TRANSIENT BONE OEDEMA OF THE TIBIA MIMICKING A TUMOROUS PROCESS

D. ROBINSON, Y. KOSSASHVILI, J. SANDBANK[1], N. HALPERIN, D. ALK

The authors describe a distinct clinical entity consisting of bony tenderness, increased isotope uptake along the metaphyses and/or diaphyses and magnetic resonance changes simulating a bone marrow- replacing lesion. Bone biopsies indicate the presence of bone marrow fibrosis and some new bone formation. Nine such cases were prospectively evaluated according to a standardized protocol including clinical examination, xrays, bone scan and CT scan as well as MRI scans including contrast medium injection.

All patients presented with tibial tenderness. In one case the bone was noticeably thicker as compared to the other side. The ages ranged from 6 years to 64 years and 6 of the patients were female. Xrays were normal in 6/9 patients ; the rest had minimal periosteal reaction, and mild intramedullary sclerosis. Uniform imaging findings were longitudinal increased uptake along the metadiaphysis of the tibia on bone scans, and increased bone marrow density on CAT scans without a fracture line. A magnetic resonance study indicated bone marrow replacement as demonstrated by an area of low signal intensity on T_1-weighted images and high signal intensity on T_2-weighted images. Some enhancement of signal was observed following gadolinium injection. This clinical entity, which the authors attribute to be a medullary stress reaction, is self-limited, and pain resolves within 3 months. However the radiographic changes appear to be permanent. A biopsy is not required provided no cortical penetration or soft tissue mass is demonstrated by MRI scan.

Keywords : bone tumors ; stress fractures ; bone-marrow fibrosis ; bone bruise.

Mots-clés : tumeur osseuse ; fracture de fatigue ; fibrose de la mœlle osseuse ; contusion osseuse.

INTRODUCTION

Patients presenting with bony tenderness, normal xrays or non-specific radiographic changes and an increased segmental uptake on a bone scan, are often suspected to harbor either a neoplasm or an infectious process. Stress fractures are another cause of bone tenderness and increased radioisotope uptake. As the fracture line is usually transverse, the bone scan usually reveals a focal area of increased uptake. Sometimes a longitudinal stress fracture occurs (1-2). In this type of fracture, the fracture line is parallel to the diaphyseal axis. The fracture line often eludes detection on conventional xrays, but is easily seen on CT scans (9) or MRI scans (2). In most cases the combination of the last two modalities allows the diagnosis to be made, obviating the need for a bone biopsy (2). In most stress fractures, a history of increased bone stress leading to fatigue failure can be elucidated.

The current study aimed at defining an entity of bone tenderness, normal or non-specific xray changes that is not a stress fracture as defined by bone scans, CT scans and MRI scan.

Departments of Orthopedics and [1]Pathology, Assaf Harofe Medical Center, Zeriffin 70300, Israel.

Correspondence and reprints : Dror Robinson, Department of Orthopedics, Assaf Harofe Medical Center, Zeriffin, 70300, Israel. E-mail : robinson@bezeqint.net.

MATERIALS AND METHODS

Patients

The patients presenting with bone tenderness without evidence of a neoplasm, infection or stress fracture were included. Inclusion criteria were : 1. Bone tenderness over the tibia. 2. Lack of radiographic evidence of a stress fracture or other pathology. 3. No history of direct trauma to the region. 4. Segmental increased uptake on a bone scan deemed atypical for a stress fracture (such a bone scan might occur in a longitudinal stress fracture but not in the more common transverse type). 5. No demonstration of a fracture line on a CT scan (such a fracture line is diagnostic of longitudinal stress fractures). 6. Diffuse segmental bone marrow edema demonstrated on an MRI scan. Exclusion criteria included evidence of irradiating pain, i.e. limited range of lumbar spine motion or positive SLR test. Nine such patients presented in our outpatient department from January 1998 to June 2001. Six had no history of increased physical exertion, two had begun recreational sports activity within 3 months prior to symptom appearance and one had a ski injury of the knee treated conservatively 2 months prior to symptom appearance. The ages ranged from 6 to 64 years, and six were female. In all cases, xrays, bone scans, CT images and MRI were performed. In the first three cases, as a neoplasm was suspected an open biopsy was performed.

Protocol of Imaging Studies

X-rays were performed in anteroposterior and lateral projections. Three-phase bone scans were performed. CT scans were performed with 3-mm thick axial slices. MRI scans were performed with T1-weighted and T2-weighted sequences as well as STIR sequences. All patients underwent gadolinium injection.

Follow-up

All patients underwent repeat x-rays and repeat MRI scan 3 months and one year after presentation.

RESULTS

Clinically all patients presented with bone pain, and a well-defined bony tenderness elicited by gentle percussion or firm digital pressure. Xrays are not a sensitive modality in these lesions, being abnormal in 3/9 cases (33%). Two abnormalities were encountered : a periosteal reaction and a cumulus cloud-like sclerosis of the medullary cavity. The most sensitive studies were bone scans and MRI scans, which were abnormal in all cases. CT scans were abnormal in all cases (in 3/9 patients demonstrating a periosteal lesion or cortical irregularities) ; in all patients increased bone marrow density was observed. MRI scans demonstrated a diffuse abnormal bone marrow signal (high T2-weighted signal) with enhancement by gadolinium. Bone scans showed minimal or no blood flow increase during the first two phases. Third-phase scans (2 hours postinjection) demonstrated increased uptake over large segments of bone (table I, II). Biopsy performed in three cases revealed

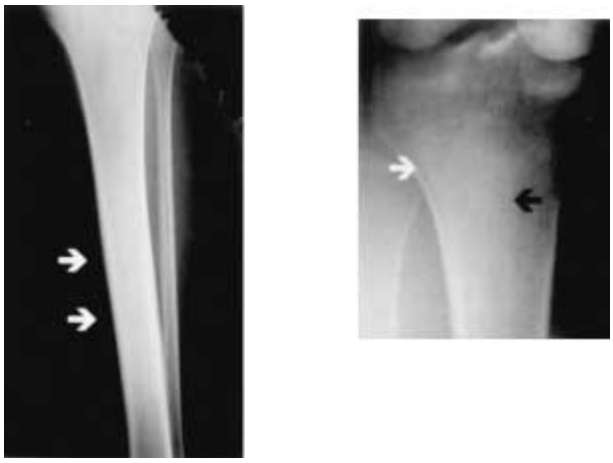

Fig. 1. — Xrays demonstrate intramedullary sclerosis (arrow heads) without cortical reaction in two cases (a : tibial diaphysis in a 16-year-old patient, no history of trauma, b : Proximal tibial metadiaphysis in a 31-year-old patient, with a history of a ski accident 3 months prior to presentation. Xrays at the time were completely normal).

Table I. — Features of nine patients with medullary stress syndrome

Age	6-64 years old
Sex	6/9 females
X-rays	3/9 periosteal reaction with intramedullary sclerosis
Bone Scan	Segmental increased uptake
CT Scan	Periosteal irregularity in some patients, increased bone marrow density in all patients
MRI Scan	Bone marrow edema, signal enhancement with Gd

Table II. — Clinical features of patients

Patient Number	#1	#2	#3	#4	#5	#6	#7	#8	#9
Age (years)	6	8	18	24	43	20	64	27	32
Sex	F	F	M	M	M	F	F	F	F
Location	D	D	PMD	D	D	D	DD	PMD	PMD
Concomitant Medical Conditions	None	None	None	STS, same leg, NED 1y	None	None	OP	None	None
Duration of Symptoms	2 M	3 M	2 M	No symptoms	3 M	3 M	4 M	2 M	2 M
Prior Trauma	None	None	None	None	None	None	None	2 M prior to symptoms	None
Prior increased physical activity	Dancing	None	Military recruit	Weight bearing post cht	None	None	None	None	None
X-rays at presentation	MS	N	PR	N	N	N	MS	N	N
Treatment	Biopsy	Rpt img	Rpt img	Rpt img	Rpt img	Rpt img	Biopsy	Biopsy	Rpt img
Biopsy	MF	—	—	—	—	—	MF	MF, PC	—
Time to healing	3 M	2 M	2M	3 M	2 M	2 M	6 M	2 M	3 M
Sequelae	None	None	None	None	None	None	CP	CP	None
Final MRI	N	N	N	N	N	N	N	N	N
X-rays at one year follow-up	MS	MS	MS, PR	N	N	MS	MS	N	N

Cht = chemotherapy ; CP = continued pain ; D = diaphysis ; DD = distal third of diaphysis ; M = months ; MF = medullary fibrosis ; MS = medullary sclerosis ; N = normal ; NED = no evidence of disease ; OP = osteoporosis ; PMD = proximal meta-diaphysis ; PR = periosteal reaction ; Rpt img = repeated imaging studies over a one year period ; STS = soft tissue sarcoma.

bone marrow fibrosis. In one patient the presence of focal lymphoid infiltration suggested a lympho-proliferative process. However, polyclonality as demonstrated by immuno-histochemistry proved the reactive nature of the process.

DISCUSSION

The differential diagnosis in patients presenting with tibial bone pain without an obvious trauma includes a space-occupying lesion, stress fracture or irradiated pain usually of sciatic origin. A stress fracture often occurs in patients who are involved in strenuous exercise. In most cases, the fracture line is transverse. In a small proportion of cases the fracture line is longitudinal (5). The unusual feature of the reported series of cases is that no fracture line was demonstrated on a CT scan. Instead a large area of bone marrow edema was present involving the entire thickness of the medullary canal. Biopsies performed in three cases demonstrated bone marrow fibrosis, and in one case lymphocytic infiltration of the bone marrow. This might be a healing reaction of the bone. The finding of medullary sclerosis in some cases supports this theory. It might be a similar phenomenon to bone bruise often found in subchondral bone following rotational knee injuries (4).

The appearance of long areas of edematous bone marrow might lead to the erroneous diagnosis of a bone-marrow replacing neoplasm such as Ewing's sarcoma or a hematologic malignancy (6). In some cases the presence of a periosteal reaction might be misinterpreted as representing tumor invasion of

Table III. — Comparative features of stress related bone disorders

	Conventional Stress Fracture	Longitudinal Stress Fracture	Bone Bruise	Intra-medullary Stress Reaction
Clinical Findings	Focal Pain, Increased Stress	Segmental Pain, Increased stress	Joint Pain, History of Trauma	Variable history of trauma or increased stress
History of Increased Stress	Usual	Usual	Not common	Unusual
Preceding Trauma	None	None	Common	Unusual
Typical Location	Diaphysis	Diaphysis	Epiphysis	Diaphysis or meta-diaphysis
X-rays Early	N	N	N	N
X-rays Late	Fracture line and callus	Callus	N	Medullary sclerosis or periosteal reaction
Bone Scan	Focal uptake	Longitudinal uptake	Subchondral increased uptake	Segmental uptake
CT Scan	Fracture line	Fracture line usually detected	N	Increased bone marrow density
MRI Scan	Fracture line and medullary edema	Fracture line and medullary edema	Medullary edema	Medullary edema
Follow up x-rays	Healed fracture	Healed fracture	N	Medullary sclerosis

N = normal.

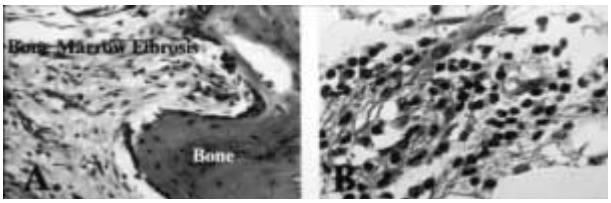

Fig. 2. — Histological examination of the same cases reveals a : bone-marrow fibrosis (original magnification × 200, H&E stain). b : Plasma cells clustered within an area of bone marrow fibrosis (original magnification × 400, H&E stain).

Fig. 3. — Bone scan indicates an area of increased uptake involving the lateral aspect of the tibial metaphysis (same case as b. in previous figures).

surrounding soft tissues. In such cases the MRI scan was noted to always demonstrate the fracture line, when a longitudinal stress fracture was present (6). The series reported above, includes patients in whom no fracture line was visible. Two treatment strategies might be entertained when such a patient is encountered ; i.e. a biopsy versus careful follow-up with sequential MRI scans. Lack of soft tissue edema, despite the presence of extensive bone marrow edema and/or a periosteal reaction, lends support to the conservative option. In addition, lack of necrosis on gadolinium-enhanced T1-weighted sequences argues against a malignant process (6).

In conclusion, an entity consisting of a bone marrow healing reaction, without an accompanying bone fracture, is described and termed medullary stress reaction. The lesion involves cancellous bone of the diaphysis or the metaphysis in contrast to the well-described bone marrow contusion occurring in subchondral bone (7). Despite the lack of clinical history of increased stress, it is the authors'

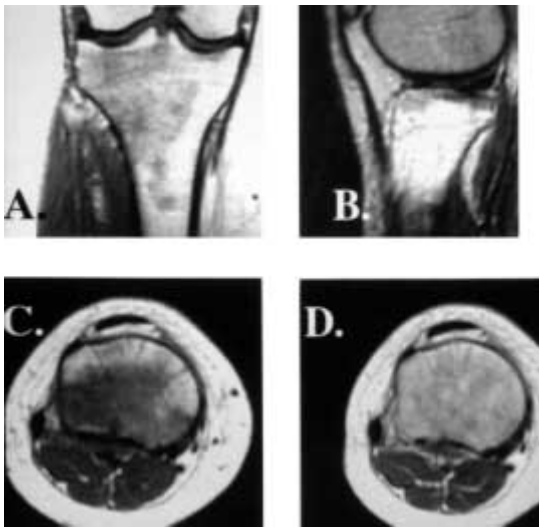

Fig. 4. — An MRI scan of the same case as fig. 3. a : T_1-weighted AP-image demonstrates an area of low signal intensity within the proximal tibial cancellous bone. b : T_2-weighted lateral image demonstrates high signal intensity supporting the presence of bone marrow edema. c : Axial T_1-weighted scan shows an area of low signal intensity. d : following gadolinium enhanced signal is noted.

opinion that this entity should be considered as part of the spectrum of stress-related phenomena (table III). This conclusion is based on the finding of fibrotic changes in the bone marrow that appear to represent a reparative process. The transient bone marrow signal change on MRI appears to represent transient bone marrow oedema as commonly seen around the hip joint. Transient osteoporosis is also typified by bone pain, normal radiographs and abnormal MRI scan. However, in the medullary stress syndrome xrays tend to eventually demonstrate a callus-like lesion that is restricted to cancellous bone. It is of interest to note that the proportion of abnormal xrays increased from 33% (3/9) to 55% (5/9) at the one year follow-up xray. This observation appears to confirm that the lesion observed is an unusual type of a callus-like repair reaction restricted to cancellous bone.

Previously described entities are distinct from the medullary stress syndrome. Conventional or longitudinal stress fractures are also sometimes mistaken for malignancies (3), but the use of MRI scans and especially CT scan often demonstrates the fracture line (8). Bone bruises are subchondral

Fig. 5. — Xray of the same case as shown in figure 1a. demonstrates persistent bone marrow sclerosis, and some periosteal reaction at the site of the bone biopsy.

in location and are trauma related (7). The medullary stress reaction is typified by a diaphyseal or meta-diaphyseal location and the absence of a fracture line on any diagnostic modality. A history of trauma appears unusual. Apparently the main involvement is of the trabecular bone while the cortical bone is spared in most cases. A combination of several imaging modalities might prevent unnecessary biopsies.

CONCLUSION

Stress fractures in bone usually involve the diaphysis in a transverse fashion. Unusual variants occur in a longitudinal fashion. The current series describes a stress reaction in bone that involves entire segments of the cancellous bone without cortical involvement or fracture lines. This entity mimics bone tumors but can be differentiated from them by a combination of imaging modalities.

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SAMENVATTING

D. ROBINSON, Y. KOSSASHVILI, J. SANDBANK, N. HALPERIN, D. ALK. Voorbijgaand botoedeem van de tibia, verdacht voor een medullair tumoraal proces.

De auteurs beschrijven een klinisch beeld ter hoogte van de tibia, bestaande uit botpijn, verhoogde isotoopopname in meta- en/of diaphysis en NMR veranderingen suggestief voor beenmerginvasie, met bioptische kenmerken van mergfibrosis en discrete nieuwbeenvorming. Negen gevallen werden prospectief geevalueerd volgens een vast protocol bestaande uit klinisch onderzoek, radiologie, botscan, CT en NMR met contrast.
Tibiale drukgevoeligheid was telkens aanwezig. Het bot was zichtbaar verdikt in één geval. De leeftijd wisselde van 6 tot 64 jaar. Zes patiënten waren vrouwelijk. Radiografies waren negatief in 6/9 gevallen ; bij de drie overblijvende was er lichte periostale reactie en matige medullaire sclerosis. De verdere beeldvorming bracht in alle gevallen op botscan een longitudinale hypercaptatie ter hoogte van de metaphysis van de tibia en op Ct een vermeerderde densiteit van het merg, aan het licht, zonder een breuklijn aan te tonen. NMR suggereerde beenmergvervanging : T1 geladen beelden toonden een zwak signaal, T2 beelden daarentegen een sterk signaal. Na Gadolinium inspuiting, nam het signaal toe.
Deze klinische entiteit wordt door de auteurs beschouwd als een stressreactie van het botmerg. De verschijnselen verdwenen spontaan binnen de drie maanden, maar bestaande radiologische afwijkingen waren blijvend. Biopsie is nutteloos, op voorwaarde dat het NMr beeld geen corticale betrokkenheid of geen weekdeel massa suggereert.

RÉSUMÉ

D. ROBINSON, Y. KOSSASHVILI, J. SANDBANK, N. HALPERIN, D. ALK. Oedème osseux transitoire du tibia simulant un processus tumoral.

Les auteurs décrivent une entité clinique particulière associant une douleur osseuse, une hyperfixation à la scintigraphie au niveau d'une métaphyse et/ou d'une diaphyse et des anomalies en IRM simulant une lésion développée au sein de la mœlle osseuse. La biopsie osseuse montre une fibrose de la mœlle osseuse et une discrète néoformation osseuse.
Neuf cas de ce type ont été étudiés de façon prospective selon un protocole standardisé qui comprenait l'examen clinique, l'examen radiologique, une scintigraphie osseuse et un CT scan ainsi qu'une IRM avec injection de produit de contraste.
Tous les patients se plaignaient de douleurs au niveau du tibia. Chez l'un d'entre eux, l'os était clairement épaissi par rapport au côté opposé. L'âge s'étalait de 6 à 64 ans ; 6 des patients étaient de sexe féminin. Les radiographies étaient normales chez 6 patients sur 9 ; chez les autres, on notait seulement une réaction périostée minime et une sclérose médullaire modérée. De façon uniforme, l'imagerie montrait en outre une zone d'hypercaptation longitudinale au niveau de la métadiaphyse du tibia à la scintigraphie, et une augmentation de densité de la mœlle osseuse au CT scan, sans trait de fracture. L'étude en IRM montrait un remplacement de la mœlle osseuse, qui se traduisait par une zone de signal de faible intensité sur des images en pondération T1 et par un signal d'intensité élevée sur les images en T2. Après injection de gadolinium, on observait une certaine augmentation du signal. Cette entité clinique, que les auteurs attribuent à une réaction médullaire aux contraintes, est spontanément résolutive ; la douleur disparaît endéans les trois mois. Cependant, les anomalies radiologiques semblent être permanentes. La biopsie n'est pas nécessaire à condition que l'IRM ne montre pas d'entreprise du cortex ou de masse dans les tissus mous.