CASE REPORT

Femoral diaphyseal stress fracture as the initial presentation of acute leukaemia in an adolescent

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Accepted 13 June 2016

SUMMARY

A 14-year-old boy was referred to the orthopaedic clinic by his general practitioner, reporting of a 6-week history of left thigh pain. Clinical examination was unremarkable. Radiographs demonstrated a periosteal reaction at the proximal femur. MRI scans demonstrated a stress fracture of the femur, with no associated sinister features and no evidence of a pathological lesion. As the fracture healed and symptoms improved, the patient became unwell with weight loss, lethargy, chest and jaw pain and fevers. After multiple blood tests over a 25-day period, including five full blood counts and two normal blood films, a third blood film finally demonstrated blasts in keeping with acute leukaemia. We discuss a literature review of musculoskeletal manifestations of leukaemia and the often atypical presentations found.

BACKGROUND

Atraumatic bone and joint pains are very common in the paediatric patient. This case highlights the importance of a detailed history in these cases, including the presence of systemic symptoms such as weight loss, fevers and night sweats, to identify those situations where further investigation is warranted. To the best of our knowledge, this is the first report in the literature of a long bone stress fracture as the initial presentation of acute leukaemia. This case not only highlights an innocuous orthopaedic presentation of haematological malignancy, and also the fallibility of imaging and laboratory investigations in the specific diagnosis of this condition.

CASE PRESENTATION

A 14-year boy was referred to the orthopaedic clinic by his family physician, with a 6-week history of intermittent left thigh and knee pain. The patient reported two discrete acute episodes of knee pain, 2 and 4 weeks prior to presentation, each lasting several days and without precipitant. At the time of each episode he reported a pain score of 10/10, with a baseline at presentation of 2/10. He had no systemic symptoms, with normal appetite and energy levels. He remained fit and active, regularly attending the gym, including during the week of attendance. He had no medical history and no relevant familial history of note.

On examination, he was an athletic young man, walking with a normal gait. He was afebrile with no evidence of lymphadenopathy. There were no skin changes, and no swelling or masses palpable in the thigh. The thigh was non-tender, with a full range of movement in ipsilateral hip and knee.

Plain radiograph demonstrated a periosteal reaction along the diaphyseal region of the left proximal femur ([figure 1](#)), with neither bony destruction nor soft tissue mass evident. Laboratory investigations demonstrated C reactive protein (CRP) 45 mg/L, white cell count (WCC) $3.8 \times 10^9/L$, erythrocyte sedimentation rate (ESR) 35 mm/h and normal blood film.

The patient was provided with crutches and started partial weight bearing on the affected limb.

The following week, an MRI scan demonstrated a benign periosteal reaction with a fine longitudinal cortical fracture in keeping with a stress fracture. There were no associated sinister features nor any evidence of a pathological lesion in the affected area ([figure 2](#)).

Follow-up at 3 weeks after initial presentation found the patient to be relatively asymptomatic from the left thigh. He was not tender to clinical examination of the leg, and had a full range of movement. He had, however, been feeling unwell, with lethargy and weight loss of almost 2 kg over the preceding 3 weeks.

Plain radiographs demonstrated that the fracture was healing. Repeat bloods revealed increasingly raised inflammatory markers (CRP 108 mg/L, ESR 101 mm/h and WCC $3.5 \times 10^9/L$). The results were discussed with a consultant haematologist, who felt that the mild neutropenia was in keeping with a viral illness such as infective mononucleosis.

The patient was acutely admitted the following day with a temperature of 39°C, jaw pain and chest pain. CRP was 86 mg/L, WCC $2.8 \times 10^9/L$ and ESR 78 mm/h. Another blood film was reported as demonstrating reactive lymphocytes, likely secondary to inflammation or infection. While the lower limb pain completely settled, the patient's chest and jaw pains continued. Inflammatory markers continued to rise (CRP 273 mg/L, ESR 112 mm/h and WCC $3.0 \times 10^9/L$).

A further repeat blood film was performed, and on this occasion, found to have numerous blasts, consistent with acute leukaemia. A diagnosis of acute lymphoblastic leukaemia with high-risk cytogenetics was made following bone marrow aspirate at the regional specialist centre.

INVESTIGATIONS

This patient underwent multiple haematological, biochemical and radiological investigations in order to make the diagnosis.

At presentation, his complete blood count was normal. This changed over the following weeks, with decreasing levels of WCC, neutrophils and platelets, as detailed in [table 1](#) below.

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To cite: Chase HE, Pang JH, Sanghrajka AP. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-215551

Figure 1 Plain radiograph of left femur at initial presentation demonstrating a periosteal reaction within the proximal femur.

The levels of CRP and ESR were mildly elevated at presentation, but rose significantly over the course of the next few weeks.

Plain radiographs (figure 1) demonstrated a periosteal reaction in the left proximal femur. MRI scan of the pelvis and left thigh (figure 2) showed periosteal reaction and a fine cortical line in the proximal femur with oedema, in keeping with a stress fracture. No other pathological features, such as lesions within the bone, were apparent. Repeat X-ray 3 months later demonstrated that the fracture had united (figure 3).

While no significant abnormalities were found on analysis of the patient's initial two blood films, a third test 24 days postpresentation demonstrated numerous blasts, which on immunophenotyping would be in keeping with B cell acute leukaemia.

Bone marrow biopsy confirmed a diagnosis of acute lymphoblastic leukaemia with high-risk cytogenetics.

Other relevant blood results: vitamin D—57 nmol/L (50–120), Ca 2.58 nmol/L (2.1–2.6).

DIFFERENTIAL DIAGNOSIS

In this particular case, the differential diagnosis for this periosteal reaction could have been infection (osteomyelitis), primary bone tumour (Ewing's sarcoma or osteosarcoma) or a healing stress fracture. The inflammatory response would have been expected to have been greater at the initial stages with infection or malignancy.

Figure 2 Coronal MRI stir sequence of femurs demonstrating a fine cortical stress fracture affecting the proximal femoral shaft and associated periosteal reaction. Prominent red marrow within the medullary canals of femurs, a normal finding at this age.

TREATMENT

After initial presentation, the patient was given crutches and instructed to weight-bear as tolerated until the MRI had been performed.

Stabilisation of the stress fracture with an intramedullary nail was considered, and discussed with the patient and his family. As the thigh pain was improving and a repeat radiograph demonstrated the fracture to be uniting, conservative management was continued.

Once the diagnosis of high-risk cytogenetic ALL was made on bone marrow aspirate, the patient was started on Regimen C of the UKALL 2011 treatment protocol.¹

OUTCOME AND FOLLOW-UP

The patient's treatment continues under the care of the Oncologists. At 6 months following initial presentation, the patient's stress fracture remains asymptomatic.

DISCUSSION

This case was most unusual in several respects. The patient in this case was an athletic individual, and so a stress fracture was the most likely diagnosis, especially given the lack of systemic symptoms at presentation.

Table 1 Serial complete blood counts from presentation to diagnosis

Blood results (normal values and units)	Days following initial presentation				
	0	20	22	23	24
White cell count ($4-10 \times 10^9/L$)	3.8	3.5	2.8	3.0	2.1
Haemoglobin ($130-170 \times 10^{12}/L$)	154	132	140	141	175
Neutrophils ($2-7 \times 10^9/L$)	0.76	0.6	0.42	0.47	0.33
Lymphocytes ($1-3 \times 10^9/L$)	2.72	2.43	1.98	2.27	1.48
Monocytes ($0.2-1 \times 10^9/L$)	0.25	0.44	0.38	0.24	0.28
Eosinophils ($0.02-1 \times 10^9/L$)	0.04	0.02	0.00	0.01	0.00
Basophils ($0-0.1 \times 10^9/L$)	0.02	0.01	0.02	0.01	0.01
Platelets ($150-410 \times 10^9/L$)	246	195	168	163	123

Figure 3 Plain radiograph of left femur taken 4 months following presentation demonstrating the periosteal reaction is incorporating into the underlying bone as the fracture unites.

An MRI scan was performed in this case, to identify any localised pathology (such as tumour or infection) at the site of the periosteal reaction, and was falsely reassuring as it did not demonstrate any pathology other than the stress fracture. This was not a pathological fracture through a bone lesion, but rather an insufficiency fracture through bone with no associated abnormality evident on MRI. The observation that the periosteal reaction settled on serial radiographs is consistent with the diagnosis of a healing stress fracture.

Diagnosis was also made difficult by the lack of systemic symptoms at initial presentation, with only slightly elevated inflammatory markers and normal peripheral blood smear. Even after the onset of systemic symptoms, the peripheral blood smears did not demonstrate any significant abnormalities.

Leukaemia is one of the commonest childhood malignancies.² Symptoms are usually non-specific, such as lethargy, anaemia, fevers and bruising.³

Musculoskeletal (MSK) pathology is commonly found in these patients, with pain being the most common manifestation.^{3–5} Other symptoms include limping and functional impairment.⁴ From 16% to 18% of patients are reported to present with joint abnormalities^{3,4} such as arthritic symptoms due to bony, periosteal or capsular infiltration,² effusions⁴ or septic arthritis-like presentations.³

Patients with leukaemia presenting with fractures usually have vertebral crush fractures.^{2,3,6,7} There has been one report of a

case of osteochondral fracture of the left femoral epiphysis secondary to avascular necrosis.⁶

Stress fractures are now well recognised in the adolescent population, but the femoral diaphysis is an uncommon location, and, consequently, there are very few reports in the literature.⁷ A literature search found only 5 reports (12 cases) of stress fracture specifically affecting the femoral diaphysis.^{8–12} Stress fractures in the femur have been associated with non-ossifying fibromas or fibrous cortical defects,¹³ but we have been unable to find any previous reports of an association with leukaemia in the literature.

Learning points

- ▶ This is the first report of acute leukaemia presenting with a stress fracture of the femoral diaphysis. Clinicians should be aware of this association, in order not to miss a difficult diagnosis.
- ▶ These types of stress fracture can still unite without operative stabilisation.
- ▶ Musculoskeletal manifestations of leukaemias are relatively common, so the orthopaedic practitioner must be vigilant and have a high index of suspicion when assessing these patients.
- ▶ Peripheral blood smears can be normal in acute leukaemia, so clinicians should have a low threshold for bone marrow aspiration in cases of musculoskeletal pathology with associated systemic symptoms.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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