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Clinical report

Delayed presentation of congenital tibial pseudarthrosis and neurofibromatosis: a difficult union

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Background: A new case of congenital pseudarthrosis of the tibia (CPT) presents yearly to CSC, but treatment is prolonged, and not always successful.
Objective: To study the outcomes of treatment, and to determine whether a relationship with neurofibromatosis (NF) was of significance.
Methods: A review of the medical records at our centre revealed 11 cases of CPT, 5 of which were associated with neurofibromatosis.
Results: Most patients had multiple operations for their case of CPT, which did finally lead to union in 6 out of 6 cases with no NF, but in only 1 case out of 5 when NF was present.
Conclusion: Late presentation and severe deformity can be overcome, and union can be achieved, but NF has a deleterious effect on obtaining union.

Keywords: Cambodia, congenital pseudarthrosis of tibia, Ilizarov, neurofibromatosis, non-union

Congenital pseudarthrosis of the tibia (CPT) is a rare paediatric malformation occurring in 1/150,000 births [1]. It remains one of the most challenging orthopaedic conditions to treat. Presentation occurs from infancy to childhood as tibial dysplasia, with anterolateral bowing, eventually leading to pathological fracture, which typically occurs at the junction of the middle and distal thirds of the tibia [1-5]. Neurofibromatosis type 1 (NF), (Von Recklinghausen's disease), is a genetic disorder frequently associated with CPT [3, 6] and bone remodelling defects are further exaggerated in this condition [4-7].

The natural history of CPT towards worsening, deformity and shortening, necessitates surgical intervention or prophylactic bracing. Surgical treatment is aimed at achieving union, restoring alignment, and preservation of bone growth [1]. Association with NF was long believed to be a negative predictive factor for CPT union, but the recent literature rejects this notion [1, 9-12]. However, prognosis is poorer in older children, markedly progressive disease, shortening, severe deformity with bone atrophy, fibular involvement, and rapid resorption of bone grafts [1, 8, 11]. Late presentations of CPT are functionally and prognostically problematic, because the distal segment becomes shorter because of resorption, therefore difficult to fix, and the reduced vasculature impairs healing [9, 11, 12].

Treatment of this serious disorder is challenging because of difficulties in achieving union, and the persistence of angulation, joint stiffness, and limb length discrepancy (LLD) [1]. Despite numerous acceptable approaches, there is yet to be consensus regarding the optimal operative procedure, fixation, timing, or adjunctive pharmaceutical therapy [4]. Research from optimal settings suggests the three techniques with the highest rates of union are intramedullary nailing with bone graft (>80%), vascularised free fibular transfer (>70%), and the Ilizarov technique (50–90%) [1]. Despite the improvements in prognosis with these techniques, multiple surgeries are frequent and the risk of amputation never ameliorated [1].

The Children's Surgical Centre (CSC) in Cambodia is a non-governmental surgical centre aiming to improve the quality of life of disabled Cambodian children and adults through a wide range of rehabilitation surgical services, free of charge. Our cases of CPT can present decades after the age of recognition because of the lack of affordable healthcare elsewhere. This is a difficult surgical environment, but with improving facilities, such as the

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acquisition of Ilizarov frames in 2005, the centre has the operative facilities to achieve good outcomes. To our knowledge, this is the first published study, from a developing world setting, to examine such late presenting and difficult cases and is a retrospective review of success rate of treating patients with CPT at the CSC.

Methods

Patients with CPT treated at the CSC were identified using the centre's electronic database. The first author (MH) then reviewed both electronic and paper records. Data was collected for gender, side, presentation date, age at initial operation and final consultation visit, associated NF, pre-operative deformity, operations performed, outcome, time to outcome, complications, and presence of residual deformity. Unequivocal radiographic evidence was required to confirm union. Ethical considerations have been upheld through written consent regarding the use of patient records for research purposes in accordance with guidelines of the Helsinki Declaration.

Results

This review identified 11 patients presenting to the CSC for CPT between October 2000 and March 2012. Five male and six female patients were included. NF was present in five people (45%); two male and three female. Side of pathology showed minimal variance with five right and six left sided cases. Mean age was 9.4 years (range 0.8 to 25) at first operation. Excluding one case of immediate amputation, mean age at final consultation was 11.6 years (range 2.8 to 26.9). At the time of data collection, mean follow up was 29 months (Range 3.6 to 60).

The majority of cases undertaken were late presentations with severe pre-operative deformity (**Table 1**) including two cases of apex anterior angulations of over 100 (cases 2 and 10). The severity of some cases is highlighted in **Figures 1, 2, and 3**.

Table 1. Demographics, pre-operative deformity, surgery and outcome

#	Age at first op (years)	NF	Pre-op deformity	Method of fixation	Outcome	Time to outcome (months)	Residual deformity
1	7	No	N/A	1. Tibia K wire	Union	2.4	Nil
2	25	No	130° apex anterior	1. Tibia and fibula IM pins 2. Additional bone graft	Union	14	9 cm LLD
3	11.3	No	35° apex anterior 30° apex lateral	1. Free fibular transfer 2. Ilizarov apparatus	Union	16	Nil
4	1.7	Yes	35° apex anterior 20° apex lateral	1. Tibia IM pin, bone graft 2. Free fibular transfer	Non-union, in brace	14	Non-union
5	24.1	No	80° apex anterior; AP NI	1. Tibia and fibula IM pins, bone graft 2. Bone graft 3. Ilizarov apparatus	Union	34	4 cm LLD
6	2.6	Yes	50° apex anterior 25° apex lateral	1. Tibia IM Rush rod 2. Ilizarov apparatus	Union	12	3 cm LLD Valgus deformity (20°)
7	3	No	40° apex anterior 15° apex lateral	1. Ilizarov apparatus, bone graft 2. Tibia K wire, Ilizarov apparatus, bone graft 3. Tibia IM pin, bone graft, Ilizarov apparatus 4. Tibia IM Rush rod, bone graft 5. Tibia IM Rush rod (larger), bone graft	Union	20	2.5 cm LLD
8	14	Yes	50° apex anterior 20° apex lateral	1. Ilizarov apparatus, tibia IM pin, bone graft 2. Ilizarov apparatus, tibia IM pin, bone graft 3. Tibia IM Rush rod, bone graft	Non-union. Brace and shoe lift		Likely non-union

Table 1. Demographics, pre-operative deformity, surgery and outcome (Continue)

#	Age at first op (years)	NF	Pre-op deformity	Method of fixation	Outcome	Time to outcome (months)	Residual deformity
9	0.75	No	25° apex anterior 30° apex lateral	1. Tibia IM Rush rod	Union	41	LLD 1 cm Left foot smaller 10° valgus deformity
10	11	Yes	120° apex anterior AP NI	1. BKA	Amputation	Immediate	BKA
11	2.5	Yes	70° apex anterior 40° apex medial	1. Ilizarov apparatus	Non-union. Abandoned. Brace until further review	2.4	Non-union

NF = neurofibromatosis type 1, AP = Anteroposterior X-ray image, NI = not interpretable, BKA = below knee amputation

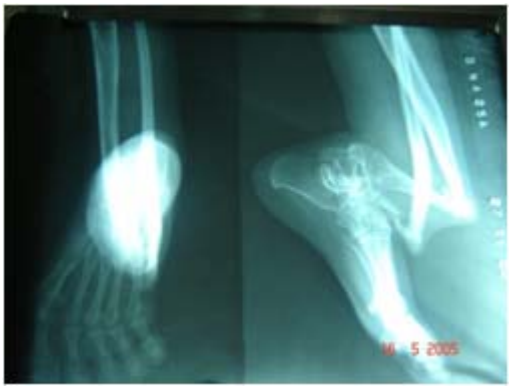

Figure 1. Patient 2 pre-operative X-ray image

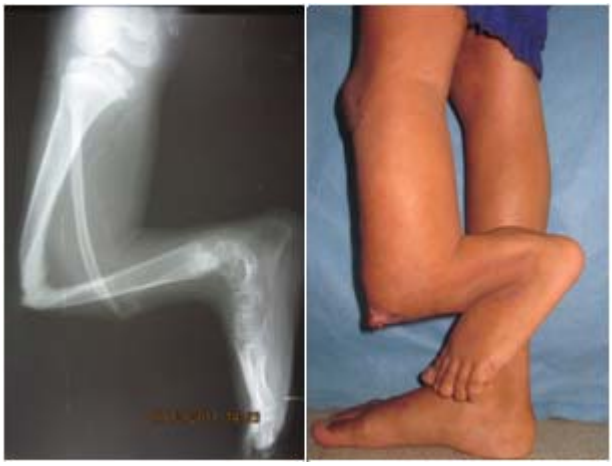

Figure 2. Patient 10 pre-operative X-ray image and clinical presentation

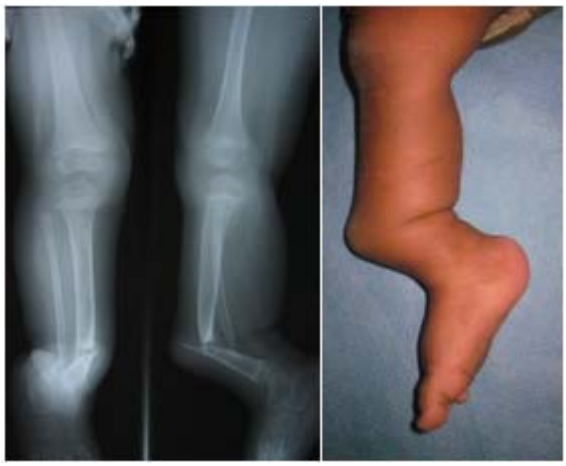

Figure 3. Patient 11 pre-operative X-ray image and clinical presentation

Union was achieved in 7 of 11 cases (64%). However, in patients with NF, only 1 of 5 (20%) achieved union while in non-NF patients it was 6 of 6 (100%). Operative methods not only varied between patients, but different methods were also used in individual patients. Intramedullary nailing was used in 11 operations on seven patients, with union achieved in five, and as the final effort to achieve union, in three. Free fibular transfer was used on a single occasion each, in two patients, with union in one case after additional procedures. The Ilizarov technique was used 9 operations in 6 patients, with union achieved in four patients, and as the final method in three. Patient 11 is classified as a non-union, but will return in the future for further surgical attempts. Union was achieved in one case solely using a K-wire.

Three cases of persisting non-union occurred, despite use of the Ilizarov technique on two, intramedullary nailing in two, and free fibular transfer in one. NF was present in all three with ages at presentation of 20 months, 30 months, and 14 years. The single case of union in a person with NF (case 6) was a 31-month-old boy who achieved union at 12 months using intramedullary nailing followed by the Ilizarov technique. A further two operations to reduce valgus deformity were performed and the patient is continuing to do well. **(Figure 4)**.

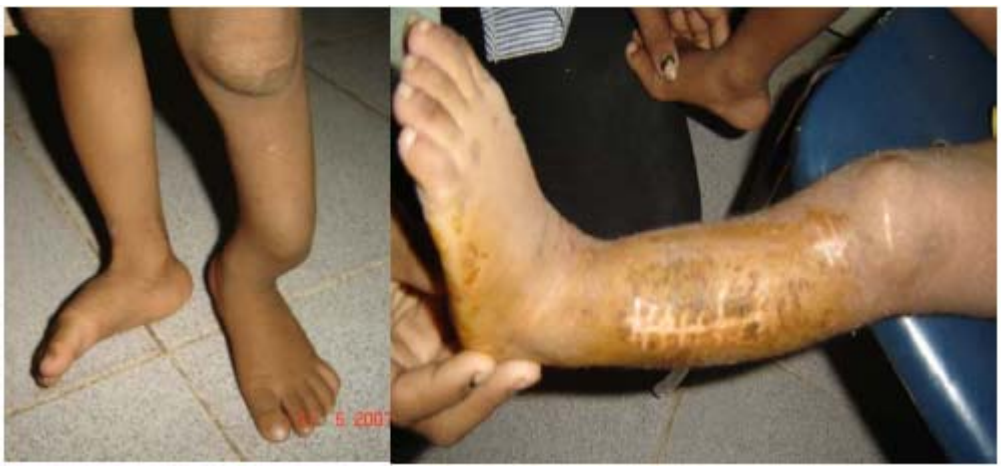

Figure 4. Patient 6 presentation and outcome

Given the late presentations and degree of deformities, we have encountered a number of challenging cases. Patient 5, a 24-year-old woman, presented in November 2004 with a severe left sided CPT **(Figure 5)**. Following three separate operations, union was achieved after 34 months with a 4 cm difference in LLD **(Figure 6)**.

Patient 8, a 14-year-old boy with NF, presented in September 2008 with a right sided CPT **(Figure 7)**. A previous attempt at union had occurred at a separate hospital with no success. Despite use of intramedullary nailing with bone grafts and the use of the Ilizarov technique, union was not achieved and he remains in a brace with a shoe lift to improve his quality of life **(Figure 8)**.

Minor complications were present in nine patients and managed conservatively; the majority were pin site or wound infections. Residual deformity was present in patients; four cases of non-union, five cases of LLD, one BKA (which was considered too unlikely to unite and so received a primary amputation), and two valgus deformities.

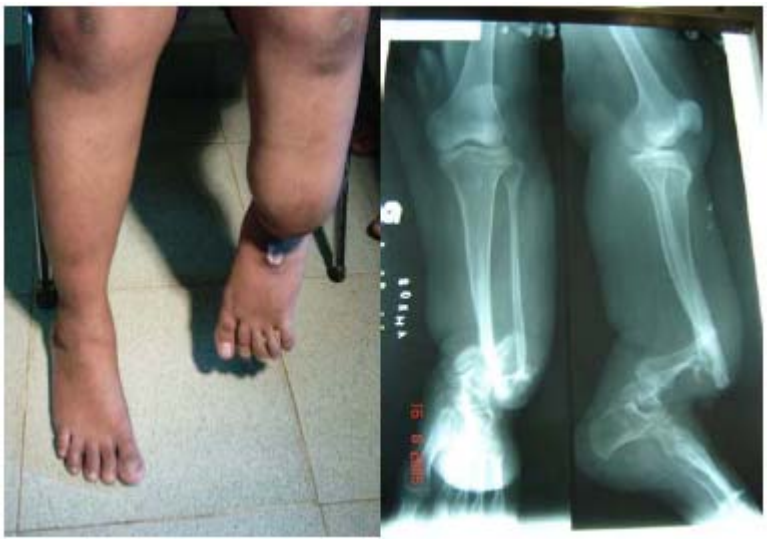

Figure 5. Patient 5 clinical presentation and pre-operative X-ray image

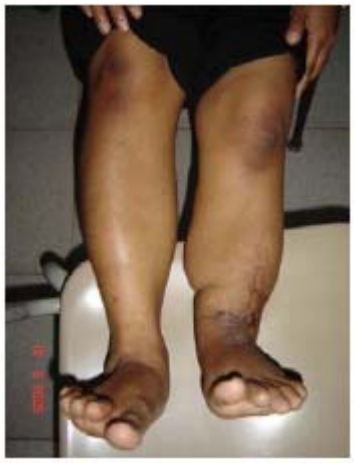

Figure 6. Patient 5 outcome

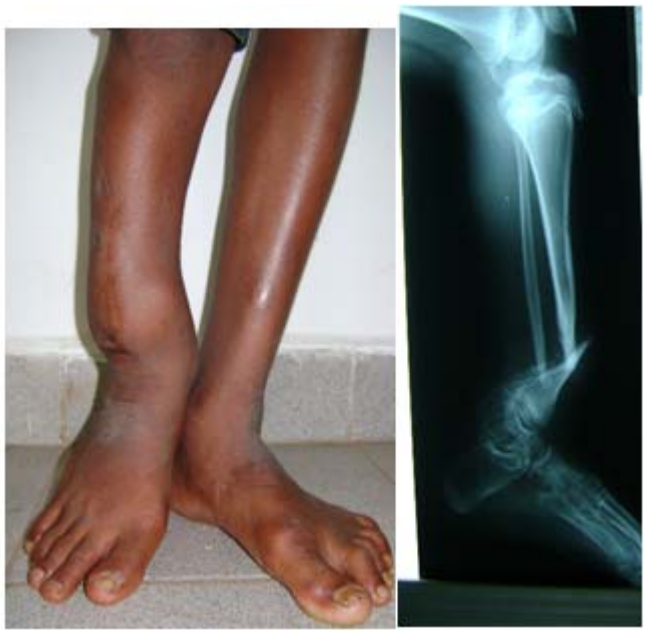

Figure 7. Patient 8 clinical presentation and pre-operative X-ray image

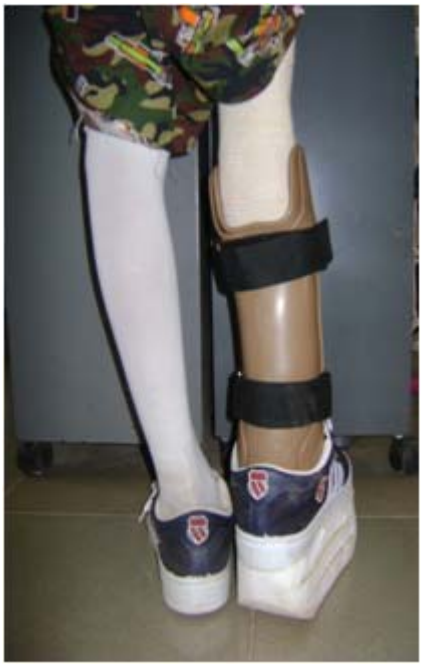

Figure 8. Patient 8 brace and shoe-lift

Discussion

Treatment of CPT remains one of the most formidable orthopaedic problems. Multiple surgical procedures and protracted medical care can have profound effects on quality of life. Achieving union remains only the first step of a long-term treatment plan including promoting leg length equality, limiting deformity, improving limb strength, and optimising function [4]. Considering our setting, we are attaining good results with a 7 of 11 (64%) union rate, and one amputation. Only one union was achieved in those with NF and is inconsistent with the literature that suggests equal rates of union [1, 9-12]. Our circumstances differ from the literature because of

delayed presentation, degree of progression, and deformity severity at presentation.

The mean age at first operation of 9.4 years is high and attributable to the paucity of free medical care in Cambodia. In most developed settings, care is received shortly after recognition. In many of our patients, years have passed from recognition to treatment. This delay promotes disease progression with bone-end resorption and impaired vascularisation of the distal segment [11, 12]. Morrissy et al., in a series of 40 cases, reported no patient achieved a good result if union had not been achieved by the age of six years [11]. This delay also abrogates our potential for optimal timing of surgery; the European Paediatric Orthopaedic Society (EPOS) recommendation is after the age of three [13].

Most case series do not consistently encounter the degree of progression and deformity that we have encountered. Prognosis is better when the disease is not markedly progressive [1]. Given our experience and success with markedly progressive non-NF cases, and the poor results in the NF cohort, we are led to believe that the presence of NF confers a poorer prognosis in late presenting, markedly progressive cases. This may relate to the effects of time on the decreased osteoblastic and increased osteoclastic bone metabolism that is exaggerated in NF [4, 6].

Because of the variations in procedures used, not only between patients, but also in individual cases, the results are difficult to interpret. The CSC relied heavily on the use of intramedullary nailing for this condition before the acquisition of the Ilizarov technique. Intramedullary nailing offers alignment, correction of the deformity and guides bone lengthening. This method achieved union with a good outcome in one child receiving five operations. Some authors believe the number of operations performed does not seem to affect the chances of obtaining union [14], but this is in contrast with previous reports suggesting amputation should be considered if a persistent non-union were present after three surgical attempts [9].

The availability of the Ilizarov technique has greatly improved our ability to treat CPT. The Ilizarov technique offers adaptability to many situations. Small bone fragments can be stabilised, deformity corrected and limb equality restored in a single procedure [1]. These advantages bode well with the presentations we encounter. Negative features include recurrent fractures because of persistent axial deformities and high rates of pin infections; the latter is consistent with our experience [1]. EPOS, in a study of 108 patients, concluded the Ilizarov technique is the optimal method, having the highest rates of fusion (75.5%) and success in deformity correction [13]. A Japanese multi-centre series supports either the Ilizarov technique or vascularised fibular transfers [15]. Our experience with vascularised free fibular transfer has been limited, given our situation. In the developing world and the late presenting cases we are faced with, the Ilizarov technique offers good rates of union and correction of deformity.

Advancements in the biological understanding of CPT have promoted the trial of new treatment options. These include adjunctive pharmacological therapy such as bone morphogenetic proteins and bisphosphonates, mesenchymal stromal cell therapy, pulsed electromagnetic fields, and the induced membrane technique [1, 4, 5]. The benefits are yet to be established and are outside the current resource capabilities of CSC [1].

The limitations of this review include the retrospective nature and reliance on recorded data. Long-term follow up for patients is difficult because of the travel and financial difficulties for those we serve. Some patients are yet to achieve skeletal maturity and the possibility of refracture remains.

Conclusion

CPT remains one of the most difficult orthopaedic conditions to treat. Late presentations are not common in the developed world, but are frequent in the developing world, where access to care is limited. The use of intramedullary nailing and the Ilizarov technique in the developing world, can achieve good union rates, but the presence of NF appears to worsen outcomes in late presenting, severe deformities.

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The authors wish to declare no conflict of interest.

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