosis and correlation with bone scintigraphy can prevent erroneous upstaging as metastatic disease. The coexistence of osteopoikilosis and osteosarcoma appears to be exceptionally uncommon, and current evidence is insufficient to establish a causal relationship.

Categories: Oncology, Orthopedics
Keywords: diferential diagnosis of malignancy, giant cell-rich osteosarcoma (gcro), lower limb malignancy, orthopedic oncology, osteopoikilosis

Introduction

Osteopoikilosis is a benign sclerosing bone dysplasia characterized by multiple small, well-defined foci of compact bone within cancellous bone, commonly referred to as bone islands or enostoses. These lesions typically have a bilateral, relatively symmetrical periarticular distribution, particularly in the epiphyses and metaphyses of long bones, pelvis, and small bones of the hands and feet [1,2]. The condition may be inherited in an autosomal dominant pattern or occur sporadically, and it is usually detected incidentally in otherwise asymptomatic individuals [2,3]. Its clinical importance lies principally in its resemblance to osteoblastic skeletal metastases. In a patient undergoing investigation for a primary malignancy, misinterpretation of these benign sclerotic foci may affect assessment of disease extent and subsequent management. Recognition therefore depends on the combined evaluation of lesion morphology, anatomical distribution, and clinical context, with bone scintigraphy providing complementary information when the distinction remains uncertain [2-4].

Giant cell-rich osteosarcoma presents a different but equally important diagnostic challenge. This uncommon histological variant contains numerous osteoclast-like giant cells admixed with a malignant mononuclear cell population and variable amounts of tumor osteoid, the unmineralized bone matrix produced by malignant cells [5,6]. Its predominantly osteolytic appearance and giant cell-rich morphology may closely resemble giant cell tumor of bone, particularly when biopsy specimens contain limited osteoid or only subtle stromal atypia [5,6]. The distinction requires integration of imaging with representative histopathological examination, rather than reliance on the presence of giant cells alone. A calcaneal origin adds to the diagnostic complexity because primary malignant tumors of the heel bone are uncommon and may be difficult to recognize promptly [7]. When a suspected malignant calcaneal lesion occurs together with multiple sclerotic skeletal foci, accurate evaluation must therefore address both the identity of the primary tumor and the nature of the additional bone lesions.

We present the case of a 20-year-old man with a calcaneal tumor diagnosed as giant cell-rich osteosarcoma and additional skeletal lesions interpreted as osteopoikilosis. The report focuses on two distinct diagnostic questions: differentiating the primary lesion from giant cell tumor of bone and distinguishing the accompanying sclerotic foci from skeletal metastases. Its educational value lies in demonstrating the need for coordinated pathological and radiological assessment during diagnosis and staging. The coexistence of

these findings in a single patient does not establish a causal relationship.

Case Presentation

A 20-year-old male patient has been referred for assessment of a four-month history of progressive right foot symptoms. The patient reported continuous pain, including pain at rest and nocturnal pain, accompanied by an antalgic gait. He had no significant past medical history. On physical examination, a palpable soft-tissue mass was noted on the lateral aspect of the right calcaneus. Plain radiographs of the calcaneus in two projections demonstrated osteolytic changes with an associated soft-tissue mass in the lateral calcaneal region, as well as multiple small sclerotic foci in other bones of the same foot, consistent with bone islands (Figure *1*). Magnetic resonance imaging with gadolinium contrast revealed an extensive tumor involving the lateral portion of the calcaneus, with destruction of the lateral cortical bone and extension into the surrounding soft tissues (Figure *2*). Routine laboratory investigations did not demonstrate any findings suggestive of concomitant infectious disease.

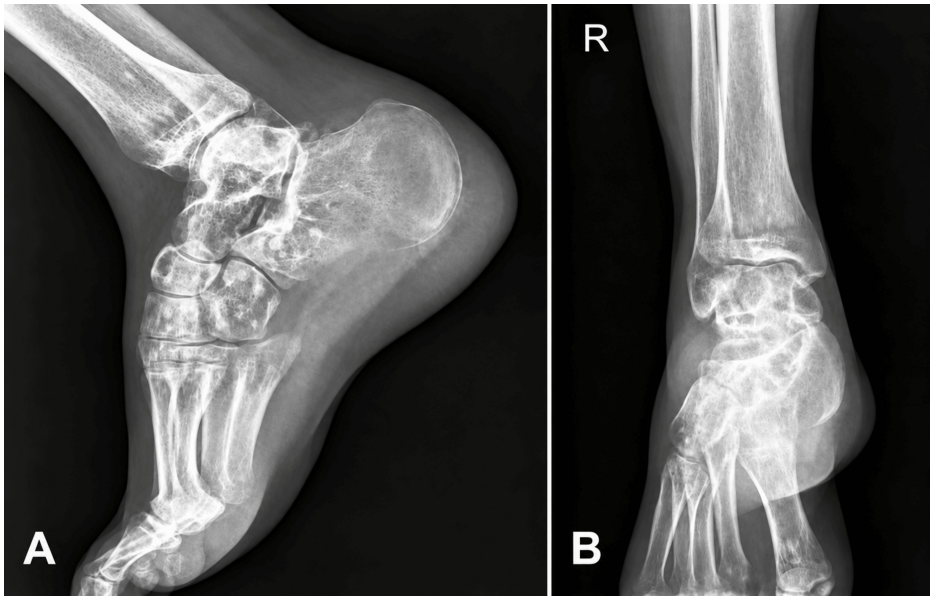


FIGURE 1: A) Lateral and B) anteroposterior (AP) X-ray of the patient at presentation show a large osteolytic lesion of the right calcaneus with soft tissue mass and destruction of the lateral cortex of the calcaneus.

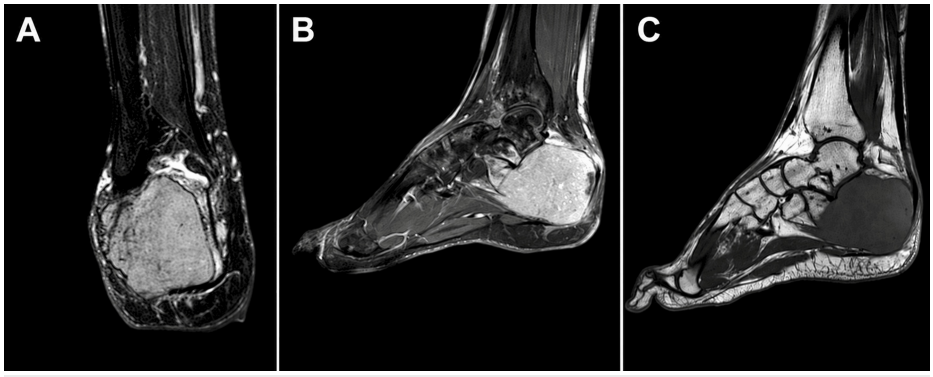


FIGURE 2: MRI examination of the right foot. (A) Coronal T2-weighted MRI with gadolinium shows a high-signal lesion. (B) T1-SPIR sagittal image of the calcaneus demonstrates a large expansile lesion involving nearly the entire calcaneus. (C) T1-weighted sagittal image.

Based on these findings, the initial clinical impression was that of a primary osseous tumor with soft-tissue extension. To establish a definitive diagnosis, an open biopsy was performed through a lateral approach to the calcaneus, in accordance with standard oncologic biopsy principles. Histopathological evaluation posed

a diagnostic challenge in differentiating between giant cell tumor and giant cell-rich osteosarcoma. The presence of moderately atypical mononuclear stromal cells, rare atypical mitotic figures, and abundant lace-like osteoid production supported the diagnosis of giant cell-rich osteosarcoma of the right calcaneus. For complete disease staging, computed tomography of the chest and abdomen was performed. Although no visceral metastases were detected, multiple small, high-density sclerotic bone lesions ranging from 1.5 to 9.5 mm were identified throughout the skeleton, predominantly in the regions of the shoulders, pubic symphysis, sacroiliac joints, and hips (Figure 3). These lesions were not associated with cortical destruction or periosteal reaction.

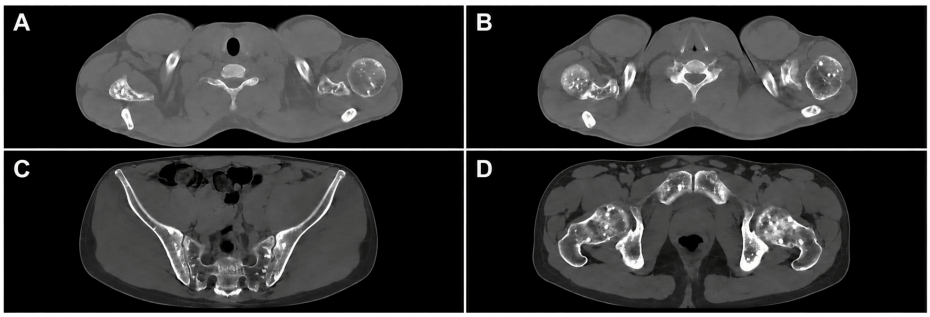


FIGURE 3: Chest and abdomen CT. Small, round osteosclerotic lesions, mostly in the epiphyses of the large bones (A, B, and D) and the sacroiliac joints (C).

Additional radiographic evaluation of the hands and shoulders, together with the chest radiograph findings, supported the diagnosis of osteopoikilosis. To further differentiate these sclerotic lesions from osteoblastic metastases, bone scintigraphy was performed. The scan demonstrated increased radiotracer uptake exclusively in the region of the right calcaneus corresponding to the primary tumor site (Figure 4). By contrast, no abnormal uptake was observed in the remaining sclerotic skeletal lesions. The combination of characteristic radiographic findings in the extremities (Figure 5) and the absence of scintigraphic activity in the sclerotic foci confirmed the diagnosis of osteopoikilosis. Finally, microscopic examination revealed focal areas of mononuclear cells exhibiting mild to moderate atypia, occasional atypical mitotic figures, and abundant lace-like osteoid (Figure 6).

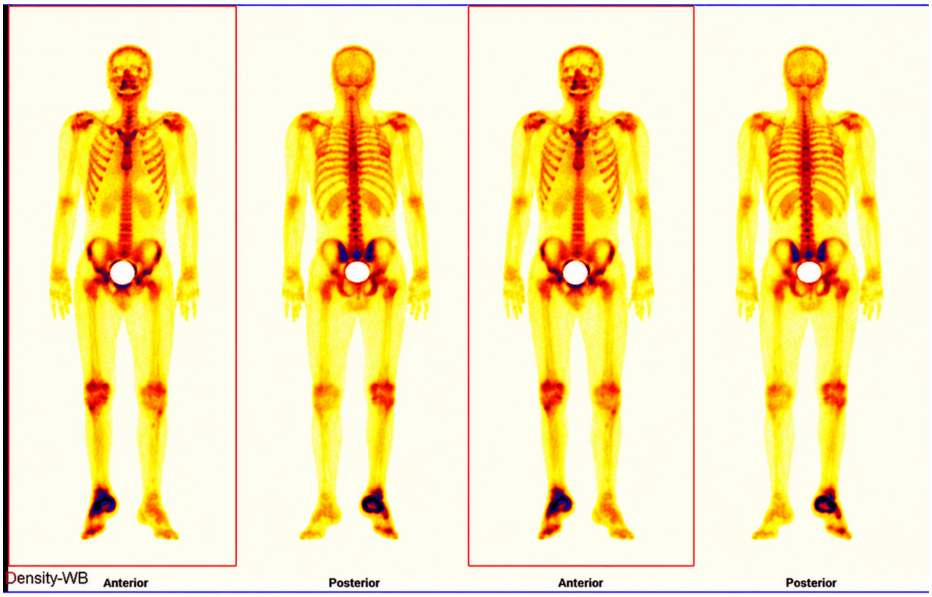


FIGURE 4: Bone scintigraphy showing increased uptakearound around the right foot.

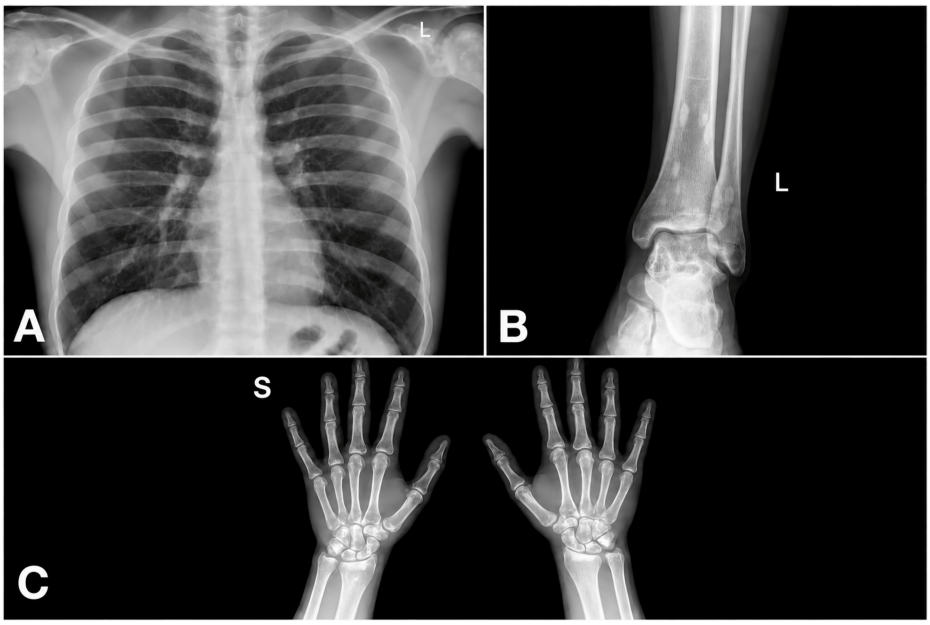


FIGURE 5: X-rays of the patient showing bone islands all over the skeleton: A) chest, B) distal tibia, and C) both hands.

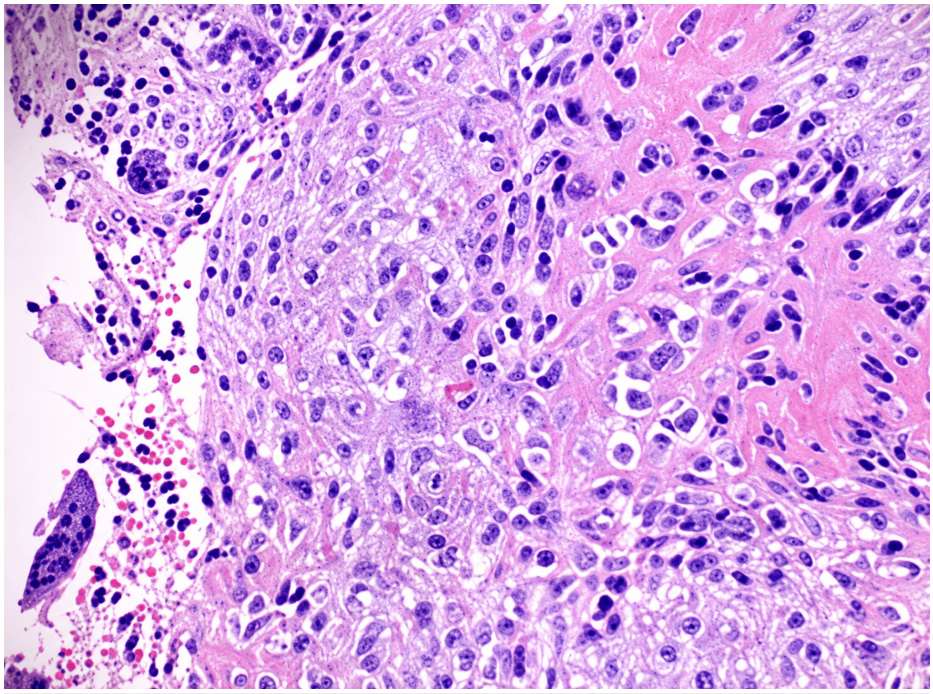


FIGURE 6: Microscopic examination is suggestive of focally located mild to moderate atypical mononuclear cells, a few atypical mitotic figures, and abundant lace-like osteoid.

VAS scores and follow-up

At initial presentation, the patient reported severe persistent pain in the right heel and hindfoot, including rest pain and nocturnal pain. The baseline visual analogue scale score was 8/10 during weight-bearing, 7/10 at rest, and 8/10 at night. His pain was associated with progressive limitation of ambulation and an antalgic gait. Following open biopsy, the patient experienced a transient increase in local pain, with a VAS score of 7/10 during the first postoperative week, which improved to 5/10 with analgesic treatment and protected weight-bearing. At the 12-month follow-up after the surgery, the patient reported no significant pain at the

primary tumor site, with a VAS score of 0-1/10 (Table *1*).

Time point	Clinical status	VAS pain score
Initial presentation	Continuous heel pain, rest pain, nocturnal pain, antalgic gait	8/10 weight-bearing, 7/10 rest
Post-biopsy, week 1	Local postoperative pain, controlled with analgesia	7/10
Pre-definitive treatment	Persistent mechanical and rest pain	5–6/10
12 months	Pain-free or minimal occasional discomfort; no clinical or radiological evidence of local recurrence or distant metastasis	0–1/10

TABLE 1: Presentation of Visual Analog Scale (VAS) scores from initial presentation to 12 months postop.

Discussion

Interpretation of the sclerotic lesions

The principal staging challenge in this patient was the interpretation of multiple sclerotic skeletal lesions in the presence of a malignant primary bone tumor. The reported small lesion size, rounded morphology, bilateral periarticular distribution, and absence of cortical destruction or periosteal reaction favored osteopoikilosis. Their distribution contrasted with the destructive calcaneal lesion and its soft-tissue extension. These observations should be interpreted collectively: neither a rounded sclerotic focus nor the absence of aggressive features is independently sufficient to establish benignity. The imaging pattern described in osteopoikilosis provides the relevant framework for this distinction [1-3]. Comparison with previous or subsequent imaging can provide further support through demonstrated stability, but stability should not be claimed for this patient unless serial examinations are available [2].

Contribution and limitations of scintigraphy

The absence of abnormal radiotracer uptake corresponding to the additional sclerotic foci supported the imaging interpretation of osteopoikilosis. Tsai et al. described concordant anatomical and functional findings using Tc-99m MDP scintigraphy with regional SPECT/CT [4]. Di Primio and Ng et al. discuss the value of characteristic imaging patterns and the generally low scintigraphic activity of osteopoikilosis, while also noting that occasional uptake can occur [2,3]. In this patient, the scintigraphic findings should therefore be interpreted alongside the morphology, symmetry, and distribution of the sclerotic lesions, rather than presented as an independently conclusive exclusion of metastases. The scintigraphic technique used in this patient must be identified from the original acquisition record; the SPECT/CT protocol of another report must not be attributed to this case.

Pathological distinction from a giant cell tumor of bone

The primary tumor introduces a separate diagnostic problem. In their nine-patient series, Wang et al. described the close clinical, radiological, and pathological resemblance of giant cell-rich osteosarcoma to giant cell tumor of bone, including initial diagnostic errors when malignant osteoid was inconspicuous or inadequately sampled [5]. Chow further demonstrated the morphological diversity of this tumor and emphasized the relationship between atypical mononuclear cells, pericellular osteoid, and infiltrative growth [6]. In the present manuscript, mononuclear atypia, occasional atypical mitoses, and lace-like osteoid are reported. The final pathological account should explicitly establish that the osteoid was deposited directly by malignant cells and describe the abundance and distribution of osteoclast-like giant cells. Neither the term “giant cell-rich” nor an aggressive radiological appearance can substitute for these observations. Representative low-power images of the architecture and higher-power images of malignant osteoid are particularly important to make the diagnostic reasoning reproducible.

Genetic context

Ben-Asher et al. reviewed the role of LEMD3 in osteopoikilosis and the biological implications of the genetic findings [8]. This genetic background concerns the sclerosing dysplasia and must be distinguished from the histological classification of the calcaneal tumor. LEMD3 testing was not performed in the present case, limiting molecular characterization of osteopoikilosis without establishing or excluding osteosarcoma. The coexistence of osteopoikilosis and a malignant bone tumor in this patient does not establish that the dysplasia caused the tumor or quantify an increased risk of sarcoma.

Calcaneal location and clinical implications

The calcaneal site provides additional context. Newman et al. assembled a pooled cohort of 131 patients with calcaneal malignancies, including osteosarcoma, illustrating both the rarity of these tumors and the challenges posed by this functionally important anatomical location [7]. Because that study included several malignant diagnoses, its outcomes should not be interpreted as giant cell-rich osteosarcoma-specific estimates or used to predict this patient's prognosis. In the present case, progressive pain at rest and at night, cortical destruction, and soft-tissue extension warranted investigation of the primary lesion independently of the benign-appearing sclerotic foci. The final report should state the documented tumor dimensions, clinical stage, and immediate management decision, then explain how interpreting the additional lesions as osteopoikilosis influenced that decision. It should not infer a particular stage, treatment intent, or outcome from the absence of abnormal uptake alone.

Limitations and educational contribution

As a single-patient observation, this report cannot establish the diagnostic accuracy of scintigraphy, determine the frequency of coexistence, or demonstrate improved clinical outcomes from a particular diagnostic strategy. The lack of LEMD3 testing should be acknowledged specifically as a limitation of genetic characterization. Any absence of serial imaging, long-term outcomes, or ancillary pathological investigations should be stated only after checking the source records. The main educational contribution is the separation of two diagnostic tasks: establishing the nature of a giant cell-rich primary tumor and assessing additional sclerotic lesions without automatically assigning skeletal metastatic disease. Both tasks require integration of clinical, imaging, and pathological evidence.

Conclusions

Osteopoikilosis is a benign skeletal dysplasia that can closely mimic osteoblastic metastatic disease on radiographs and CT. In a patient with a primary bone malignancy, recognition of its characteristic distribution and correlation with bone scintigraphy can prevent erroneous metastatic staging. Giant cell-rich osteosarcoma is a rare diagnostic entity that requires careful correlation of imaging and histopathological findings, particularly because of its resemblance to giant cell tumor of bone. Although osteosarcoma and other primary bone tumors have been reported in patients with osteopoikilosis, current evidence is insufficient to establish a causal relationship or a clinically meaningful increased risk of malignant transformation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Konstantinos Zygogiannis, Dritan Pasku, Artan Bano, Teona Bushati

Drafting of the manuscript: Konstantinos Zygogiannis, Dritan Pasku

Critical review of the manuscript for important intellectual content: Konstantinos Zygogiannis, Dritan Pasku, Artan Bano, Teona Bushati

Supervision: Konstantinos Zygogiannis, Dritan Pasku

Acquisition, analysis, or interpretation of data: Dritan Pasku, Artan Bano

Disclosures

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References

1. Greenspan A: Sclerosing bone dysplasias--a target-site approach . Skeletal Radiol. 1991, 20:561-83. 10.1007/BF01106087
2. Di Primio G: Benign spotted bones: a diagnostic dilemma . CMAJ. 2011, 183:456-9. 10.1503/cmaj.091740
3. Ng C, Schwartzman L, Moadel R, Haigentz M Jr: Osteopoikilosis: a benign condition with the appearance of

metastatic bone disease. J Clin Oncol. 2015, 33:e77-8. 10.1200/JCO.2013.50.5222

4. Tsai SY, Wang SY, Shiau YC, Wu YW: Benign incidental findings of osteopoikilosis on Tc-99m MDP bone SPECT/CT: a case report and literature review. Medicine (Baltimore). 2016, 95:e3868. 10.1097/MD.0000000000003868
5. Wang CS, Yin QH, Liao JS, Lou JH, Ding XY, Zhu YB: Giant cell-rich osteosarcoma in long bones: clinical, radiological and pathological features. Radiol Med. 2013, 118:1324-34. 10.1007/s11547-013-0936-9
6. Chow LT: Giant cell rich osteosarcoma revisited-diagnostic criteria and histopathologic patterns, Ki67, CDK4, and MDM2 expression, changes in response to bisphosphonate and denosumab treatment. Virchows Arch. 2016, 468:741-55. 10.1007/s00428-016-1926-9
7. Newman ET, van Rein EA, Theyskens N, Ferrone ML, Ready JE, Raskin KA, Lozano Calderon SA: Diagnoses, treatment, and oncologic outcomes in patients with calcaneal malignances: case series, systematic literature review, and pooled cohort analysis. J Surg Oncol. 2020, 122:1731-46. 10.1002/jso.26205
8. Ben-Asher E, Zelzer E, Lancet D: LEMD3: the gene responsible for bone density disorders (osteopoikilosis) . Isr Med Assoc J. 2005, 7:273-4.