Correlation of bone scintigraphy and histological findings in medial tibial syndrome

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Abstract

***Objective*—To correlate bone scintigraphy and histopathological findings in patients with medial tibial syndrome.**

***Methods*—Twenty patients (32 limbs) with a clinical diagnosis of medial tibial syndrome had surgery. Bone scintigraphy before the operation was compared with the histological appearance of bone and periosteal specimens obtained at surgery.**

***Results*—Delayed bone scintigraphy showed normal appearance in 11 limbs, characteristic diffuse tubular pattern uptake in 16 limbs, and focal uptake in five. Periosteal histology disclosed fibrous thickening as the most common finding associated with increased vascularity, occasionally with chronic inflammatory cell infiltration, haemosiderin, and acid mucopolysaccharide deposition. Loss of osteocytes was the main finding of bone histology associated with some enlargement of lacunae and lamellar structure disruption. A grading system was used to score normal and abnormal histological appearance. For analysis the findings were regrouped to provide tables using Fisher's exact test. There was no correlation between bone scintigraphy and the histology of bone and periosteum, but two interesting observations were noted. Those cases with periosteal thickening had mostly normal bone scan appearance ($p = 0.0028$). Those cases with low levels of osteocyte loss had mostly abnormal bone scintigraphy.**

***Conclusion*—Abnormal histological appearance of bone and periosteum is a feature of medial tibial syndrome. These histological findings show poor correlation with bone scintigraphy. The exact pathogenesis of this syndrome remains unclear.**

(*Br J Sports Med* 2000;**34**:49–53)

Keywords: medial tibial syndrome; bone; periosteum; scintigraphy; histology

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Accepted for publication
26 August 1999

Stress related bone injuries are common in athletes and account for up to 10% of cases in sports medicine practice.[1] Pain in the lower leg brought on by exercise but relieved by rest is a common complaint in athletes. Stress injuries involving the tibia account for up to 75% of exertional leg pain,[2] and encompass several clinical syndromes such as medial tibial syndrome, chronic compartment syndrome, soleus syndrome, and stress fracture.

Medial tibial syndrome commonly affects young people active in sports such as running and soccer and is characterised by exertional pain along the posteromedial border of the middle and distal thirds of the tibia. Pain is typically felt over a much more diffuse area than in stress fracture, becomes more apparent during activity, and disappears after a variable period of rest which can be as long as 48–64 hours. On clinical examination, there is diffuse extreme tenderness along the posteromedial border of the tibia, swelling is absent, peripheral pulses are normal, and no neurological changes are apparent.[3]

Precise diagnosis of medial tibial syndrome is important for successful management of the condition. Diagnostic work up of suspected medial tibial syndrome includes: clinical examination, plain radiography, compartment studies, and bone scintigraphy. Plain radiographs are almost always normal.[4] Normal compartment pressures (exercise pressure less than 40 mm Hg) exclude chronic compartment syndrome in either the deep posterior or anterior compartments.[5] Bone scintigraphy is a valuable tool in the diagnosis of medial tibial syndrome. Characteristic intense uptake of isotope along the anterior and posterior cortices (double stripe sign) is seen.[6]

The role of magnetic resonance imaging has been described, but because of a wide spectrum of appearance, it has limited value in diagnosing medial tibial syndrome.[2]

Johnell *et al*[7] studied morphological bone changes in operative specimens of patients with shin splints.

No specific histopathological appearance for medial tibial syndrome has been described in the literature. The aim of this study was to correlate bone scintigraphy and histopathological findings in patients with this syndrome. To our knowledge, no such study has been previously published.

Materials and methods

Twenty patients (32 limbs, 12 patients had bilateral disease) with a clinical diagnosis of medial tibial syndrome were operated on between April 1993 and April 1995. There were 14 male and six female patients. The age range was 22–46 years with a mean age of 29 years (table 1). All patients had symptoms, the duration of which ranged from 15 to 22 months before operative treatment. Clinical examination showed diffuse tenderness along the inner border of the distal tibia, and radiographs and compartment pressures were normal in all patients.

Scintigraphy was performed on a Siemens large field of view gamma camera. Three phase studies (perfusion, blood pool, and delayed

Table 1 Age and sex distribution of patients with medial tibial syndrome

	Age (years)		
Sex	21–30	31–40	41–50
Male (n = 14)	7	4	3
Female (n = 6)	5	1	0

phase) after intravenous administration of 400 MBq technetium-99m methylene diphosphonate were performed. Anterior internally rotated views of each tibia were acquired. All scans were reviewed by a single radiologist.

All patients had initially received conservative treatment and physiotherapy. When this had failed, they were treated by fasciotomy of the deep posterior compartment, stripping of periosteum from the posteromedial border of the tibia, and 3 mm drill holes in the medial tibial cortex. After the operation, patients were allowed non-contact exercise—for example, swimming and cycling—after four weeks and contact ground work after three months. Biopsy specimens of periosteum and bone were obtained during surgery from 32 operated limbs. They included periosteum from the medial edge and splinters of cortical bone from the tibia. Histopathological findings of 32 specimens of periosteum and 26 specimens of bone were reviewed by one histopathologist.

All tissues were routinely fixed in unbuffered formal saline. The bone samples were subjected to acid decalcification. Paraffin sections of bone and periosteum were stained with haematoxylin and eosin, Perls stain for haemosiderin, and alcian blue/periodic acid-Schiff stain (PAS) for mucopolysaccharide content.

The following variables were recorded for histopathology of bone and periosteum: for the periosteum, periosteal thickness, fibrosis, vascularity, mucin production, and iron deposition; for bone, lamellar structure, osteocyte loss, and chronic inflammation changes. A grading system was used to assess the variables and to identify normal and abnormal appearance. In each case, a four point grading scale (1 (lowest) to 4 (highest)) was used for each variable. For analysis, it was usually necessary to regroup into low (grades 1 and 2) and high (grades 3 and 4) to provide tables using Fisher's exact test.

Periosteal thickness was measured using a microscope stage Vernier scale together with an eyepiece graticule.

Periosteal thickness greater than 1 mm was considered abnormal. Using the grading scale, fibrosis and increased vascularity, mucin production, and iron deposition giving a combined score >6 was considered abnormal.

Results

Perfusion and blood pool images of isotope bone scans were normal in all cases. The appearances of delayed images were classified into three groups: normal (fig 1), diffuse tubular pattern uptake (fig 2), and focal or patchy uptake. The scans were normal for 11 limbs, 16 limbs showed diffuse tubular uptake, and five showed focal uptake changes.

Figure 1 Medial view of the tibia on isotope bone scintigraphy: normal appearance.

In general the histological findings were extremely varied; in some cases the periosteum or the bone showed no abnormality (figs 3 and 4), and in others there was a wide variety of changes in both tissues.

The most common change in the periosteum was fibrous thickening, and this was usually associated with an increase in vascularity (fig 5), but only rarely with any chronic inflamma-

Figure 2 Medial view of the tibia on isotope bone scintigraphy: tubular pattern characteristic of medial tibial syndrome.

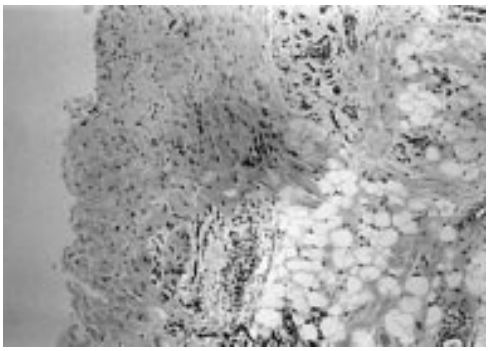

Figure 3 Photomicrograph of periosteum showing only mild abnormalities. There is no thickening, but to the right of the centre of the photomicrograph there is an increase in the number of small blood vessels. Haematoxylin and eosin stain; original magnification × 120.

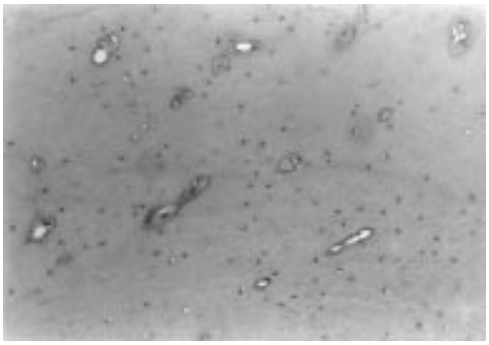

Figure 4 Photomicrograph showing normal bone. Note the presence of osteocytes in all of the lacunae. Haematoxylin and eosin stain; original magnification × 120.

tory cell infiltration. The presence of haemosiderin indicating previous trauma was seen in only a few cases. The low incidence of haemosiderin deposition and acid mucopolysaccharide deposition is in sharp contrast with our other studies on Achilles and patella tendons.[8 9]

The main finding in the bone was apparent loss of osteocytes which was usually associated with some enlargement of lacunae (fig 6). This finding was often associated with some disruption of the lamellar structure of the bone as apparent under polarised light. There was rarely any evidence of chronic inflammation.

Overall, there were 21 cases of abnormal periosteum out of 32 specimens (table 2). Ten cases showed periosteal thickness >1 mm and

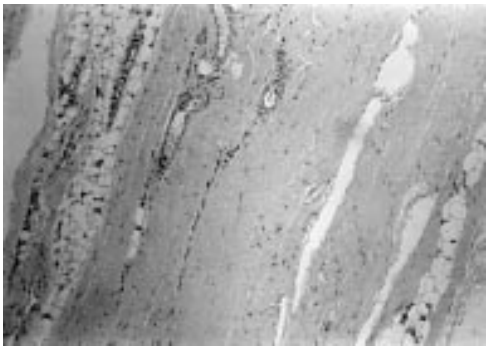

Figure 5 Photomicrograph showing periosteum that is considerably thickened. It is about three to four times the thickness of the specimen seen in fig 3. In this photomicrograph there is increased vascularity to the left of the centre. Haematoxylin and eosin stain; original magnification × 120.

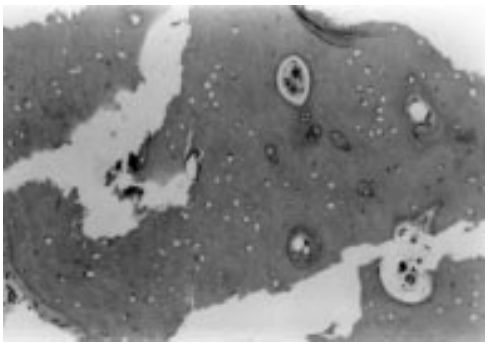

Figure 6 Photomicrograph of bone. Note the absence of osteocytes in most of the lacunae which are themselves larger than normal. The histological features are similar to those encountered in avascular necrosis. Haematoxylin and eosin stain; original magnification × 120.

combined grading score >6. Seven cases showed periosteal thickness <1 mm but combined grading score >6. Four cases showed periosteal thickness >1 mm but combined grading score <6.

Bone changes were considered abnormal if the combined grading score of chronic inflammation, nuclear loss, and damage to lamellar structure was >5. Overall 16 out of 26 specimens were positive (table 2). Initial attempts to analyse the relation between bone scans and the histological results for bone and periosteal changes (tables 3 and 4 respectively) produced no apparent statistically significant results. The number of observations in each group was small, and, for further analysis, only two groups (normal and abnormal) were used for the bone scan results. This produced two totally unexpected results as shown in tables 5 and 6. In the case of periosteal thickening (table 5) abnormal scans were seen almost exclusively in those cases of low periosteal thickness. Conversely increased thickness was mostly seen with normal scans.

When osteocyte loss was examined in this way (table 6), there was more apparent osteocyte loss in those patients with normal scans and a high proportion of the abnormal scans had only low levels of osteocyte loss. The finding for periosteal thickening was statistically highly significant whereas the osteocyte loss just failed to achieve significance.

Table 2 Incidence of significant periosteal and bone histopathological findings in patients with medial tibial syndrome

Histopathology findings	*Bone n=26*	*Periosteum n=32*
Positive	16	21
Negative	10	11

Table 3 Comparison of bone changes with bone scan appearance for patients with medial tibial syndrome

	Bone changes		
Bone scan appearance	*Lamellar structure damage*	*Osteocyte loss*	*Chronic inflammation*
Normal (n = 11)	4	6	1
Tubular pattern (n = 16)	8	8	2
Focal changes (n = 5)	3	3	0

Table 4 Comparison of periosteal changes with bone scan appearance in patients with medial tibial syndrome

	Periosteal changes				
Bone scan appearance	*Periosteal thickening*	*Fibrosis*	*Vascularity*	*Mucin*	*Iron deposition*
Normal (n = 11)	9	6	5	1	0
Tubular pattern (n = 16)	6	11	11	3	1
Focal changes (n = 5)	2	2	2	0	0

Table 5 Table of isotope bone scan by periosteal thickness for patients with medial tibial syndrome

	Periosteal thickness	
Bone scan	*Low*	*High*
Abnormal (n=21)	14	7
Normal (n=11)	1	10

p = 0.0028 (Fisher's exact test).

Table 6 Table of isotope bone scan by osteocyte loss for patients with medial tibial syndrome

	Osteocyte loss	
Bone scan	*Low*	*High*
Abnormal (n=15)	13	2
Normal (n=11)	6	5

p = 0.0946 (Fisher's exact test).

Discussion

Medial tibial syndrome is an ill defined disorder largely because the underlying pathology of the affected tissues has never been properly determined. In 1958 Devas[10] described pain in this area and attributed the cause to stress fracture. In 1986, Detmer[11] first proposed a classification system with which to separate inner tibial border pain into three different types. He suggested the classification of medial tibial syndrome on the basis of involvement of bone, periosteal-fascial junction, and soft tissue posterior to the tibia. Today, medial tibial syndrome is defined as a clinical entity.

Diagnosis of medial tibial syndrome is solely based on clinical features of exercise induced leg pain, compartment studies, and isotope scan appearance.

Bone scintigraphy is a very useful diagnostic tool in the diagnosis of medial tibial syndrome. Lieberman and Hemingway[6] described characteristic superficial uptake along the anterior and posterior cortices (double stripe sign) in medial tibial syndrome. Holder and Michael[12] showed localised abnormal uptake in the middle and distal third of the posteromedial aspect of the tibial cortex in shin splints. Allen *et al*[4] in their study concluded that a tubular pattern of uptake in the tibia on bone scanning is strongly associated with medial tibial syndrome. Isotope uptake in medial tibial syndrome can be focal along the tibia or even normal in appearance.

It has been suggested that medial tibial syndrome may represent a type of fatigue damage to bone (atypical stress fracture) or a traction peristalgia relating to the origin of the tibialis posterior muscle insertion. The exact pathophysiology of this syndrome remains controversial.[2]

Johnell *et al*[7] studied morphological bone changes in shin splints. In 22 of 35 bone biopsy specimens from the medial edge of the tibia, increased tissue metabolic activity, actively proliferating oestoblasts, and vascular ingrowth were evident. In 13 of 33 soft tissue biopsy samples, inflammatory changes were noted in the fascia, and in only one instance was the periosteum affected. These authors suggested stress microfracture as a common cause of shin splints.

All the patients in this study had significant symptoms. Furthermore, in 21 out of 32 cases there were changes on scintigraphy. Similarly, in 21 out of 32 cases there were abnormal periosteal histological findings. In only 16 of 26 specimens were significant bone changes observed.

Our study failed to show any significant correlation between histological and scintigraphic appearance (tables 3 and 4). The findings are disappointing but not entirely surprising. Even in cases showing histological abnormalities, changes such as osteocyte loss were often localised to small areas. This implies a potential major problem with sampling as it would be comparatively easy with the necessarily small samples obtained to miss a histological bone abnormality. The other problem is that it is not possible to ensure that biopsies are performed in all cases at equivalent stages of disease progression. We cannot be sure whether the periosteal thickening and osteocyte loss are early or late phases of the disease as no sequential biopsy material was available.

Two interesting and unexpected observations were noted in the study. The first relates to the relation between periosteal thickening and abnormal scintigraphy. Those cases with periosteal thickening had mostly normal scintigraphy and those with thin periosteum had mostly abnormal scintigraphy. At first sight this finding is the opposite of what one might perhaps expect. It is likely that a thick periosteum indicates a late phase of the disease in which reparative changes are well advanced and an abnormal scan less likely. A thin periosteum would suggest an earlier phase of the disease in which bone changes may well be more active. Differences in the length of history and sampling errors make interpretation even more difficult.

The second unexpected finding was the lack of a correlation between abnormal scintigraphy and bone abnormalities. Bone histology often showed loss of osteocytes but only a few of these cases had abnormal scintigraphy The loss of osteocyte nuclei and the enlargement of lacunae are similar features to those found in avascular necrosis as observed for example in the non-healing fractures of the femoral head. The common presence of bone pathology is certainly a good explanation for the symptoms and signs of this disease. Given the focal nature of the bone changes, it is relatively easy to understand how an abnormal scan may be associated with apparently normal histology because of random sampling of non-involved bone at the time of surgery. What is much more difficult to comprehend is the apparent inverse relation between bone histology changes and abnormal scintigraphy. It could simply be a

chance finding as the relation did not quite achieve statistical significance. Alternatively it could reflect a difference in phasing of the scintigraphy changes in relation to when the bone samples were taken. An abnormal scan could precede the development of bone changes or in other instances could follow healing. Very localised histological changes may well produce a normal scan. We have no complete explanation, and probably only a sequential study with multiple scans and histological observations would provide all of the answers.

In conclusion we have been able to show abnormal bone and periosteal histology in most cases of medial tibial syndrome. These histological changes correlate poorly with abnormal scintigraphy. We do not currently have sufficient evidence to comment on the relative diagnostic value of the two approaches and at present we would recommend that both scintigraphy and histology should be undertaken in all cases until a clearer picture of the pathogenesis of this puzzling disorder emerges.

We would like to thank Louise Stokes for secretarial assistance.

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