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Chronic anterior tibial stress fractures in athletes: No crack but intense remodelling

Stress fractures: No crack but remodelling

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Abstract

Purpose

Delayed healing of anterior tibial stress fractures in athletes is related to high tensional forces acting across a putative fracture gap. These forces lead to crack propagation and create strains that exceed tissue differentiation thresholds for new bone to form in the gap. The “dreaded black line” is a radiographic hallmark sign of stress fractures considered to represent a transverse fracture gap. However, whether a fracture gap truly exists at the microscopic level remains unclear. The aim of this study was to describe the area of the “dreaded black line” microscopically and to identify signs of delayed healing.

Methods

Between 2011 and 2016 we included seven athletes with chronic anterior mid-shaft tibial stress fractures. The fracture site was excised as a cylindrical biopsy. The biopsy was evaluated with micro-CT and histology. The formation of new bone in the defect was evaluated radiographically.

Results

The “dreaded black line” seen on preoperative radiographs in all patients could not be seen on the microscopic level. Instead, the area of the putative crack showed widened resorption cavities, lined with active osteoblasts, and surrounded by immature bone. This area of intense remodelling seemed to create a false impression of a fracture line on radiographs.

Complete cortical continuity was restored at the biopsy site at median eight months (range six to 13 months).

Conclusion

Tibial stress fractures in athletes normally show no fracture defect, but a region of increased remodelling. The healing process is already ongoing but seems mechanically insufficient.

Key Words

Stress fracture, tibia, fracture healing, histology

Introduction

Anterior mid-shaft tibial stress fractures in athletes are prone to healing complications.¹⁻⁴ The underlying causes of the complicated healing are poorly understood, but tensile forces in the anterior tibial cortex due to bending play a major role.⁵ These forces also cause propagation of the putative crack, which ultimately might lead to a complete fracture.⁶ To counteract tensional forces, two surgical techniques are often used: intramedullary nailing and plating.^{2,7-10} Regardless of the surgical technique, the aim is to reduce strain levels in the putative fracture gap to levels that allow the formation of new bone.⁸ This treatment is based on tissue differentiation theories suggesting strain thresholds and ceilings, which determine the type of tissue that will form in a fracture gap. Ideally, to facilitate the formation of new bone, interfragmentary strain should be less than 2% to allow local osteoblast proliferation and formation of lamellar bone.¹¹

A radiographic hallmark of stress fractures in long bones is the “dreaded black line”.¹² This black line indicates the formation of a stress lesion on the tension side in the diaphyseal region of the bone and therefore may be fundamentally different from other types of stress fractures caused by compression. In the tibia, the dreaded black line is typically seen in the mid-shaft of the anterior cortex and the radiographic appearance is that of a locally thickened cortex with a lucent line¹² or V-shaped defect¹³. This specific radiographic appearance has been ascribed a high risk for non-union or secondary complete fracture.¹⁴ Based on the assumption that the black line represents a true transverse fracture gap/pseudarthrosis, surgical intervention is often recommended. However, there is little evidence to support the existence of such a gap at the microscopic level. Nonetheless, in patients with atypical

femoral fractures¹⁵ (a specific type of stress fracture associated with long-term bisphosphonate treatment) the “dreaded black line” shows a well-defined, and very narrow crack in histology, running transversely through the whole thickness of the lateral femoral cortex.¹⁶ These fractures show no signs of healing in the gap but increased remodelling (signs of healing) in the bone around it. We investigated biopsies comprising the area of the putative fracture gap in a consecutive series of athletes with chronic anterior tibial stress fractures, and hypothesised the presence of a stress fracture gap with insufficient healing.

Materials and methods

Patients

Between 2011 and 2016 we consecutively included seven athletes (5 males and 2 females) with an anterior mid-shaft tibial stress fracture, and with symptoms lasting at least six months (Table). Four of the patients were professional athletes, two were semi-professional, and one was an amateur. The mean age at the time of surgery was 25 years, (range 16 to 39). The primary objective of the initial study protocol was to evaluate the treatment effect of fracture gap widening (by use of a cylindrical drill) on fracture healing.¹⁷ Because this effect was unsatisfactory, this report focuses on the unexpected histological findings made in the bone biopsies acquired during widening of the putative fracture gap. The study was approved by the regional ethics committee (DNR 2013/214-31) and all patients formally agreed to participate in the study.

Surgery

The fracture line was identified with an image intensifier. A longitudinal skin incision followed by an incision of the crural fascia was made slightly lateral to the anterior margin of the tibia at the level of the fracture line. In the wound, a periosteal callus reaction could be palpated in all cases. After a longitudinal incision of the periosteum, the bony prominence (periosteal callus) could be seen in all cases (Figure 1A). The site was excised with a cylindrical drill (diameter: 7.3 to 9.4 mm) as a cortical full-thickness biopsy under image intensification (Figure 1B). Postoperative weight-bearing was allowed as tolerated.

Biopsy imaging

Computational 3D radiographs were obtained on a Sky-Scan 1174 micro-CT (Bruker-micro-CT, Kontich, Belgium) to identify the fracture line. All scans were performed at 180 degrees with a voltage of 50 kV and a 1-mm aluminium filter. Reconstruction was carried out with NRecon software (Sky-Scan); beam hardening and ring artefact reduction was applied. In all cases the biopsy was cut into two half-cylinders, with the section parallel to the longitudinal axis of the bone, using an Exact saw. The saw cut was planned using 3D images from micro-CT.

One half of each biopsy was fixed in 4% formaldehyde and stored in 70% alcohol. The samples were embedded undecalcified in polymethyl methacrylate and sectioned by Histo-center AB (Västra Frölunda, Sweden). Hematoxylin and Eosin staining, Goldner's Trichrome and Toluidine Blue stains were obtained.

Macroscopic imaging

All patients underwent preoperative plain radiographs and CT. In five out of seven patients, a preoperative MRI was also performed. After surgery, the formation of new bone was evaluated with CT at two and four months postoperatively and until cortical continuity could be seen in the defect.

Clinical

All patients were followed clinically and reported functional recovery and return to sports.

Results

Biopsy imaging

On macroscopic inspection of the biopsies, after sectioning in two half-cylinders, the section surface showed a discernible lesion in the subperiosteal cortical bone structure in all cases.

The micro-CT sections of the cylindrical specimens did not show a fracture or a fracture crack in any of the cases. Instead, the lesion corresponded to an area in the cortex with wide resorption cavities and an irregular bone structure (Figure 2) corresponding to the histological findings.

Histology showed a 1-2 mm thick periosteal callus in all cases. The callus was well integrated into the underlying cortical bone. Corresponding to the intracortical changes seen on CT and visual inspection, histology showed changes that can be described as resorption and increased remodelling (four cases) or a crevice (two cases). In the cases with resorption and increased remodelling, the lesion comprised wide resorption lacunae (Figure 3), some of them lined with active osteoblasts (Figure 4), and areas of irregularly structured woven bone.

The lesion extended roughly halfway from the periosteal to the endosteal surface, meaning that the inner, endosteal half consisted of normal-looking osteonal bone, with a structure clearly in contrast to the lesion (Figure 3).

In the two cases with a crevice in the periosteal surface, there were no certain structural changes deeper in the cortex. At the periosteal surface, the crevice contained mature-looking fibrous tissue extending from the fibrous section of the external callus less than two millimetres into the cortex. The crevice was surrounded by immature woven bone.

In one patient, a micro-CT and histology were not available for analysis.

Interpretation of microscopic findings

Most importantly: There was no fracture gap visible in histology in any of the cases. In four cases, resorption and increased remodelling were ongoing, possibly as a chronic process sustained by iterated microdamage. The cases with a periosteal crevice might represent the resolution of the lesion, or more likely, a process where the initiating microdamage was located close to the periosteal surface and left the deeper cortex unharmed.

Macroscopic imaging

On plain radiographs or CT reconstructions, all patients showed a horizontal or short oblique putative fracture line (Table, Figure 5). In one patient with available consecutive plain radiographs, this radiolucent line changed in shape between examinations. Initially it appeared as a fracture line. Two months later it appeared as a circular lytic lesion, and 11 months later, it looked like a fracture line again (Figure 6).

In two of five patients with available MRI, a focal bone marrow oedema was noted at the level of the fracture. No pathologic MRI changes were noted in the remaining patients.

After two months, new bone could be seen in parts of the cylindrical defect in four patients.

At four months, all patients showed new bone filling more than 50% of the defect. Complete cortical continuity was restored at median eight months (range six to 13).

Clinical

Four patients returned to the same level of sporting activity as before the stress fracture. The remaining three decreased their level of activity due to discomfort at high performance (two patients) or reasons unrelated to the stress fracture (one patient).

One patient suffered an undisplaced complete fracture of the tibia through the drill hole. The fracture occurred during the first team-based exercise 2 months postoperatively, when the patient accelerated to catch a ball. The fracture was treated with a patella tendon bearing cast and healed uneventfully.

Discussion

In histology and micro-CT, we found that one crucial assumption underlying pathophysiological theories on delayed healing in stress fractures was not fulfilled: there was no fracture gap. Instead, we found an area of increased resorption and remodelling with irregularly structured immature bone. This area gave the false impression of a fracture line on clinical plain radiographs and CT.

One might ponder what inferences can be drawn from our case series of only six available biopsies. The number however, is sufficient to falsify the hypothesis that all chronic stress fractures consist of a fracture crack. Moreover, with zero fracture cracks in a sample of six biopsies, it is unlikely that the majority of patients with clinical stress fractures would actually show a fracture crack on a microscopic level. The 95% confidence interval for zero out of six ranges zero to 0.45. This allows the conclusion that if our patients can be regarded as a random sample, at most 45% of all patients with this kind of clinical fracture in fact have a fracture crack, in spite of the “dreaded black line” on radiographs.

Based on the primary microdamage hypothesis,¹⁸ stress fractures initiate as a focal area of microdamage and microcracks that coalesce to form a stress fracture under persistent loading.^{19,20} When our patients were operated, more than six months after the initiation of symptoms, the damaged area that appeared as a fracture gap on preoperative radiographs appeared remodelled, leaving no visible fracture gap in histology.^{21,22}

Another possible explanation for the lack of a visible fracture gap in histology is based on the primary remodelling hypothesis, meaning that stress concentrations lead to accelerated focal bone remodelling without the formation of a fracture line.¹⁸ According to this theory, the lag time between osteoclastic bone resorption and subsequent osteoblastic bone formation weakens the bone,¹⁸ and as a consequence of the mechanical deterioration of the area, initiates the formation of microdamage which further triggers bone remodelling in a positive feedback loop.²² These focal areas of excessive bone remodelling might be misinterpreted as a fracture gap on clinical radiographs. Similar findings of excessive bone remodelling (increased cortical thickness, periosteal new bone formation, and deformities at the whole bone level) were noted in the tibiae of rabbits that were exposed to forced running and jumping exercises over a 60-day period.²³ A visible fracture line was only seen in one animal

of 20 in the study. Based on their findings in the rabbit model, Li et al²³ hypothesised that disturbances of blood circulation in the Haversian system might be responsible for excessive osteoclast activity and degeneration and necrosis of osteocytes. The hypoxic conditions in the anterior tibial cortex might lead to disturbances in the equilibrium between resorption and bone formation with an overweight of resorption. A recently detected specific type of trans-cortical vessel might be responsible for these specific circulatory conditions and the sensitivity to mechanical overload in the anterior tibial cortex.²⁴ These trans-cortical vessels appear to contribute extensively to the total blood flow of long bones, and connect endosteal vessels with the periosteal blood circulation. These vessels appear to interact with canaliculi of intra-osseous osteocytes and thereby might have a direct influence on bone remodelling. A decreased number of these vessels might play an important, yet unexplored role in the pathogenesis of stress fractures.²⁴

Despite the lack of a fracture gap, our patients still had symptoms preventing most sports activities. One possible explanation might be that immature and poorly mineralised bone is less stiff than mature cortex and therefore the area of immature bone might have made a limited contribution to the mechanical function of the tibia: the newly remodelled area might have biomechanical consequences similar to a true fracture crack. This also implies that the immature bone has undergone considerable strain at loading, which might explain the recurrence of symptoms after periods of rest and our observation that the “dreaded black line” changed in shape over time on radiographs (Figure 3). Deteriorations of the mechanical function of the tibia, despite the absence of a fracture gap, would also explain the higher risk for progression to a complete fracture.¹⁴

The idea to perform this study came from our observations of bisphosphonate-associated atypical fractures of the femoral shaft. Although these fractures are also stress fractures (insufficiency fractures) they show a completely different histological appearance, with a well-defined, and very narrow crack running transversely through the whole cortical thickness of the lateral femoral cortex.¹⁶ They also show the “dreaded black line”.¹⁵ Also in atypical fractures, the line reflects a zone of resorption and immature bone rather than the crack (which is too thin to be macroscopically visible). The most important difference seems to be that in spite of increased local remodelling around the crack of the atypical fracture, the crack is devoid of any living tissue, which could be related to insufficient resorption due to bisphosphonates.²⁵ Similar to our clinical samples, bisphosphonate treatment in animal stress fracture models has been shown to depress remodelling activation and to inhibit healing.^{26,27}

Descriptions of the histology of tibial stress fractures in humans are rare and most are dated several decades ago. We have found in total 10 cases in the literature. All of the patients were described as athletes, with a history of local pain lasting for several years and radiographic and clinical findings that fit rather well with the modern definition of stress fractures. The description and documentation of histological findings and their interpretation differ widely. Most commonly, periosteal thickening, subperiosteal bone apposition, compact bone and empty osteocyte lacunae are described. A fracture crack or fissure in histology is described only in a case description of two ballet dancers from 1956.²⁸ The authors present a histological picture of a fracture crack in one patient, located in the periosteal callus reaction and subperiosteal bone. They suggest that a widening of the Haversian canals might have contributed to the transradiency of the defect on preoperative clinical radiographs. Interestingly, in no other publication a fracture gap is actually described or shown in

histology. Nevertheless, stress fractures are often referred to as pseudarthroses based on histological evaluations.^{4,7,29}

In our study radiographic findings of the stress lesion changed over time in the same patient (Figure 3). Similarly, the histological picture is likely to depend on the timing of the biopsy in relation to the onset of symptoms. In all our cases, the biopsy was taken within one month of the last radiograph showing a fracture line. This limits our findings to a specific time interval in a long-term clinical process.

Perspective

The clinical implications of our findings are clear: Chronic anterior tibial stress fractures are neither biologically passive cracks, nor pseudarthroses, but show intact biological activity. In consequence, there is limited use trying to accelerate healing with bone grafts,¹⁴ transversal drilling² or drugs, such as teriparatide, or widening of the fracture gap. The reasons for the poor healing in these fractures might be similar to those that caused the fracture in the first place – high exercise volume. The traditional treatment seems well motivated: reducing strain, either by plating^{2,9} or nailing,⁷ or by reduced weight-bearing for a sufficiently long time without interruption. Given that the remodelling period in cortical bone in humans is roughly 100 days, and at least two or three remodelling cycles are required to achieve a new equilibrium,^{30,31} the period for protecting a stress fracture region may be longer than generally appreciated by physicians, and particularly by impatient athletes.

Widening of the fracture gap had no obvious positive effect on recovery but allowed the formation of new bone in the defect at normal speed.

Acknowledgements

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Figure legend

Figure 1. The anterior tibial shaft exposed intraoperatively (A). The arrow indicates an area of a cortical crevice with surrounding periosteal callus (Case 6). The cortical defect after resection of the biopsy (B).

Figure 2. Micro-CT showing areas of increased resorption in the subperiosteal bone (arrow).

Figure 3. Histological section (toluidine blue) showing increased resorption in the subperiosteal area (to the left) compared to the cortical bone close to the medullary canal (to the right). The picture consists of two superimposed images to cover the whole thickness of the anterior tibial cortex.

Figure 4. Resorption cavities (r), lined with active osteoblasts surrounded by immature woven bone (arrows) and osteoid (x).

Figure 5 A transverse “fracture line” in the anterior cortex of the tibia on plain radiograph (A) and CT (B) in Case 1.

Figure 6. Plain radiograph of a stress fracture showing a transverse “fracture line” (A). Two months later (B) the fracture line was replaced by a circular area of bone resorption. Another 11 months later a clear “fracture line” can be seen again (C).

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Table. Patient characteristics and background information

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age	16	16	39	23	28	24	26
Sport	Orienteering	Football	Running	Football	Basketball	Running	Hand-ball
Gender	Male	Male	Female	Male	Male	Female	Male
MRI	NA	No changes indicating a stress fracture	No changes indicating a stress fracture	Bone marrow edema. Signal change indicating previous stress fracture	Bone marrow edema. No fracture line	No changes indicating a stress fracture	NA
CT	NA	Intracortical lesion	Cortical indentation	Intracortical lesion	Intracortical lesion	Mild intracortical lesion	Intracortical lesion
Symptom duration (months)	12	12	12	20	7	30	24
Symptom debut	Unspecified	Increase in exercise volume	Change in running style	Change in league level and exercise intensity	Intensified exercise volume after break	Change from street running to track running	Change in league level and exercise intensity
Relevant drug treatment	None	None	None	None	Diclofenac	None	Diclofenac
Relevant comorbid conditions	None	None	None	None	None	Female athlete triad	None
Fracture location	mid-diaphysis	mid-diaphysis	mid-diaphysis	mid-diaphysis	mid-diaphysis	mid-diaphysis	mid-diaphysis





