■ CASE REPORT

Bone morphogenetic protein 7 in the treatment of congenital pseudarthrosis of the tibia

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We describe a 13-year-old boy with atrophic tibial pseudarthrosis associated with neurofibromatosis who had undergone nine unsuccessful operations. Eventually, union was obtained by the use of bone morphogenetic protein 7 in conjunction with intramedullary stabilisation and autologous bone graft.

Congenital pseudarthrosis of the tibia is a rare disorder, usually appearing during the first two years of life. Neurofibromatosis is present in approximately 40% to 50% of patients with pseudarthrosis and approximately 10% of patients with neurofibromatosis develop pseudarthrosis of the tibia. Treatment is challenging and often disappointing and unsatisfactory outcomes may lead to amputation.¹

Operative treatment includes intramedullary rodding and grafting, limb lengthening, vascularised fibular transfer and the Ilizarov techniques.²⁻⁵ However, even after multiple attempts to achieve bony union,²⁻⁴ amputation may be needed.

The osteogenic proteins are a class of natural growth factors of the bone morphogenetic pro-

tein family (BMP) which stimulate bone regeneration.⁶ A specific member of this family is BMP-7, known as human recombinant osteogenic protein number 1 (rh OP-1), which accelerates bone repair compared with a control fracture when injected into a fresh fracture model.⁷

Case report

The patient was born by normal delivery after an uneventful pregnancy. There was no family history of congenital problems. At the age of nine months, 'café-au-lait spots' appeared on his back and abdomen. At 14 months, there was anterior bowing of the right leg and neurofibromatosis was diagnosed. When he had reached 20 months and began to walk, the leg was protected by an ankle-foot orthosis with an anterior shell.

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Fig. 1a

Fig. 1b

Radiographs showing the tibia pre-operatively a) lateral and b) anteroposterior views. The boy had undergone nine unsuccessful surgical treatments.

Fig. 2a

Fig. 2b

Radiographs showing early bony union five weeks after surgery a) anteroposterior and b) lateral views.

Fig. 3

Radiograph at five months post-operatively following removal of the transarticular pins.

Fig. 4

Radiographs showing the fracture is united two years after surgery.

At 30 months, he fell and fractured his tibia and fibula in the region of the deformity. After six months of unsuccessful cast treatment, he underwent intramedullary nailing. Five subsequent operations, combining intramedullary nailing with autograft and casting, were unsuccessful. Each

time after the protective cast or the intramedullary rods were removed, the leg refractured.

When he was eight years old, the Ilizarov technique was tried for a period of seven months during which several pin-track infections required treatment with antibiotics. Union

Fig. 5

Clinical appearance of the limb.

was not achieved and the bone ends became tapered and sclerotic. After two further failures using the Ilizarov technique, amputation was advised. This was refused by the family.

On referral to our hospital an alternative option was investigated. We were aware of several challenging cases of pseudarthrosis which were successfully treated using BMP-7.⁶ Although all were adults and none had neurofibromatosis, it was decided, with parental approval, to attempt that treatment.

At the time, there was 50° of anterior angulation and a 20° varus deformity at the pseudarthrosis (Fig. 1), which was mobile. The ankle had only 15° of plantar flexion and no dorsiflexion. The child had local pain and the leg was shortened by about 4.0 cm.

After resection of the pseudarthrosis, intramedullary nailing and grafting were performed. A mixture of one vial of Osigraft (Stryker Biotech, Hopkinton, Massachusetts) containing 3.5 mg of human recombinant Osteogenic pro-

tein 1 (eptoterminal alpha) with 1 g of purified collagen matrix and cancellous bone from the ipsilateral posterior iliac crest was packed into the nonunion. Because of the location of the pseudarthrosis two rods were not enough for mechanical stability. The fixation was completed by three further 2-mm K-wires and the wound closed without drainage. The leg was immobilised in a plaster cast for six months, with partial weight-bearing allowed three months after operation.

Bony union was noted five weeks after surgery (Fig. 2). The transarticular pins were removed at five months when the patient was allowed full weight-bearing (Fig. 3). Although he had no pain, walking was limited to less than one hour per day for one month and thereafter was not restricted.

The fracture was united at 28 months (Fig. 4) and the new bone appeared of good quality. Ankle mobility was unchanged. The patient had no complaints, other than minor concern about the appearance of the leg (Fig. 5). The leg was 5 cm shorter and he walked unrestrictedly with a 4 cm shoe raise. He had a good school record but did not participate in sport except cycling for a few hours a week. He and his family are very satisfied with the result.

Discussion

To our knowledge, this is the first use of BMP-7 (OP-1) for tibial pseudarthrosis associated with neurofibromatosis in a growing child.

The recognised indication for BMP-7 (Osigraft) in the tibia is for long standing post-traumatic pseudarthrosis in skeletally mature patients when autograft has failed or is unfeasible. We decided to use BMP-7 in our 13-year old patient because all other treatments had failed and the attending surgeon recommended amputation.

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