

Bilateral congenital pseudarthrosis of the tibia with neurofibromatosis type 1

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Abstract

Neurofibromatosis type 1 is an autosomal dominant, common genetic disorder that affects many systems, including the skeleton and neurocutaneous system. Skeletal involvement is seen in 38% of patients with NF1. Bowing deformity and pseudarthrosis are observed in 5.7% of the long bones, most of which are common in the tibia.

A 13-year-old Somalian girl visited our orthopaedic clinic with complaints of deformity, inability to walk and pain in both legs. The deformity in both legs was present at birth and progressed further. A pathological fracture in the right tibia and a wide range of pseudarthrosis, hamartomatous bone tissues, medullary canal and diaphyseal narrowing towards the pseudoarthrosis range and cortical thickening were observed on her radiographs. Ilizarov technique was used for the case in this study.

Keywords: Congenital pseudarthrosis of the tibia, Neurofibromatosis type 1, Patients

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Introduction

Congenital pseudarthrosis of the tibia (CPT) is very rare in the early stages of life and is characterised by spontaneous pathological fractures of the anterolateral part of the tibia, bowing deformity of the tibia and narrowing of the medullary canal and cysts.¹ Pseudarthrosis occurs in the fracture site usually due to insufficient bone regeneration.² CTP prevalence is approximately 1 in 140,000 births.³ Treatment of CTP is the most complex and difficult among orthopaedic surgeries. The general principles of surgery consist of the excision of the abnormal bone tissue, defined as hamartoma and internal or external fixation.⁴ Several surgical methods including autologous free bone grafting, vascularised fibula grafting, internal fixation and adjuvant chemical, physical and biological methods have been described in the recent literature.⁵ However, rates of surgical failure are high and the prognosis is poor. In

addition, multiple surgeries are applied but amputation of the limb may still be required.⁵ Although, the involvement of the left tibia is more common in the literature than in the right, bilateral involvement is very rare.⁶

The aetiology of CTP has not been fully revealed; however, relationship of CTP with neurofibromatosis type 1 (NF1), fibrous dysplasia and osteo-fibrous dysplasia has been defined.⁵ A study conducted recently, reported that the incidence of NF1 was found to be 84% in all patients with CTP.⁷ A very rare case of bilateral involvement of CTP in a 13-year-old girl diagnosed with NF1, which has been rarely discussed in the literature is presented in this article.

Case Report

A 13-year-old Somalian girl visited our orthopaedic clinic with complaints of deformity, inability to walk and pain in both legs. The deformity of both legs was present since birth and developed progressively over a period of time. It was also observed that the patient had occasional bouts of high blood pressure and during these attacks, her blood pressure increased to 220 mmHg systolic and 140 mmHg diastolic. On physical examination, there were genu varum, genu recurvatum and anterolateral bowing deformities compatible with tibial pseudarthrosis in both distal 1/3 of the tibia. The genu varum deformity was 30° in the right leg and 10° on the left leg and the anterior angulation was 35° in both legs. Ankle movements were restricted with no changes in the knees. No pathology was observed on her feet and on the other extremities. As the suspicion of neurofibromatosis was suspected, café au lait spots were investigated and large-base café au lait spots that had spread to the head and neck were detected. There was no history of neurofibromatosis or similar disease in the patient's family.

A pathological fracture in the right tibia and a wide range of pseudarthrosis, hamartomatous bone tissues, medullary canal and diaphyseal narrowing towards the pseudoarthrosis range and cortical thickening were observed on her radiographs. Pathological fracture line, medullary canal towards the fracture line, narrowing and cortical thickening in the diaphysis were seen in the left tibia. While 25° varum and mild cortical thickening was observed in the right fibula, no pathology was found in

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Figure-1: Preoperative radiographs of the right and left tibiae (2a: anteroposterior, 2b: lateral).



Figure-2: Intraoperative image of the patient after the Ilizarov fixation method was applied.

the left fibula (Figure-1). The patient's diagnosis was compatible with CTP on radiographs; therefore, computed tomography or Magnetic Resonance Imaging (MRI) showed that her MRI (brain) findings were normal except for the 25x17 mm arachnoid cyst in the left temporal lobe anteriorly localized at the Sylvian fissure. The diagnosis of pheochromocytoma was excluded by the patient's abdominal imaging reports and laboratory findings and preoperative and postoperative blood

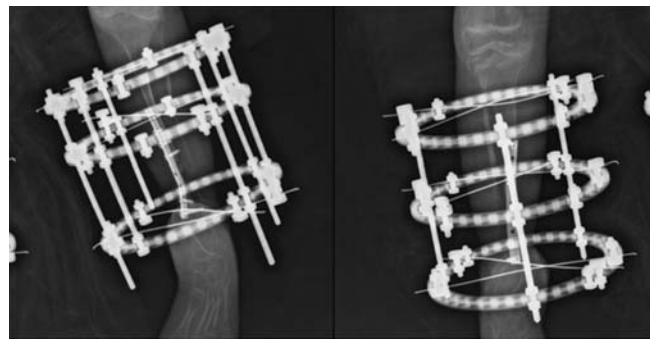


Figure-3: Follow-up radiographs of the patient in the postoperative 13th month.

pressure levels. The BT result reported that pseudarthrosis was apparently in both the tibia. As a result of the patient's NF1 gene mutation analysis, 17 exon heterozygous p.Trp571 * (c1713G> A) mutation was detected and she was diagnosed with NF1.

Fibular grafting and external fixation of the tibia with internal and Ilizarov technique was undertaken. The surgery under general anaesthesia started with an incision from the anterolateral aspect of the right tibia. Fibrous hamartomatous tissues in the pseudarthrosis line were cleaned. Fibular graft was removed and one 1/3 semitubular plate and five screws were fixed. Correction osteotomy was done and grafted with 20 cc synthetic bone graft on the part of the right tibia where bowing deformity was proximally observed. After closing the anatomical layers, one Ilizarov fixation device with four rings was applied (Figure-2). Similar procedures were

performed on the left side; however, because the bowing deformity in the left tibia was slightly less, it was not osteotomised and only 10 cc of synthetic bone graft was used. During the 13-month follow-up, signs of bone union were observed in the left tibia (Figure-3).

Discussion

CTP is one of uncommon congenital diseases seen in about 140,000 births.^{1,8} The prevalence of NF1 varies from 1:2190 to 1:7800.⁹ NF1 affects multiple organ systems including skeletal and neurocutaneous and shows a broad clinical spectrum. The clinical diagnosis of NF1 is made according to the criteria defined at the NIH conference held in 1987.¹⁰ Neurofibromas, cafe-au-lait spots and Lisch nodules are the most common signs of NF1. It is also characterised by various skeletal system diseases including macrocephaly, scoliosis, short stature, sphenoid wing dysplasia, CTP, congenital bowing and decreased bone mineral density.¹¹ The prevalence of skeletal system abnormalities is about 38% in patients with NF1, while the rate of CTP ranges from 2% to 4% in such patients.^{1,12} Recent review studies investigating the relationship between NF1 and CTP have reported that NF1 gene was positive in 84% of the patients along with CTP.⁷ The studies also report, that the patients with CTP who do not have NF1 may also have a genetic basis of the disease. However, it may be related to the localised loss of NF1 allele in patients with CTP who cannot be genetically diagnosed. No environmental factor other than genetic factors has been reported in the aetiology of CTP. According to the review study published in 2019, examined the genetic basis of patients with and without NF1, CPT patients without NF1 may have a genetic basis of the disease, but they are not consistent with NF1 variants.¹

Studies conducted on patients with bilateral CTP are very rare. NF1 has been detected in all the bilateral CTP cases that are reported in the literature.¹³ First, Berkshire et al., presented a case of bilateral symmetrical pseudarthrosis in an infant in 1970.¹³ In their first large and multicenter study, Hefti et al., examined 340 patients with CTP from 13 countries, and found only 3 patients to have bilateral involvement.⁶ However, it was not stated whether these cases had NF1 or not. Heikkinen et al., examined 14 patients with CTP and performed bilateral distal tibial osteotomy using vascularised fibular graft together with NF1 in 1 patient among all of them.¹⁴ Borzunov et al. conducted a study with 28 children with CTP and reported bilateral involvement in a case with NF1.⁵ Finally, Zhu et al. revealed that only 3 patients with CPT out of 75 had bilateral involvement and all of them had NF1.¹ They emphasised in the same study that NF1 could be seen in

patients with bilateral involvement and that CPT was a genetical disease. In the present study, a 13-year-old girl was diagnosed with bilateral CTP disease and NF1 mutation was detected in her genetic analysis. Considering only these studies, bilateral involvement was reported in 10 patients (2.19%) among 459 cases.

The surgical method with the highest success rate in the treatment of CPT is vascularised autologous fibular grafting and fixation with Ilizarov technique. The most important advantage of this method is that it protects blood flow to the area of pseudarthrosis. Elimination of the deformity using the Ilizarov technique provides a hard and controlled fixation to the resection area for bone transplant, distraction and compression.⁵

Conclusion

CTP is a genetic disease which leads to dysplasia in the tibia and significantly affects the quality of life. Also, it has been reported that CTP is associated with high rates of NF1 gene mutations. Genetic factors are known to contribute in aetiology. In addition, studies discussing bilateral CTP cases are very rare which was found to be 2.18% as a result of the review carried out by the researcher of this study. NF1 gene mutation has been reported in almost all patients with bilateral CTP. The change in osteoblast and osteoclast activity as a result of a lack of neurofibromin protein in the pathophysiology of CTP cases seen with NF1 complicates the management of the treatment. The most effective treatment method described so far is fixation with the vascularised autologous tibia grafting using the Ilizarov technique. Despite the most successful Ilizarov technique, the prognosis is poor and high amputation rates have been reported in the literature.

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Conflict of Interest: None

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