Lack of hypervascularity on three phase bone scan : Osteoid osteoma revisited.

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Abstract

Osteoid osteoma is a benign skeletal neoplasm of unknown aetiology that is composed of osteoid and woven bone. The tumor is usually smaller than 1.5 cm in diameter. Osteoid osteoma can occur in any bone, but in approximately two thirds of patients, the appendicular skeleton is involved. The skull and facial bones are involved exceptionally. Radionuclide Scans virtually always show increased uptake of isotope. The average time from the onset of symptoms to diagnosis is reported to be 28 months with spinal tumours. Radionuclide bone scanning reduces the time to diagnosis in 66% of patients. The sensitivity of radionuclide bone scans is extremely high as it can demonstrate the tumour before abnormal radiographic findings are apparent. Classically a three phase bone scan shows increased vascularity and increased uptake in an osteoid osteoma. But it is not always the case. We present here a pictorial assay of our experience in imaging osteoid osteoma in twenty six patients. It is evident that scintigraphic evidence of hypervascularity is not always present in osteoid osteomas.

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Introduction

Osteoid osteoma is the third most commonly occurring benign tumour of the bones (1). Most patients with osteoid osteoma are young. Rarely, an ossification centre is affected. The classic presentation is that of focal bone pain at the site of the tumour. The condition worsens at night and increases with activity, and it is dramatically relieved with small doses of aspirin. The lesion initially appears as a small sclerotic bone island within a circular lucent defect. This central nidus is seldom larger than 1.5 cm in diameter, and it may be associated with considerable overlying cortical and endosteal bone sclerosis. The tumours may regress spontaneously. The mechanism of this involution is not known, but tumour infarction is a possible cause.

Radionuclide bone scanning using Tc-99m phosphonates shows intense activity at the site of the tumour. Occasionally, a double-density sign is seen in which a small focus of radioactivity in the nidus is superimposed on a larger area of radioactivity (2). CT scan and MRI are also useful in evaluation of these lesions although in most instances, radionuclide bone scan is often the first test to suspect the abnormality. It is commonly believed that osteoid osteomas are hypervascular on radionuclide imaging (3,4). However, in the present series of twenty six cases, majority of osteoid osteoma lesions did not show evidence of hypervascularity in the perfusion and blood pool images.

Materials and methods

Twenty-six cases of histologically proven osteoid osteoma were retrospectively analyzed for their clinical profile, radiologic and scintigraphic features. The patients were in the age group 3.5 to 53 yrs (mean age = 22.7 yrs). There were 24 males and 2 females. All the patients underwent three phase bone scans using 250 to 740 MBq of Tc-99m methylene diphosphonate (MDP: Amersham, UK). Images were acquired using low energy high-resolution collimator on Millennium MPR and Ecam gamma cameras. SPECT images were acquired wherever considered necessary. First pass images (Phase-1)were obtained with the region of interest under the gamma camera at the acquisition rate of two seconds per frame and with matrix size of 64x64. Blood pool images (Phase-2) were obtained between two and five minutes after injection with the matrix size of 128x128. Delayed static planar images with approximately 700-1000 KCounts (Phase-3) were obtained at three hours using image matrix size of 256x126. SPECT images were obtained in a matrix size of 128x128 using step

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S.No.	Age	Presentation	Nocturnal	Bone Involved	Bone Scan 1st Phase	Bone Scan 2nd Phase	Bone Scan 3rd Phase	X-Ray	CT	MRI
1	22y/M	Backache	No	D 7	-	-	*	Normal		Yes
2	17y/M	Pain	Yes	Femur	-	+	* #	Sclerotic Lesion-central lytic	Cortical thickening	No
3	22y/M	Swelling	No	Ulna	-	-	* #	Sclerotic Lesion	Cortical thickening	No
4	28y/F	Backache	Yes	L 4	-	-	*	Normal		Yes
5	14y/M	Pain	Yes	Femur	-	-	* #	Sclerotic Lesion- central lytic		Yes
6	20y/M	Pain	Yes	Femur	-	-	*	Sclerotic Lesion	Cortical thickening	No
7	13y/M	Pain	Yes	Femur	-	-	*	Sclerotic Lesion		No
8	28y/M	Backache	No	D 6	-	-	*	Normal	Cortical thickening	Yes
9	30yM	Pain	Yes	Femur	-	-	* #	Normal	Nidus seen	No
10	53y/M	Pain	No	Tibia	-	-	*	Sclerotic Lesion		Yes
11	18y/M	Pain	No	Femur	-	-	* #	Sclerotic Lesion		Yes
12	3.5y/M	Pain	Yes	Femur	-	-	*	Sclerotic Lesion	Nidus seen	No
13	30yM	Backache	Yes	L 2	-	-	*	Normal		Yes
14	14y/M	Pain	Yes	Femur	-	+	*	Sclerotic Lesion	Cortical thickening	Yes
15	24y/M	Pain	Yes	Fibula	+	+	* #	Sclerotic Lesion-central lytic	Cortical thickening	Yes
16	12y/M	Pain	Yes	Tibia	-	+	*	Sclerotic Lesion	Cortical thickening	Yes
17	20y/M	Pain	No	Humerus	-	+	*	Sclerotic Lesion		Yes
18	20y/M	Pain	No	Tibia	+	+	* #	Sclerotic Lesion	Osteoid Osteoma/ Chronic Infection/Paraosteal Tumor	Yes
19	13y/M	Pain	Yes	Tibia	-	+	* #	Cortical Thickening/ ?Osteoid Osteoma	Cortical thickening	Yes
20	24y/M	Pain	Yes	Femur	-	+	*	Normal	Cortical thickening	No
21	23y/M	Pain	No	Femur	-	-	*	Sclerotic Lesion	Cortical thickening	No
22	24y/M	Pain	No	Femur	-	-	* #	Sclerotic Lesion	Sclerotic Lesion/Osteoid Osteoma	No
23	41y/M	Pain	Yes	Femur	-	-	*	? Lesser Trochanter lesion		Yes
24	34y/F	Pain	No	Fibula	-	+	* #	Normal		Yes
25	15y/M	Pain	No	Femur	-	-	* #	Sclerotic Lesion		No
26	30y/M	Pain	Yes	Femur	-	-	*			Yes

(+): Hypervascular; (-): Non-hypervascular; (*): Increased uptake; (#): Double density sign

Table-1. Brief demographic profiles, clinical presentations and salient findings of radionuclide, x-ray, CT and MRI investigations of all 26 patients

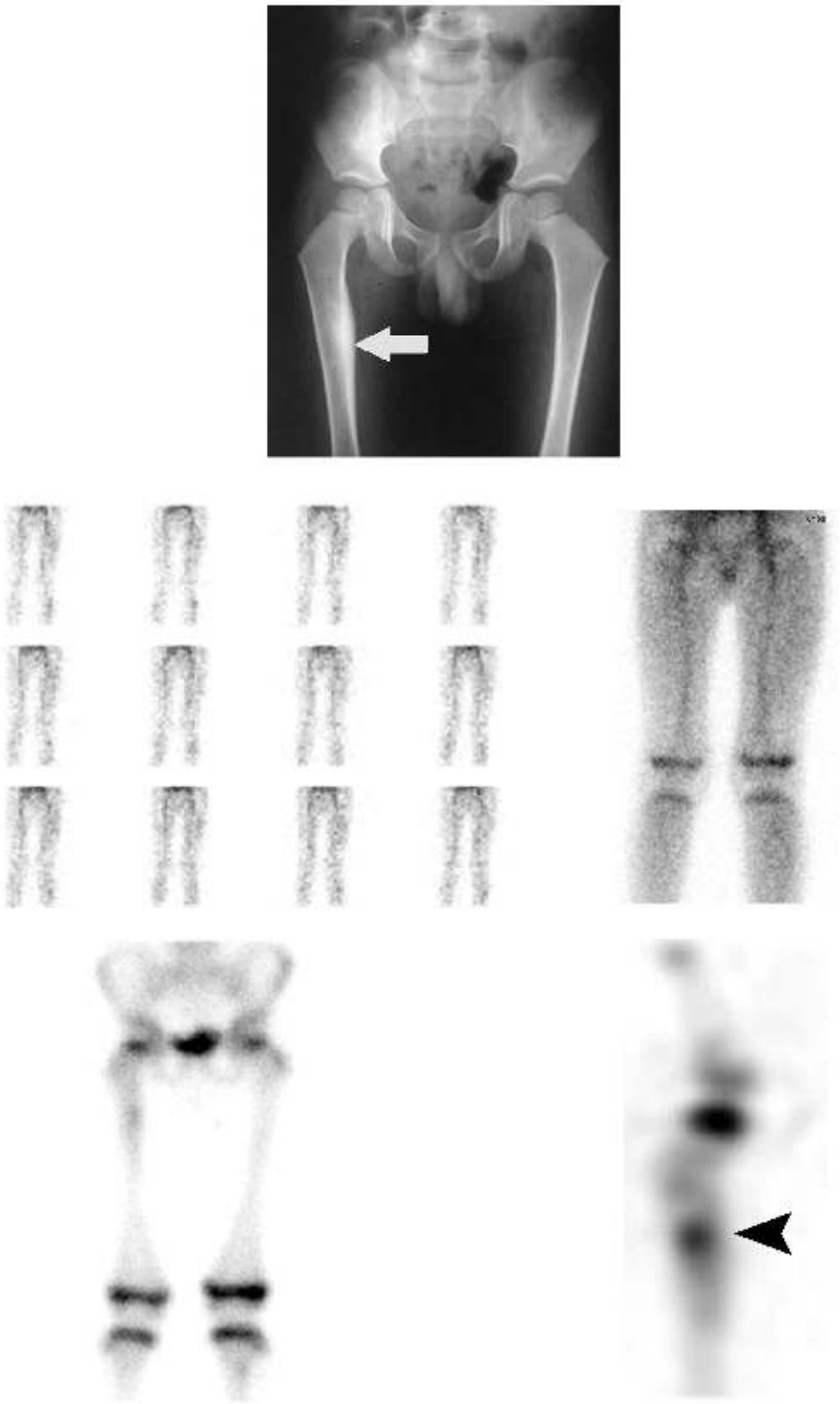

Figure1. Plain x-ray (top row) and radionuclide bone scans (middle and bottom rows) of an 18 year old male (Patient No.11 in table-1) who presented with pain in the hip and thigh with nocturnal aggravation of symptoms lasting few weeks. Plain radiograph (top row) revealed cortical sclerosis on the medial surface of right femur in its upper third (white arrow). Three phase bone scan showed absence of hypervascularity in the first and second phases (middle row) and a well circumscribed lesion with double density sign in the shaft of right femur in the delayed static scan (bottom row left) which is better appreciated on the SPECT study (➤).Final histopathological diagnosis: Osteoid Osteoma.

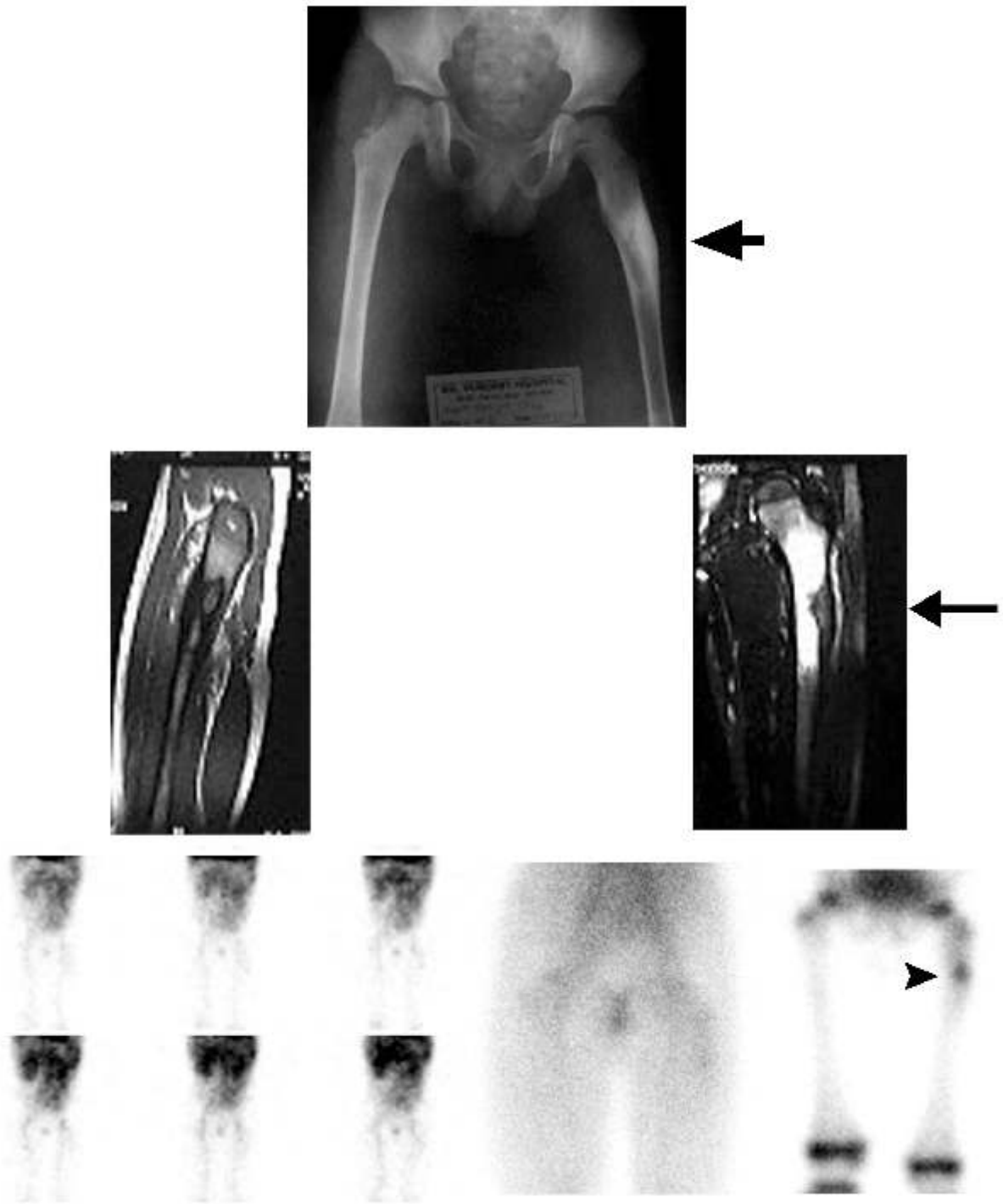

Figure 2. Plain x-ray (top row), MRI (middle row) and three phase radionuclide bone scans (bottom row) of a 14 year old male (Patient No. 5, table-1) who presented with pain in the thigh, which was predominantly nocturnal. Plain radiograph (top row) revealed a sclerotic lesion in the upper shaft of left femur (➧). MRI images (middle row) showed extensive area of sclerosis thus raising a suspicion of malignancy (➧). The three phase bone scan (bottom row) did not show hypervascularity in the first and second phases, but revealed a well-defined hot spot with double density sign in the upper shaft of left femur (➤) in the static third phase image, thus suggesting the diagnosis of Osteoid osteoma. Final histopathological diagnosis: Osteoid Osteoma.

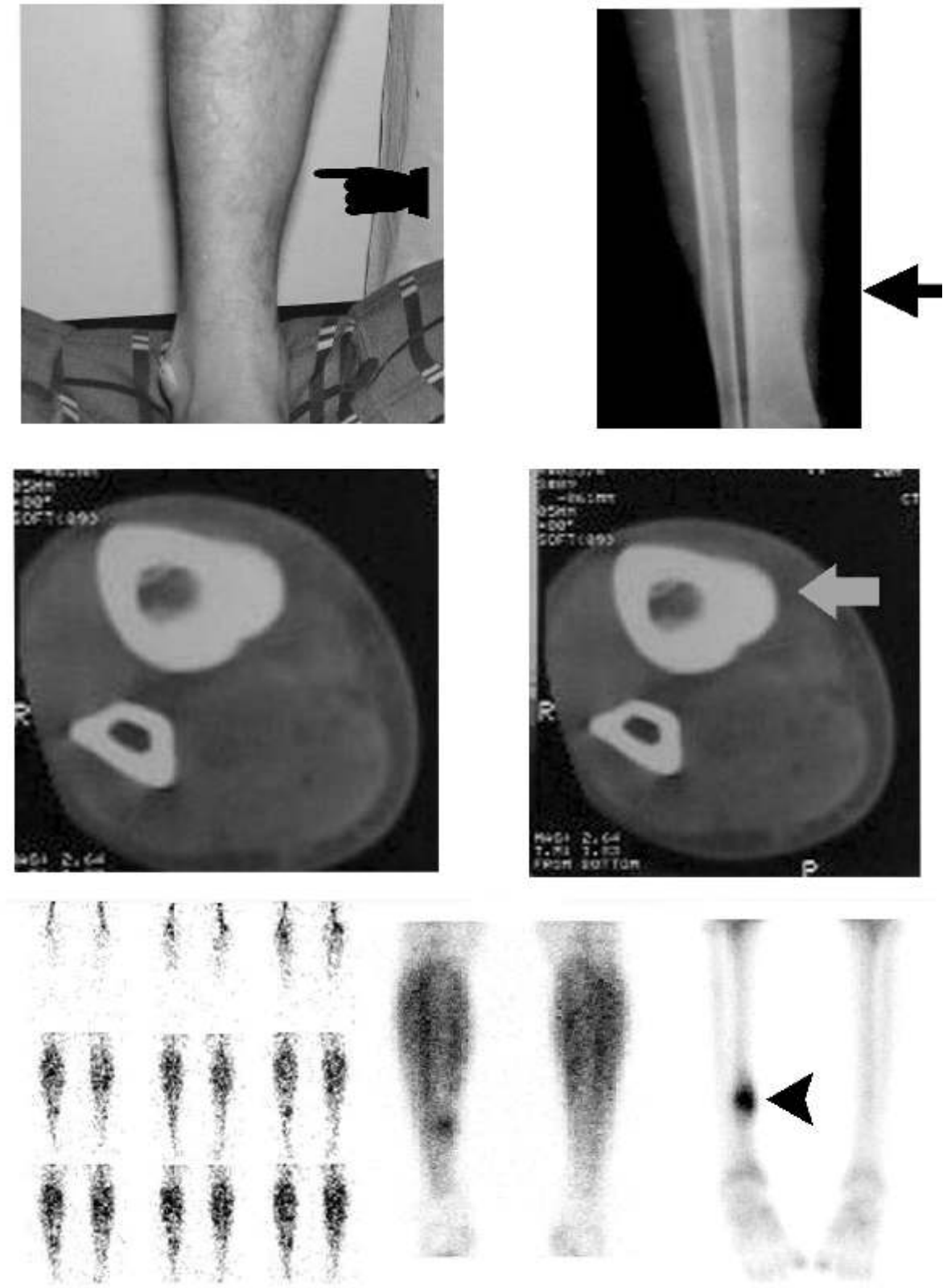

Figure 3. Clinical presentation and plain x-ray (top row), CT scan (middle row) and three phase radionuclide bone scans (bottom row) of a 20 year old male (Patient No. 18, table-1) presented with pain and swelling in the right leg (➧**).** Plain X ray (top row right) revealed sclerosis in the mid shaft of right tibia (➧). CT scan (middle row) revealed prominence of the tibial cortex in its middle third (white arrow). Three phase bone scan (bottom row) did not show hypervascularity in the first pass perfusion images. However the second phase revealed a focus of high soft tissue uptake in the middle third of shaft of right tibia. In the third phase the delayed static bone scan revealed a hot spot in the middle third of shaft of right tibia with double density sign (➤). Final histopathological diagnosis: Osteoid Osteoma

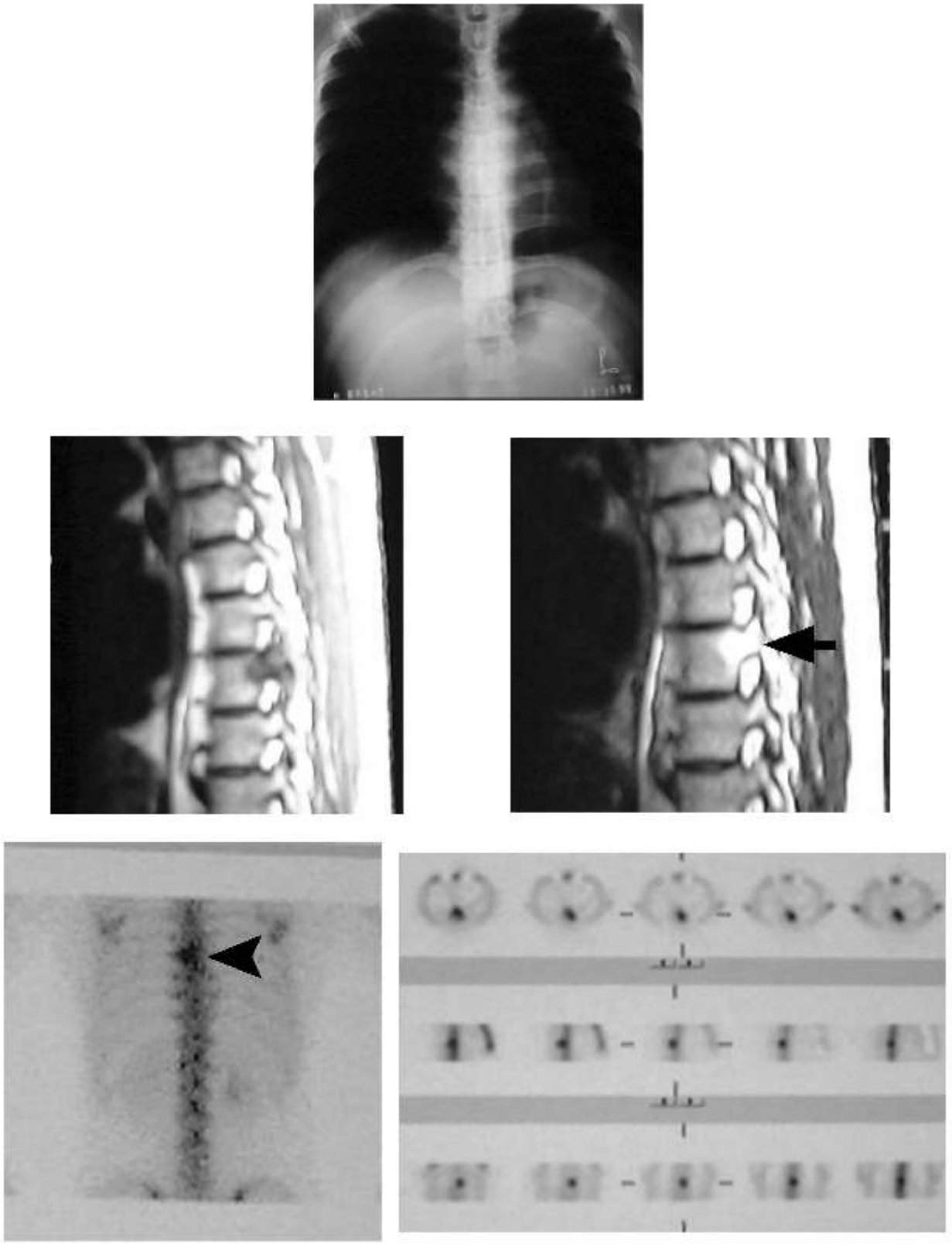

Figure 4. Plain x-ray (top row), MRI (middle row) and planar and SPECT bone scans (bottom row) of a 22 year old male (Patient No. 1, table-1) who developed backache, which was mostly nocturnal. Plain X ray of the dorsal vertebrae was normal. MRI revealed a lesion at the 7th thoracic vertebra (◄) the nature of which was reported to be inflammatory. Based on this the patient was subjected to empirical anti-tubercular treatment to which he did not respond. Bone scan was requested at a later date which revealed hot spot in the 7th Thoracic vertebra which was better defined on SPECT images (◄). Excision of the lesion promptly brought about relief in symptoms. Histology confirmed the diagnosis of osteoid osteoma.

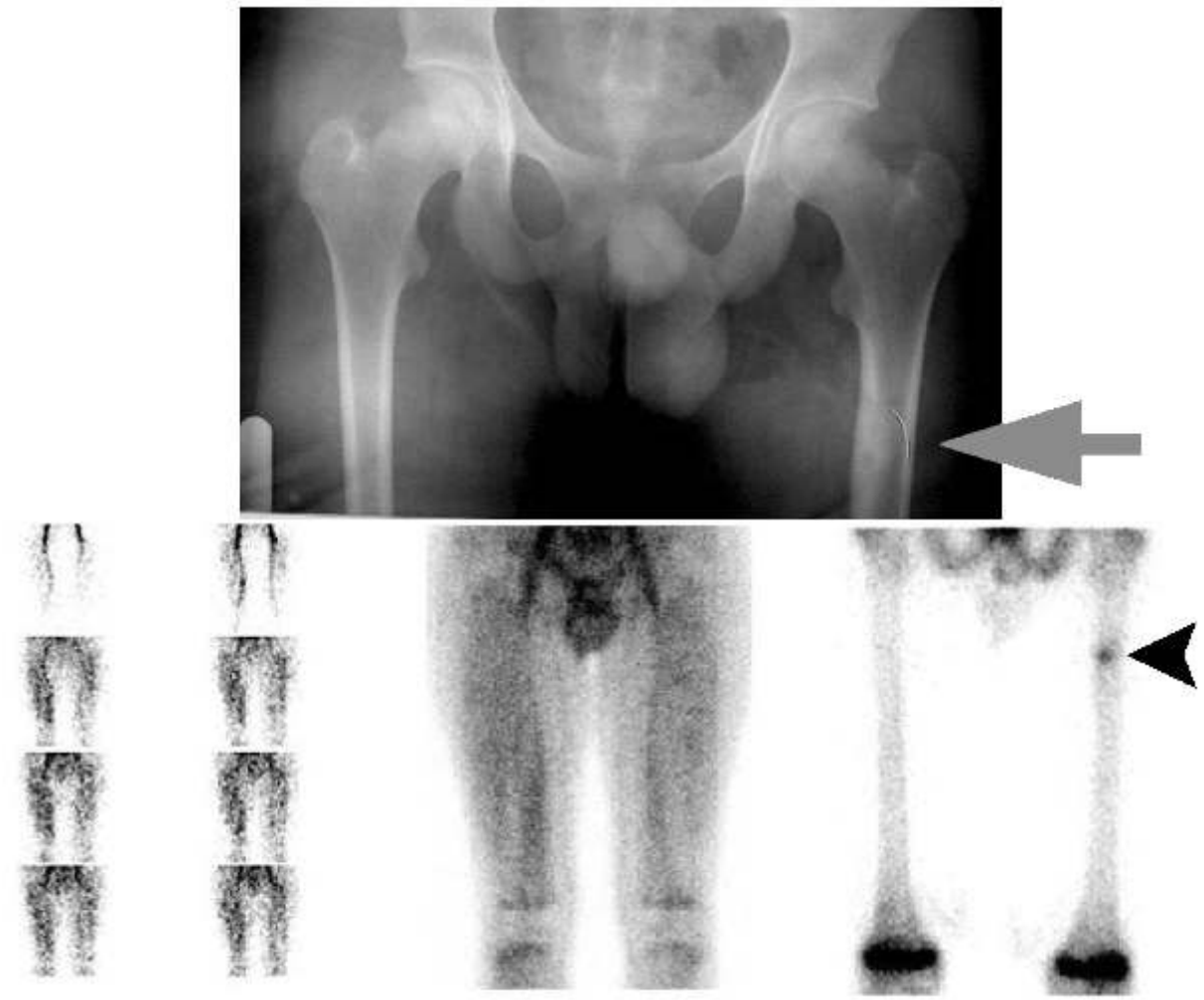

Figure 5. Plain x-ray (top row) and three phase bone scans (bottom row) of a 14 year old male (Patient No. 14, table-1) who presented with left thigh pain that aggravated at night. Plain X ray revealed sclerotic lesion with central lytic focus (➔). Three-phase bone scan revealed normal first and second phases and a hot spot in the upper shaft of left femur medially in the third phase (➤). Excision of the lesion brought about complete relief in symptoms. Histology confirmed the diagnosis of osteoid osteoma.

and shoot rotation at the rate of 30 seconds per slot, and rotating over 360 degrees.

Results

In the present study the average duration of symptoms in our patients was 3 months. Fifteen out of 26 patients had nocturnal aggravation of symptoms. The bones involved were femur (N=14), tibia (N=4), fibula (N=2), humerus (N=1), ulna (N-1) and vertebrae (N=4). Hip synovitis was observed in two cases. Both of them had osteoid osteoma in the neck of femur. One patient, with backache and a lesion in the dorsal vertebra on an initial MRI examination, was suspected to have inflammatory lesion secondary to tuberculosis and was given a six months trial of anti-tubercular treatment to which he did not respond and was subsequently subjected to a radionuclide bone scan, which suggested the diagnosis of osteoid osteoma. Five patients had clinical suspicion of osteoid osteoma.

Plain x-ray of the bones

The plain x-ray of the bones revealed abnormality in 18 cases. Central lytic lesion with surrounding zone of sclerosis was observed in three cases. In three cases the plane x-rays were reported as normal. But on subsequent reviews following an abnormal bone scan, the reports were modified and reported as abnormal.

Radionuclide Bone Scan

In 16 patients radionuclide bone scanning was the first test to show the abnormality. The first phase (perfusion) was abnormal in two of these cases; the second phase (blood pool) was abnormal in 9 of these cases and the third phase (delayed static bone scan) revealed abnormality in all the cases. Seventeen lesions did not reveal evidence of hypervascularity in the first and second phase of bone scans. Double density sign was seen in eleven cases. In three cases where bone scans suspected osteoid osteoma , the confirmation was done using a CT scan prior to histology. (Two of these in the vertebra and one in the neck of femur). SPECT studies were done in ten cases. Double density sign was better appreciated on SPECT scan. The

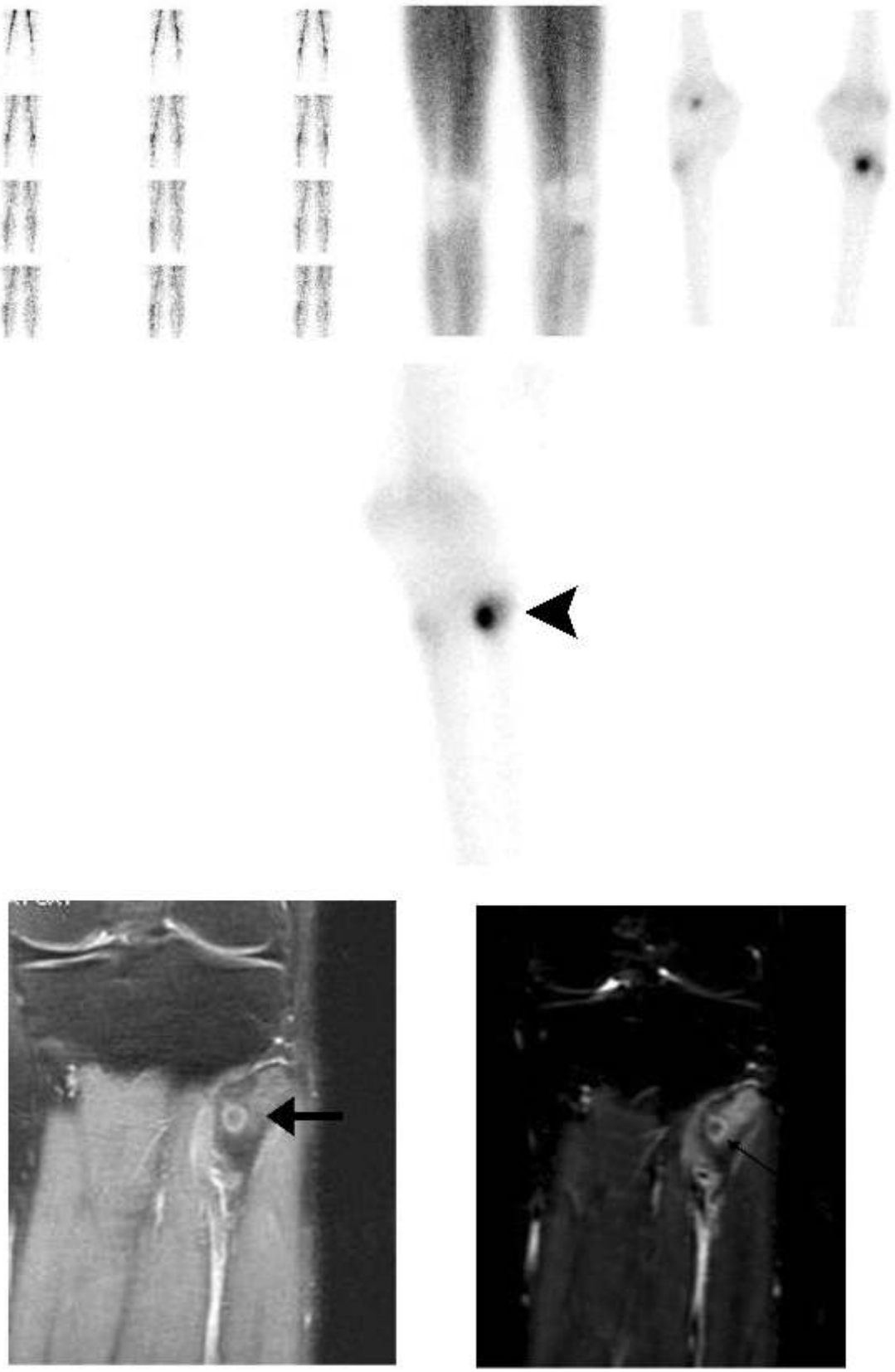

Figure 6. A 34-year-old gentleman (Patient No. 24, table-1) presented with pain in the region of left knee with nocturnal aggravation in symptoms lasting several months. On examination it was noticed that he had also developed wasting of the muscles around the left knee. Bone scan revealed normal perfusion in the first phase, a focus of high soft tissue uptake in the second phase and a well-defined double density lesion in the upper end of left fibula in third phase (➤). MRI (bottom row) revealed abnormal signal intensity on T1 and T2 weighted images in the same region (➤**).** Surgical excision of the tumour resulted in total relief of symptoms. Histology confirmed the diagnosis of osteoid osteoma.

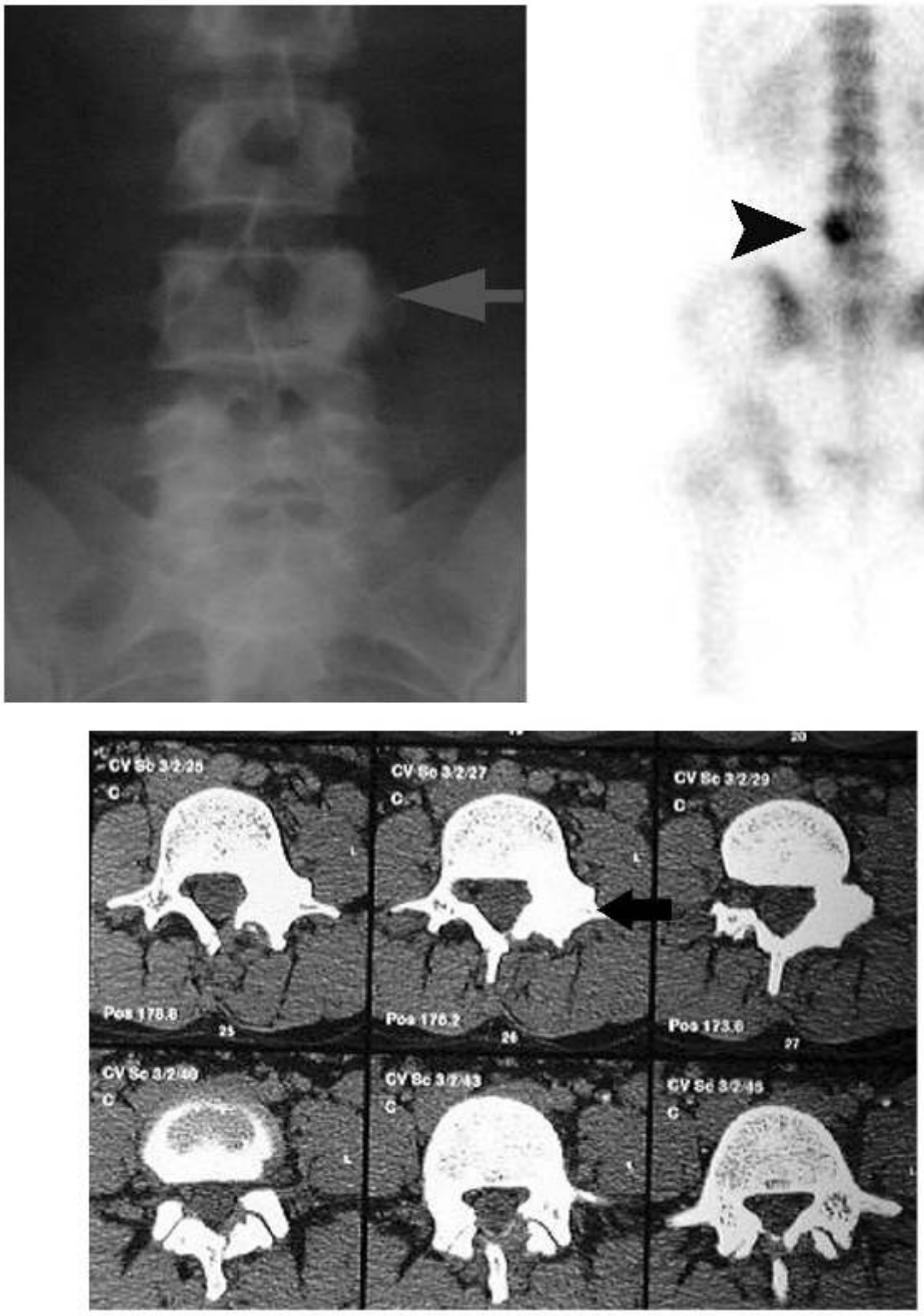

Figure 7. A 28-year-old female (Patient No. 4, table-1) presented with backache. There was no specific history of nocturnal aggravation of pain. Plain radiograph (top row left) revealed a rounded lesion in the pedicle of 4th lumbar vertebra (⬅). A static bone scan showed hot spot in the region of the pedicle of 4th lumbar vertebra (➤). CT scan (bottom row) showed a sclerotic lesion in the same region (⬅). Surgical excision of the tumour resulted in total relief of symptoms. Histology confirmed the diagnosis of osteoid osteoma.

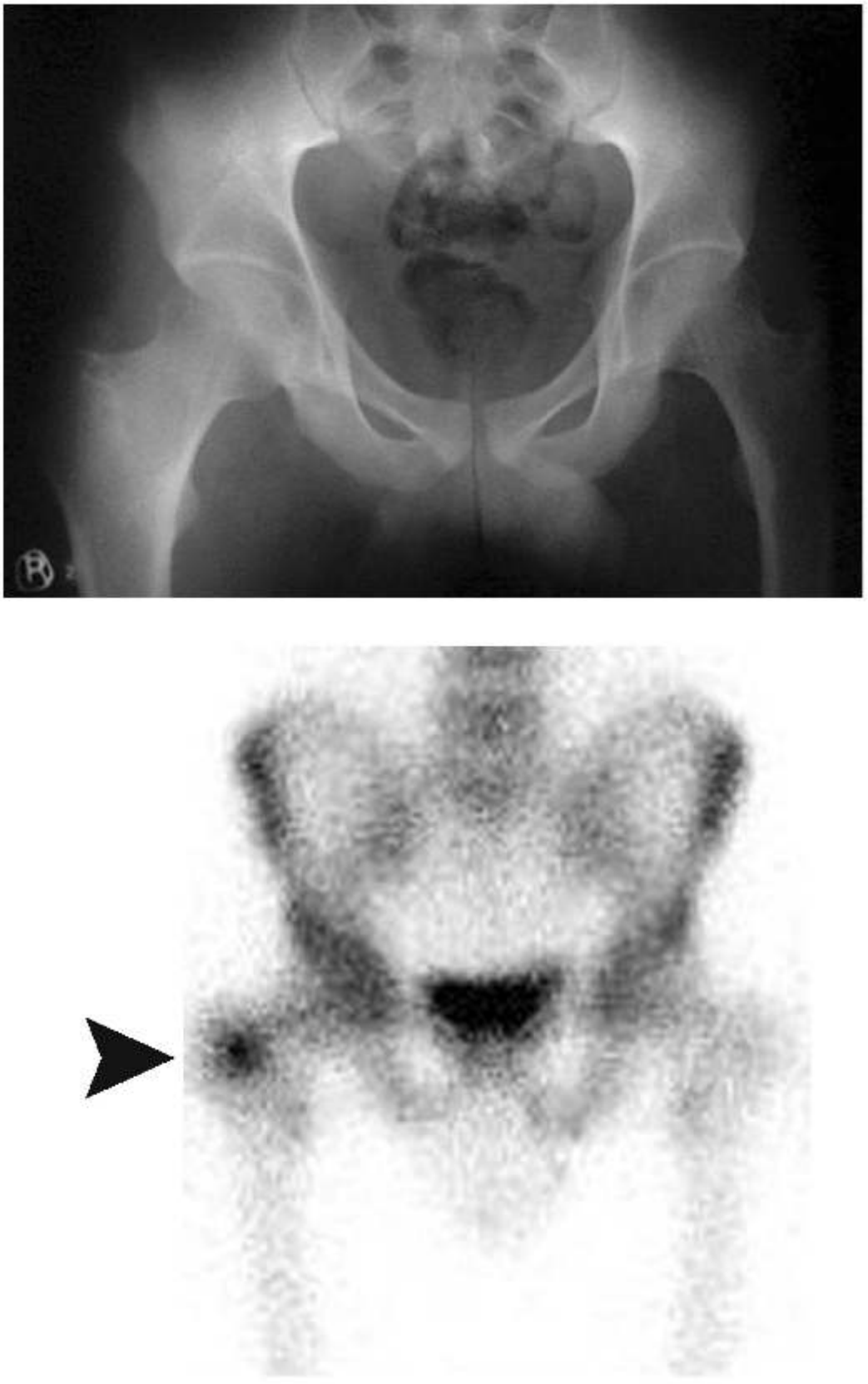

Figure 8. Plain x-ray (top) and static radionuclide bone scan (bottom) of a 20 years old male (Patient No.6, table-1) who presented with pain in the right hip region with nocturnal aggravation of symptoms. Plain X ray was normal and did not contribute to the diagnosis. A radionuclide bone scan revealed a well defined lesion in the upper shaft of right femur (➤) with double density sign better seen on SPECT images (not shown here). Histology confirmed the diagnosis of osteoid osteoma.

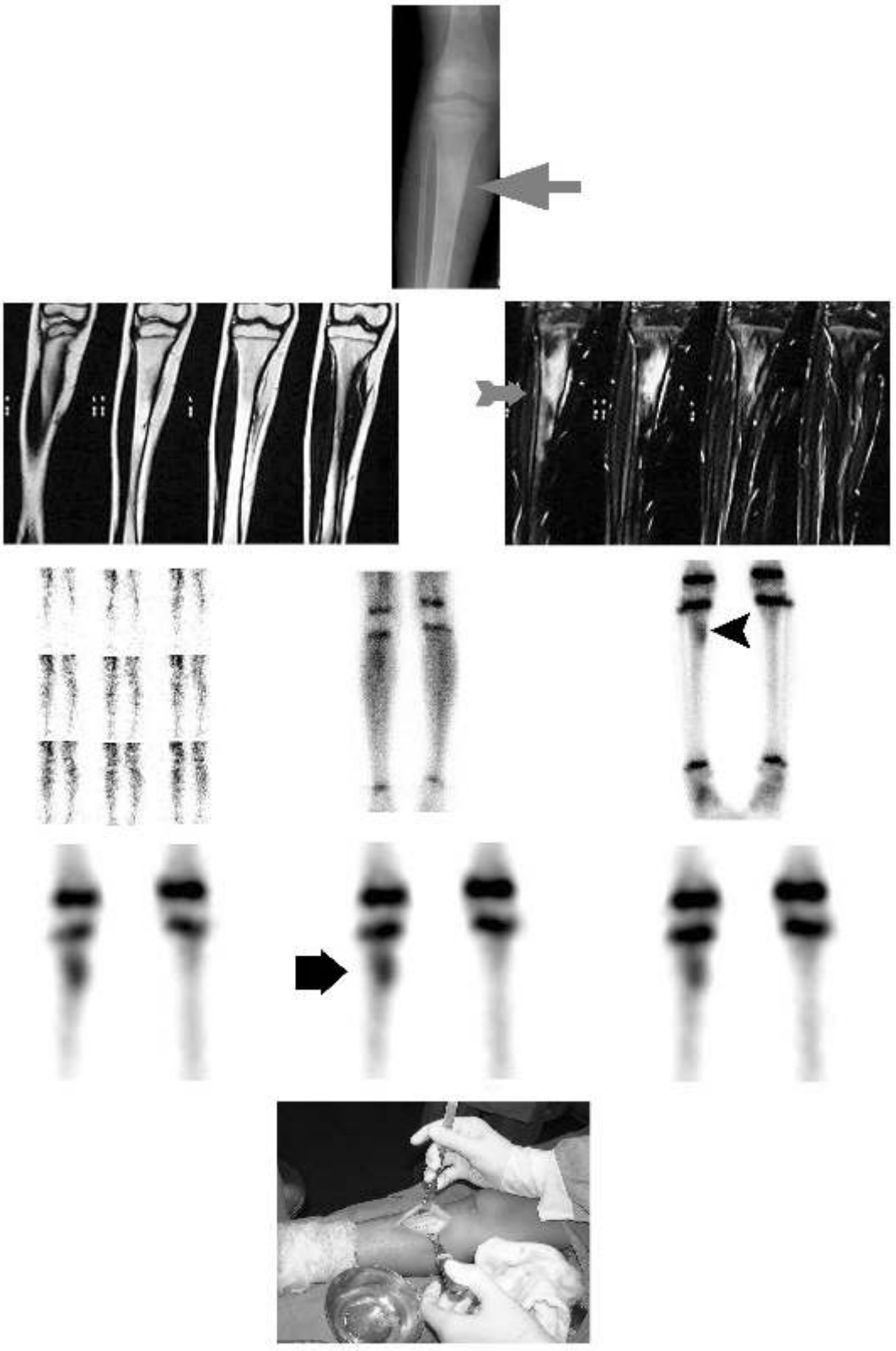

Figure 9. Plain x-ray (top row), MRI (middle row), three phase radionuclide bone scans (third row) and SPECT study (fourth row) of a 12 year old male (Patient No. 16, table-1) who presented with pain in the right leg. Plain x-ray (top row) revealed sclerotic lesion in the upper shaft of right tibia (⬅). MRI showed hypo-intense lesion on T1 and hyperintense lesion on T2 in the upper shaft of right tibia (➡**). Three phase** bone scan did not reveal abnormality in the first phase, minimally increased soft tissue uptake in the second phase and focal uptake in the upper shaft of right tibia in the third phase (➤). A well defined double density lesion is seen on SPECT images (➡). Per-operative localization of the lesion is also shown here in the fifth row. Surgical excision of the tumour resulted in total relief of symptoms. Histology confirmed the diagnosis of osteoid osteoma.

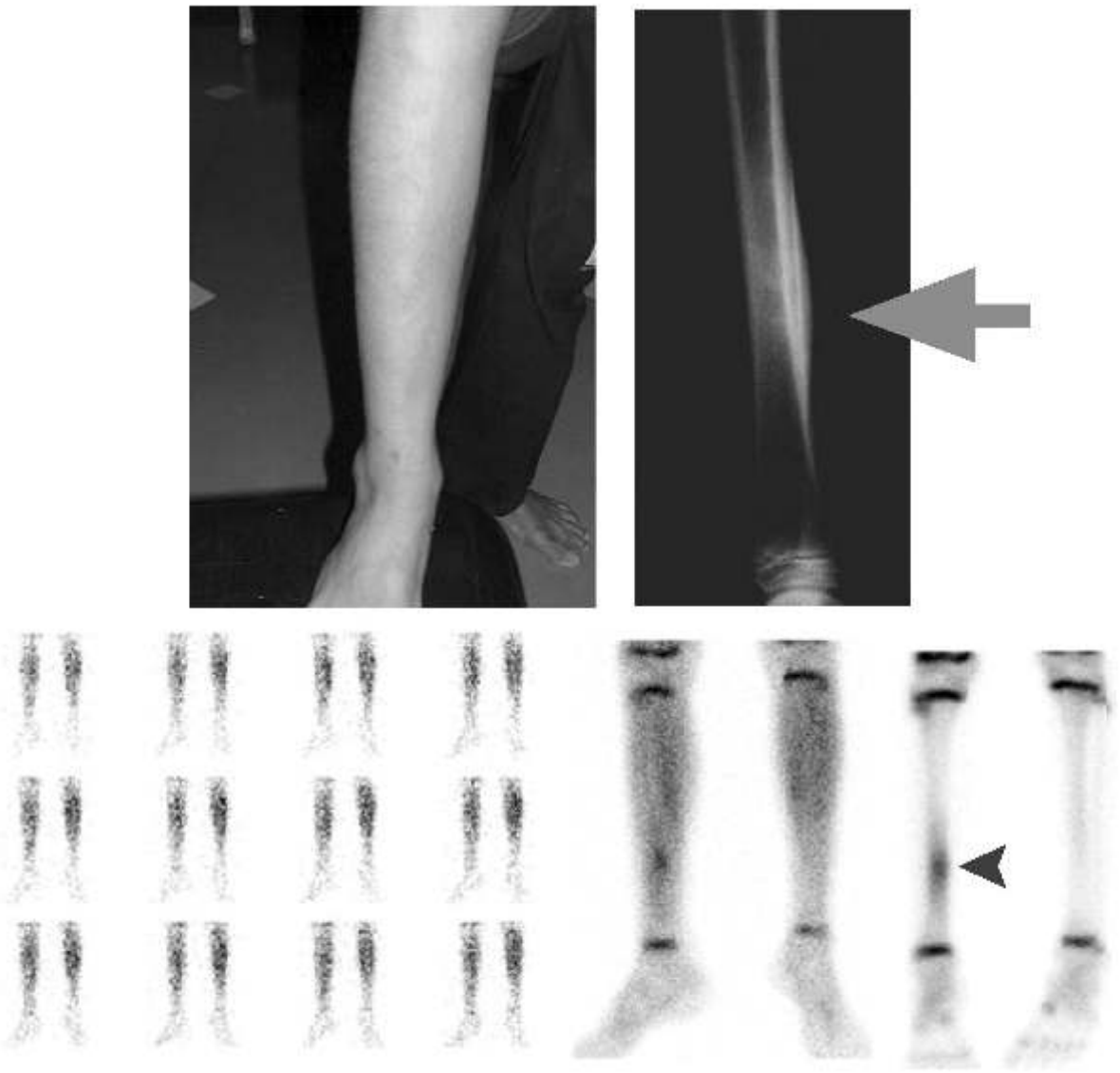

Figure 10. Clinical presentation (top left), plain x-ray (top right) and three phase bone scan (bottom row) of a 13 years old boy with history of pain and swelling in the right shin. The swelling was localized to the mid shaft of right tibia. Plain x-ray revealed a large area of sclerosis in the mid shaft of right tibia (◄). Bone scan showed normal first pass, high soft tissue uptake in the second blood pool phase and a double density hot lesion in third phase (➤) over the mid-shaft of right tibia. Surgical excision of the tumour resulted in total relief of symptoms. Histology confirmed the diagnosis of osteoid osteoma.

vertebral lesions were also better resolved on SPECT. Three of the vertebral lesions were in the posterior arch and one lesion was in the body at the junction of posterior element.

CT scan

Six patients had CT scans performed prior to radionuclide bone scan. None of these were diagnosed as osteoid osteoma based on CT scan alone, although it was suspected in two of these cases. 10 cases underwent CT scan following localization on radionuclide bone scans, and they all had demonstrable nidus on CT scan.

MRI scan

Sixteen patients underwent MRI evaluation of the lesions seen on radionuclide bone scans, and the MRI scans were positive for osteoid osteoma in all. One patient was reported to have an inflammatory lesion in the vertebra. One patient had disproproportionately large periosteal reaction, which was misleading on its own, but when reviewed in conjunction with the bone scan, the diagnosis of osteoid osteoma was confirmed.

Brief demographic profiles, clinical presentations and salient findings of radionuclide, x-ray, CT and MRI investigations of all 26 patients are given in Table 1. Selected illustrations of results of imaging studies carried out in 10 of the 26 patients are given in figures 1-10.

Discussion

Osteoid osteoma accounts for 4% of all primary bone tumours and 11% of all benign bone tumours (1,5). It is the third most commonly occurring benign tumour after osteochondroma and non-ossifying fibroma. The peak incidence of the disease is in the second decade of life.

Patients frequently present with nocturnal pain that responds promptly to salicylates. Prostaglandins are recovered in large amount from the tumour and are responsible for mediation of pain (6). The lesion is most frequently seen in the femur. This was also observed in the present study. In the hip region it has predilection for proximal portion including the femoral neck and the inter-trochanteric region (7). Lesions near the joints may produce symptoms characteristic of inflammatory synovitis (8). This was observed in two of our cases. Tibia, humerus, fibula are the other commonly involved long bones. Next to the long bones, the locations most commonly reported for osteoid osteoma are the spine and the bones of the foot and hand (9). Lumbar, cervical, thoracic and rarely the sacral vertebrae are affected. In the vertebrae, the lesion has a predilection for the posterior arch. In our study we had four cases of vertebral involvement, out of which there were three with posterior arch involvement and in one the body was involved at the junction of lamina.

The gross appearance of osteoid osteoma is typical, with the nidus being small, red and granular. It is softer than the surrounding sclerotic bone. The surgeon usually requests a radiograph of the involved bone following surgery to ensure that the nidus has been removed. The osteoid osteomas, as well as the osteoblastomas are very cellular. But benign osteoid producing tumours may simulate osteogenic sarcoma if the radiologic appearance of the lesion is not appreciated. These benign conditions exhibit osteoblasts with evidence of transition of the immature osteogenic tissue into more mature thick trabecular bone at the periphery of the lesion. The mineralization of bone is variable. The bony trabeculae are rimmed by osteoblasts. The spaces between the trabeculae show capillary proliferation and few cells. Benign giant cells are almost always found (10).

Radiographically the lesion needs to be differentiated from osteomyelitis, osteoblastoma and langerhan cell histiocytosis. The nidus of osteoid osteoma has smooth edges. Rough edges on a nidus suggest osteomyelitis. In addition osteomyelitis generally has a larger peripheral area of radiolucency because of increased oedema and necrosis. Langerhans cell histiocytosis needs to be excluded by histologic evaluation. Osteoblastoma is larger than 2.5 cm and can be as big as 10 cm in size and lacks a nidus (11).

There are several difficulties in the radiological diagnosis of osteoid osteoma. Typical radiographic findings may not become evident on plain radiograph until several months after the patient first presents with symptoms. It may also be noted that reactive tissue may obscure the location of the nidus. Besides, a few lesions, which are atypical in location may present without the easily identifiable reactive sclerosis. These are the situations where radionuclide bone scanning will invariably show abnormality despite a normal plain radiograph (12). Often bone scintigraphy is performed in osteoid osteoma as the primary diagnostic modality when the clinical history is atypical or vague, or when the radiographs are equivocal or normal (13).

It may be noted that 25% of positive bone scans are associated with normal radiographic examination (14). There is only one isolated case report of negative bone scan in a case of osteoid osteoma (15). However in this case the patient was not subjected to three phase study or SPECT.

After plain radiography has been performed, magnetic resonance (MR) imaging is considered the modality of choice for the evaluation of suspected musculoskeletal lesions because of its high sensitivity to show changes in the signal intensity of marrow and soft tissue. However in case of osteoid osteoma MRI may overestimate its aggressiveness, especially in children. Potentially misleading MRI features are commonly seen in cases of prominent marrow edema, soft-tissue edema; and in cases with overwhelming periosteal reaction as in childhood, when the periosteum is more loosely attached. Knowledge of the potential pitfalls encountered with MR imaging may help to choose plane x-ray and radionuclide bone scanning judiciously in such situations (16). In our series, it may be noted that the MRI was first reported as negative in patient No.14, which was subsequently revised after the bone scan (Table 1, Figure 5).

Summary:

Osteoid osteoma is a benign neoplasm of the skeleton with characteristic nocturnal pain promptly relieved by aspirin. It commonly occurs in the second decade of life with male preponderance. The lesion involves metaphysis or shaft of long bones and is cortical in its location. Roentgenographically it shows radiolucent nidus that is surrounded by sclerotic zone. The sclerosis is sometimes so extensive that the nidus gets masked. CT scan may help in localization of such nidus. However radionuclide bone scanning is highly sensitive in defining the lesion and shows the typical “double density sign”. Though it is commonly believed that three-phase bone scan shows abnormality in all the three phases, in our observation, majority of these lesions (65%) did not reveal abnormality in the first and second phases. Clinical features, plain radiography, computed tomography, magnetic resonance imaging as well as radionuclide bone scans may have their own limitations in a given patient. The present study highlights the profiles of 26 cases of osteoid osteoma and outlines the role of radionuclide bone scan as well as other investigations in arriving at the diagnosis.

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