Spontaneous healing of large femoral cortical bone defects : does genetic predisposition play a role ?

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Traumatic segmental femoral defects are commonly high velocity injuries and their reconstruction necessitates challenging surgical procedures. These injuries present commonly as open fractures and thorough wound debridement followed by adequate soft tissue cover is mandatory before skeletal reconstruction can be commenced. The definitive reconstructive procedure is therefore often delayed and the optimal treatment option is frequently determined by the extent of the cortical defect. The complication rate is high and femoral non-union is not uncommon in these injuries but associated head injuries as part of a polytrauma can have a positive effect on fracture healing. We are presenting a series of four cases, in which traumatic segmental femoral defects of 6, 9, 10 and 15 cm without associated head injury healed spontaneously while the patients were waiting for a definitive skeletal reconstructive procedure.

INTRODUCTION

Cortical defects of long bones are in general surgically treated with an early attempt for skeletal reconstruction (15). Treatment options include cancellous and cortical bone grafting or more complex procedures such as free vascularised bone grafting and distraction osteogenesis (2, 3, 6, 20, 25). Specific indications exist for each of the above procedures but complications during the treatment often warrant alteration of the planned strategy. This can result in multiple operations and a long rehabilitation process for the patient.

Spontaneous healing of large cortical bone defects is a rare phenomenon. To our knowledge, the literature has reported only one case for the tibia and one for the femur, in both occasions associated with head injury (18, 23).

We are describing a series of four cases, where spontaneous bridging of large femoral cortical bone defects occurred and suggesting a genetic predisposition in trauma victims.

MATERIAL

Case 1

A 26-year-old male motorcyclist sustained a polytrauma with the following injuries : fractures to the right tibia, right acetabulum, right humerus and forearm with brachial plexus injury and an open fracture to the right femur (AO 32 C3.3). After the initial wound debridement and application of an external fixator to the femoral fracture at the receiving hospital, the patient was transferred to our unit and underwent on the third day after his injury a second look and definitive treatment of
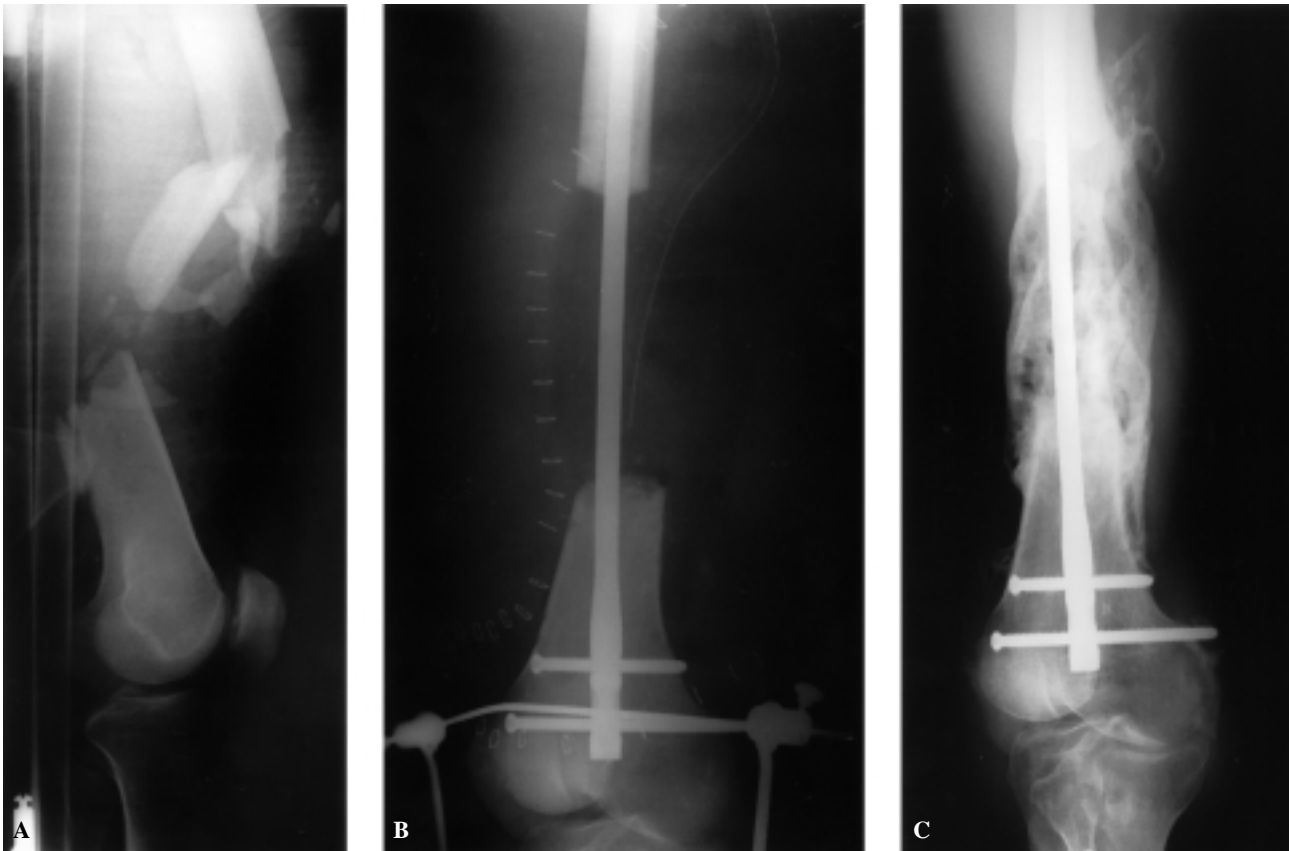
Fig. 1. — Severe open, comminuted distal femoral fracture before (A) and after aggressive wound debridement and stabilisation with retrograde femoral nail (B). The cortical bone defect measured initially 15 cm and filled up spontaneously within 6-8 months (C).

the femoral fracture with a retrograde femoral nail. The diaphyseal bone defect following this procedure measured 15 cm (fig 1A and B). Due to the surgical treatment of the other injuries and wound infection of the upper limb, the planned bone-transport procedure to his femur had to be delayed. At regular reviews in the outpatient clinic, an extraordinary new bone formation was noted and surgery therefore deferred. Six months after the injury the patient was able to fully weight bear without any pain and the radiographs showed that the callus had already bridged the long bone defect. Further reviews confirmed filling of the substantial diaphyseal defect at nine months following the injury (fig 1C).

Case 2

Following a fall of 15 metres height, a 30-year-old male sustained multiple injuries including facial fractures, fractures of both forearms, right patella, both ankles, the left neck of femur and an ipsilateral open fracture of the midshaft of the femur (AO 32-C3.3). A thrombectomy of the left femoral artery was necessary and the left femur was initially treated at the receiving hospital with a Dynamic Hip Screw (DHS) for the intertrochanteric fracture and double plating to the open femoral fracture. Seven months after the initial treatment an infected non-union with failing metal work was diagnosed and the patient underwent revision surgery. During extensive wound debridement all dead bone was excised, the previous metal work removed and a solid antegrade femoral nail inserted. The cortical bone defect after sequestrectomy measured 10 cm. A bone transport procedure was planned but deferred because an unusual amount of new bone formation was noted. Within few months the gap had been spontaneously bridged and 10 months after the nailing procedure (16 months after trauma) the patient was full weight bearing and the fracture had radiologically united (fig 2 A and B).
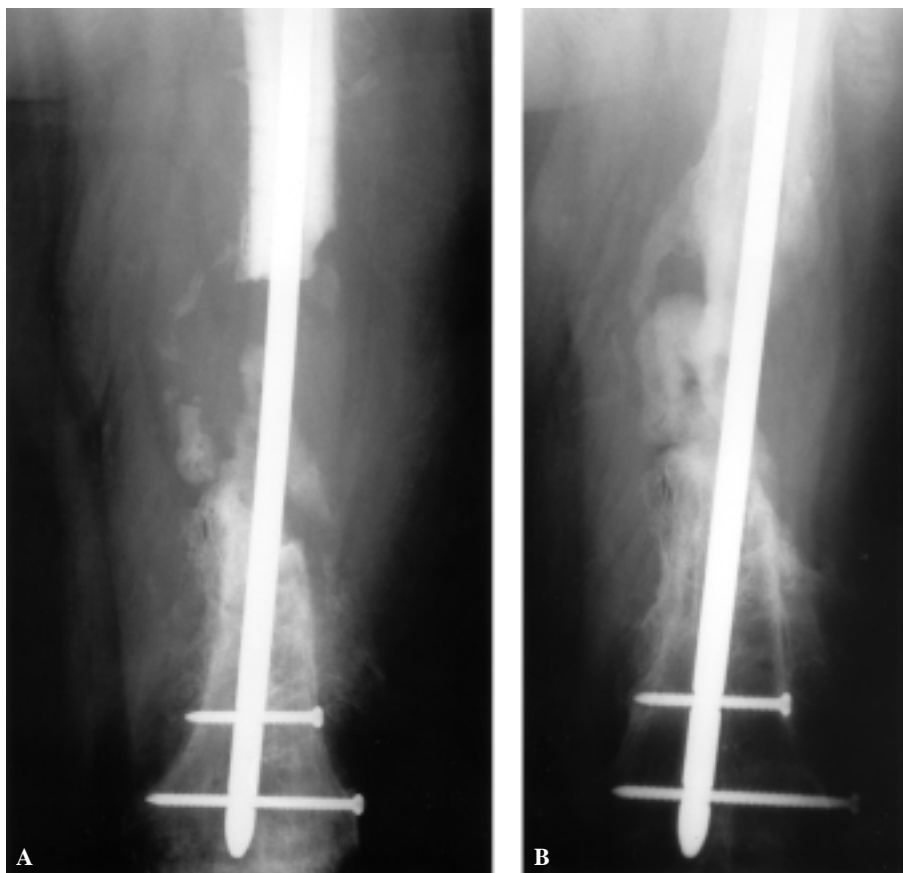
Fig. 2. — The femoral cortical defect after wound debridement and sequestrectomy measured 10 cm and was stabilised with an antegrade femoral nail (A). Figure B shows bridging of the bone gap 6 months following internal fixation.

Case 3

A 33-year-old woman sustained an isolated open fracture of the distal femur (AO 32 C3.3) after falling down 14 stairs at her home. Due to marked cachexia caused by long-standing anorexia nervosa, the initial treatment at the admitting hospital consisted of wound debridement and skeletal traction. The patient was transferred to our hospital and 13 days after the accident she underwent further wound debridement with sequestrectomy of all devitalised fragments and a 6 cm distal femoral cortical defect was bridged with an angled blade plate device. The patient was discharged home with a splint and six months after the initial internal fixation the bone gap had been filled and allowed weight bearing.

Case 4

A 21-year-old male motorcyclist sustained multiple injuries including blunt abdominal trauma causing spleenic rupture, multiple fractures to the forearm and hand and an open fracture of his left distal femur with immediate bone loss, causing a cortical bone defect of 9 cm (AO 32 C3.3). After the initial application of an external fixator to the femur the patient underwent on the fifth day reconstruction of the femoral condyles and bridging of the long cortical bone defect with a long reconstruction plate. Due to the initial open wound, bone grafting was deferred. During the following weeks extraordinary new bone formation was noted and six months after the injury the patient was weight bearing with the help of only one walking stick.

DISCUSSION

Cortical bone defects are commonly associated with motorcycle and other road traffic accidents, where the skeletal injury is part of a polytrauma. Due to the nature of these high-velocity injuries, the associated soft tissue injury often condemns the skeletal injury to an open fracture, which often prevents primary definitive stabilisation and warrants particular treatment algorithms (1).

Up to date, the treatment of open fractures with segmental bone loss remains challenging and follows several stages. Accurate assessment of the skeletal injury, the associated neurovascular structures and their soft tissue envelope is essential and can often be carried out only intra-operatively. Based on this assessment, associated surgical specialists are involved and a multi-disciplinary treatment plan developed. Meticulous wound debridement with removal of all devitalised tissues and thorough lavage is the mainstay of these complex injuries and determines the final outcome (15, 24). Adequate soft tissue cover follows internal or external skeletal stabilisation. If the expertise is available, early internal fixation with immediate soft tissue cover has shown favourable results (14). If gross contamination has occurred or any doubt about tissue viability persists, temporary external fixation might be necessary and delayed closure of the soft tissue envelope is the preferred method. Only if a clean and healthy soft tissue bed has been accomplished, should a delayed procedure for the reconstruction of the cortical bone defect be contemplated (24). Considering the individual situation, several surgical options are available. *Autologous cancellous bone grafting* is the most commonly used method for the reconstruction of segmental skeletal defects (12). However the limited amount available, the tendency for delayed revascularisation and the high incidence of non-union compromise the use in larger defects (15). To increase mechanical graft stability and to allow anatomical reconstruction in one stage, the use of cancellous bone grafting within a cylindrical titanium mesh cage over an intramedullary nail has been recently described for the reconstruction of tibial cortical defects (10). This technique might be a promising treatment option for larger femoral defects, when synthetic osteoconductive matrices as an alternative or adjunct to cancellous bone graft are more readily available. *Cortical bone grafting*, when compared with cancellous graft can bridge larger defects and gives initially greater mechanical strength. But owing to its lesser porosity it must first undergo a resorptive phase to allow osteoconduction with ingrowth of fibrovascular tissue and replacement of the graft. This process causes a decrease in mechanical strength, requires a prolonged period for incorporation and shows a higher incidence of infection (9, 11). *Vascularised bone grafting* is a technically demanding procedure and donor site morbidity can be high (17). But healing rates of 80% have been described and Pirela-Cruz and Decoster (28) described the main advantages of this technique as "more rapid and complete graft incorporation with immediate structural support, the ability of the transplanted (living) bone to form new bone and the addition of new blood supply to the recipient area". *Distraction osteogenesis* for the bridging of traumatic bone defects is based on the principle of callus distraction and has been described with unilateral and circular frame devices (26, 31). Despite the high complication rate including delayed and non-union at the docking site, wire failure, pin-track loosening and infection, soft tissue contracture and joint stiffness, this technical demanding procedure has become extremely popular in recent years (19, 30). In order to reduce time-related frame complications, Carrington *et al* (8) described the technique of combining an external ring fixator over a solid intramedullary nail for the treatment of a 13-cm tibial defect. As soon as the cortical defect was bridged the ring fixator was removed while the intramedullary device ensured mechanical stability and allowed so early mobilisation without compromising further callus consolidation. Skeletal stability and a clean and healthy soft tissue bed have been postulated as mandatory for successful bone regeneration (24). But equally important is an osteoconductive substrate functioning as a scaffold between bone ends, enabling active ingrowth of bone and fibrovascular tissue (11). As an alternative to autogenous bone grafting several synthetic substrates including

hydroxyapatite, tricalcium phosphate, collagen as well as non-biological substrates such as polylactic/glycolic acid polymers and tantalum have been experimentally and clinically used with various success (11, 22). The stimulation of the fracture healing process with fibroblast growth factor, transforming growth factor beta, insulin like growth factor and bone morphogenetic proteins as well as the use of gene therapy are subjects of ongoing research in the field of fracture healing enhancement (5, 21, 29, 32, 34).

In none of the four described cases, was any of the above-mentioned surgical procedures or healing-enhancement interventions initiated. Cortical defects of 6, 9, 10 and 15 cm bridged and filled spontaneously within 6 to 10 months following skeletal stabilisation, resulting in a mean consolidation index (C.I.) of 0.96 months per cm (0.4 – 1). This demonstrates an extraordinary potential for spontaneous bone regeneration, when compared with surgical reconstructive techniques with a consolidation index of 1.7 months per cm for elective limb lengthening (26) and 1.9 months per cm for the treatment of traumatic segmental defects (15). Raschke *et al* (31) observed the same phenomenon during distraction of an 8-cm femoral defect with hypertrophic callus formation (C.I. of 0.35 months per cm) and Horch *et al* (18) described the spontaneous bridging of a 15 cm femoral defect within 6 months (C.I. of 0.4). Both of these patients had associated head injuries, which is a well-described association for the formation of hypertrophic callus as well as heterotopic ossification (4, 27, 33). In none of the described cases was such influence present and it remains only speculative, that similar neurogenic and other humoral factors might be present, initiating and accelerating the bone healing process (7). The stimulus for such mechanisms could be genetically programmed and might explain, why different trauma victims respond differently regardless standardised treatment protocols. Some trauma patients develop a whole range of complications despite optimal trauma care while others recuperate regardless their treatment. Genetic predisposition may play a key role in the metabolic and immunological response of trauma victims and might be responsible for such extraor-

dinary healing potential as described in the observed phenomenon (16). The severity of the fracture pattern might also be an important stimulus and would correspond to findings of our earlier studies, suggesting that more complex (C-type) fracture pattern heal faster (13). An interesting observation was that the consolidation index was lower when intramedullary devices were used. This might reflect the individual implant biology with different local and systemic effects but cannot be substantiated with such a small series.

CONCLUSION

These four cases represent an extraordinary observation, demonstrating the enormous potential for bone regeneration in certain individuals. The importance of a clean and healthy soft tissue bed for successful fracture management is well known but mechanisms, which lead to the here described observation will need further research. Knowing the responsible immunological, hormonal and inflammatory factors as well the genetic make-up of predisposed individuals could ultimately help the surgeon to select from different treatment options the best suitable for the patient, therefore avoiding long-standing complications.

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