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# Bruck Syndrome: A Combination of Osteogenesis Imperfecta and Arthrogryposis

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## Abstract

**Background:** Bruck Syndrome is an extremely rare disorder that presents a challenging constellation of orthopaedic problems. Common features described in the literature include joint contractures, bone fragility with subsequent deformity and progressive kyphoscoliosis.

**Case Report:** We report on a case of a young infant referred to the outpatient orthopaedic service with suspected Erb's palsy and bilateral congenital talipes equinovarus. Further imaging revealed multiple fractures and clinical examination demonstrated contractures in both knees. Subsequent genetic testing confirmed the diagnosis of Bruck Syndrome.

**Conclusion:** The combination of arthrogryposis and osteogenesis imperfecta poses a difficult challenge in the management of orthopaedic problems in patients with Bruck Syndrome. Evidence on specific treatments for patients with Bruck Syndrome is insufficient and treatment should follow the current principles for osteogenesis imperfecta and arthrogryposis.

**Keywords:** Bruck syndrome; Arthrogryposis; Osteogenesis imperfecta

## Introduction

Bruck Syndrome is an autosomal recessive condition described as a combination of osteogenesis imperfecta and arthrogryposis [1]. Mutations in the FKBP10 and PLOD2 genes result in Bruck Syndrome type 1 and type 2 respectively, although there are no significant phenotypic differences between the two subgroups [7]. Phenotypic heterogeneity in the FKBP10 mutation, which is linked to Bruck Syndrome type 1, has been shown to be associated with isolated osteogenesis imperfecta [2]. Commonly described manifestations of Bruck Syndrome in the current literature include bone fragility, limb deformities, joint contractures and deformities of the spine, including progressive scoliosis [3]. Management of orthopaedic issues is often complex and involves a combination of surgical intervention, physiological treatment, splinting and physical therapy [4]. The rare nature of this disorder has made diagnosing and managing patients with Bruck Syndrome highly challenging. In this report, we present a case of a young infant with a confirmed diagnosis of Bruck Syndrome and highlight the different orthopaedic problems that may arise from this disorder.

## Case Presentation

The case is of a young infant who first presented to the orthopaedic outpatient clinic, having been referred by her paediatrician for evaluation of multiple orthopaedic issues. The patient was born at 41 weeks via spontaneous vaginal delivery. The pregnancy was uncomplicated and antenatal scans were reported as largely unremarkable. The patient's birth was complicated by shoulder dystocia, nuchal cord and meconium exposure. The patient's Apgar scores were 3 and 8 and temporary CPAP (continuous positive airway pressure) therapy commenced with good response. Postnatal examination revealed an infant reluctant to move the right upper limb. Knee flexion contractures were seen bilaterally, both feet had mildly increased cavus and the tendoachilles was slightly tight on the left side. The hips and spine examined normally, as did the left upper limb. The anterior fontanelle was noted to be soft. The patient was referred for an orthopaedic review with clinical impressions of right sided Erb's palsy and bilateral congenital talipes equinovarus. However, following clinical assessment in the Orthopaedic clinic, it was noted the feet did not meet criteria for congenital talipes equinovarus. Furthermore, plain films of the right upper limb were performed, revealing a healing diaphyseal humerus fracture with abundant callus around the fracture site. A full skeletal survey was ordered which demonstrated multiple bilateral rib fractures, a healing diaphyseal femur fracture on the right side and bilateral C2 pars defects. A subsequent CT (computed tomography) scan of the cervical spine showed further fractures in the right C3 lamina and right C7 pedicle.

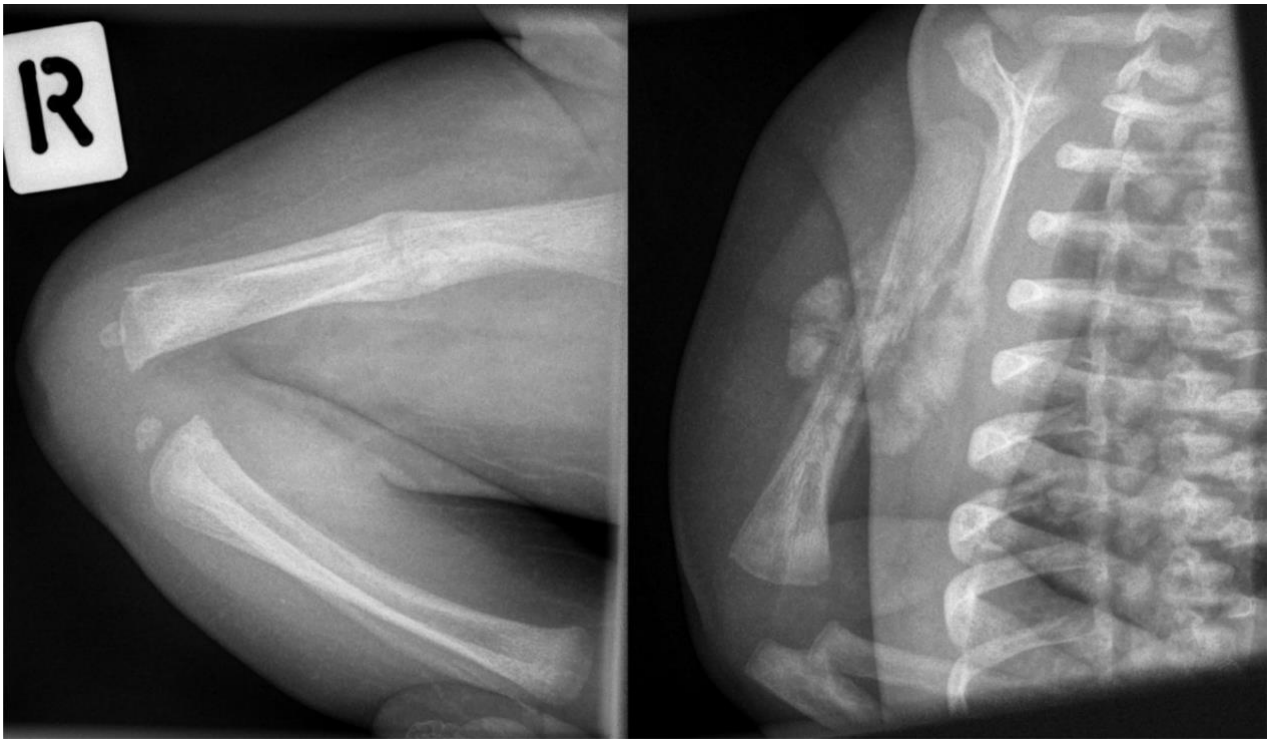


**Figure 1:** Healing diaphyseal humerus and femur fractures are seen in these plain radiographs.

The above findings prompted an acute admission for further workup of possible syndromic manifestations. Ultrasound scans of both hips showed that both had good coverage with no features of dysplasia. No signs of tethering were found on an ultrasound of the spine. Laboratory investigations showed a low vitamin D level of 37 nmol/L and a normal parathyroid hormone level.

The renal function studies and serum calcium levels were normal. A multidisciplinary approach was undertaken and immediate treatment was commenced. Vitamin D, calcium supplementation and bisphosphonate therapy were administered in conjunction with the endocrinology team. Following consultation with the spine service, the decision was made not to pursue immobilisation of the cervical spine. A follow up CT scan demonstrated progressive healing at the fracture sites in the cervical spine.

Thorough assessment of the bilateral cavus and tight tendoachilles on the left side led to the conclusion that these features were not consistent with congenital talipes equinovarus or congenital vertical talus. Therefore, no active treatment was commenced and both feet will continue to be monitored with serial clinical examinations. The patient will be monitored for surgical intervention of the bilateral knee flexion contractures in the outpatient setting, starting with passive stretches and may need further surgery at an older age. Subsequent molecular genetics confirmed the presence of a variant of the FKBP10 gene, consistent with the phenotype Bruck Syndrome type 1. The patient was referred to the genetic Services and is currently awaiting consultation with the geneticist.

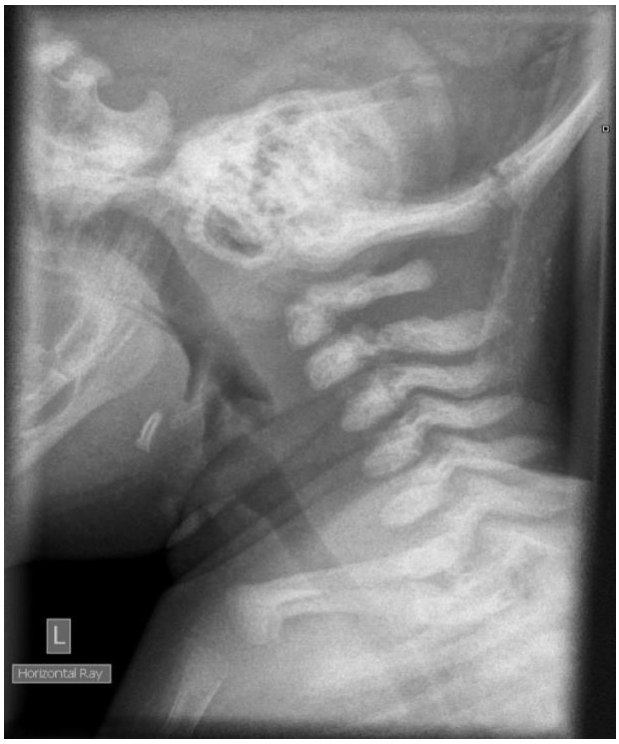


**Figure 2:** A lateral cervical spine plain radiograph of the patient. Subsequent CT imaging would confirm bilateral pars defects at C2 and multiple healing fractures.

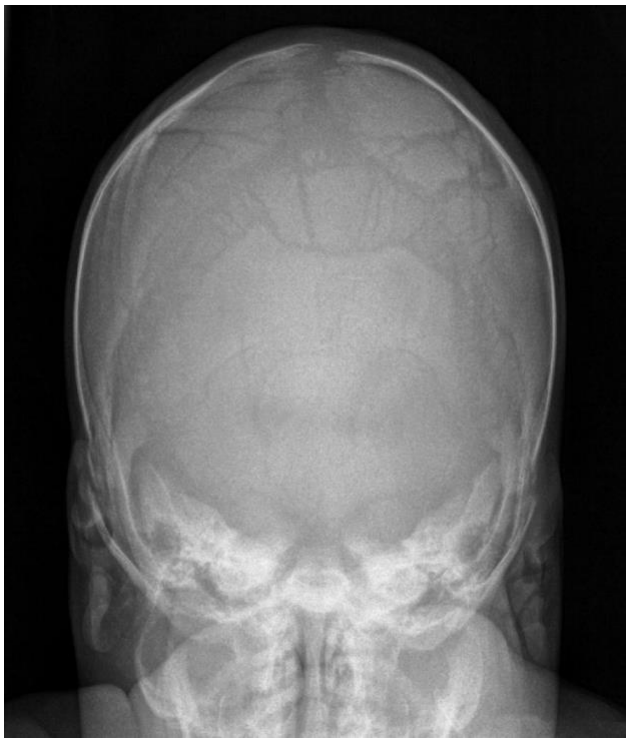

**Figure 3:** Wormian bones, a classic feature of osteogenesis imperfecta, seen in the patient's skull.

## Discussion

Due to the rare nature of the disorder, the extent of the manifestations of Bruck Syndrome is not well known. Based on case reports in the literature, it appears that the major orthopaedic abnormalities that present in patients with Bruck Syndrome can be categorised into recurrent fractures, limb deformities, joint contractures and spinal deformities [5]. The biochemical anomaly in collagen production seen in Bruck Syndrome differs from that seen in classic osteogenesis imperfecta [6].

Regardless, the management of bone fragility is the same in both patient groups. With the aid of endocrinology input, regular bisphosphonate infusions and concurrent vitamin supplementation remains the primary physiological treatment for patients with Bruck Syndrome [7]. Otaify et al. reported that biannual zoledronic acid infusions increased bone mineral density and reduced fracture rates in patients with both Bruck Syndrome and osteogenesis imperfecta with nearly no significant side effects seen [8]. Joint contractures in the upper limb and clubfeet are initially managed with serial casting during infancy. Persistent contractures despite casting treatment may require surgical intervention in the form of tenotomies to aid in further correction [7]. It should be said that great care must be taken in the process of casting in the context of bone fragility, as iatrogenic fractures have been described in the literature, particularly with Ponseti casting and iatrogenic distal tibia and fibula fractures [18]. Franzone et al. showed that guided growth for correction of coronal plane deformities in the knee and ankle in patients with osteogenesis imperfecta can be effective, provided that the procedure is performed at an early age to allow enough time for correction to occur [19]. This could prove to be an effective treatment method for lower limb deformities in Brucks Syndrome, however further evidence is needed in this area. Regular and persistent physical therapy is a critical adjunct to the management of contractures and in improving the overall functional capacity of patients with Brucks Syndrome [9].

Fractures most commonly occur in the diaphyseal region of bones in patients with Bruck Syndrome [4]. This predisposes them to the development of deformities that may preclude satisfactory function of a limb, given the relatively poorer remodelling potential of the diaphyseal region [10]. The current indications and principles of surgical treatment in patients with Bruck Syndrome align with those of classic osteogenesis imperfecta. Most deformity correction surgeries are performed in the lower limbs. While plate fixation has been historically used, this is now discouraged due to high failure rates and predisposition to recurrent fractures [11]. Various intramedullary techniques have been described with good restoration of function and improvement in ambulation following surgery. High rates of complications with these techniques have been reported, including the need for revision surgery and migration of implants [12]. Kyphoscoliosis is another common manifestation seen in Bruck Syndrome patients [4,7]. Spinal deformity is progressive, which is consistent with disease progression seen in patients with classic osteogenesis imperfecta [13].

Pathogenesis of kyphoscoliosis in patients with Bruck Syndrome is linked to defects in collagen folding and cross-linking associated with PLOD2 mutations and FKBP10 deficiency. However, the pathology is not well understood and is likely to be multifactorial, including osteopenia, vertebral body malformation and mechanical loads during childhood [14]. The role of bisphosphonate therapy in kyphoscoliosis is not yet clear. Aström et al. and Anissipour et al. both concluded that early administration of bisphosphonates may lead to improved vertebral remodelling and therefore reduced prevalence of scoliosis or slower progression of disease [15,16]. A retrospective review by Sato et al. found that although bisphosphonate therapy may slow the progression of the Cobb angle, it did not reduce the prevalence of scoliosis [17]. The management of kyphoscoliosis in Bruck Syndrome currently follows the standard practice in osteogenesis imperfecta, with early screening beginning around the age of 6 years, serial examination for neurological deficits, observation of curvature progression and surgical intervention in the form of fusion with or without instrumentation. Bracing is known to be ineffective in patients with osteogenesis imperfecta due to bone fragility [13].

## Conclusion

Bruck Syndrome is an extremely rare and complex disorder, characterised by a combination of osteogenesis imperfecta and arthrogryposis. The wide array of orthopaedic manifestations seen in this condition makes management of patients with Bruck Syndrome challenging. Early identification of syndromic features, genetic testing and engagement of a multidisciplinary team is crucial for positive patient outcome. Due to the low incidence of Bruck Syndrome, evidence regarding treatment of associated orthopaedic disorders is scarce. Treatment principles for osteogenesis imperfecta and arthrogryposis should be followed for individual problems, however clinicians should take into consideration the different manifestations that can arise in patients with Bruck Syndrome when providing treatment.

## REFERENCES

1. Mokete L, Robertson A, Viljoen D, et al. Bruck syndrome: congenital joint contractures with bone fragility. J Orthop Sci. 2005; 10: 641-646.
2. Steinlein OK, Aichinger E, Trucks H, et al. Mutations in FKBP10 can cause a severe form of isolated Osteogenesis imperfecta. BMC Med Genet. 2011; 12: 152.
3. McPherson E, Clemens M. Bruck syndrome (osteogenesis imperfecta with congenital joint contractures): review and report on the first North American case. Am J Med Genet. 1997; 70: 28-31.
4. Santana A, Oleas-Santillán G, Franzone JM, et al. Orthopedic Manifestations of Bruck Syndrome: A Case Series with Intermediate to Long-term Follow-Up. Case Rep Orthop. 2019; 8014038.
5. Breslau-Siderius EJ, Engelbert RH, Pals G, et al. Bruck syndrome: a rare combination of bone fragility and multiple congenital joint contractures. J Pediatr Orthop B. 1998; 7: 35-38.
6. Schwarze U, Cundy T, Pyott SM, et al. Mutations in FKBP10, which result in Bruck syndrome and recessive forms of osteogenesis imperfecta, inhibit the hydroxylation of telopeptide lysines in bone collagen. Hum Mol Genet. 2013; 22: 1-17.
7. Luce L, Casale M, Waldron S. A Rare Case of Bruck Syndrome Type 2 in Siblings With Broad Phenotypic Variability. Ochsner J. 2020; 20: 204-208.
8. Otaify GA, Aglan MS, Ibrahim MM, et al. Zoledronic acid in children with osteogenesis imperfecta and Bruck syndrome: a 2-year prospective observational study. Osteoporos Int. 2016; 27: 81-92.
9. Yelkur P, Mohammed S, Narayan K. Congenital Contractures and Fractures: A Variant of Bruck Syndrome Type 2. Cureus. 2024; 16: e61991.
10. Naik P. Remodelling in Children's Fractures and Limits of Acceptability. Indian J Orthop. 2021; 55: 549-559.
11. Esposito P, Plotkin H. Surgical treatment of osteogenesis imperfecta: current concepts. Curr Opin Pediatr. 2008; 20: 52-57.
12. Escribano-Rey RJ, Duart-Clemente J, Martínez de la Llana O, et al. Osteogénesis imperfecta: tratamiento y resultado de una serie de casos [Osteogenesis imperfecta: Treatment and results of a case series]. Rev Esp Cir Ortop Traumatol. 2014; 58: 114-119.
13. Wallace MJ, Kruse RW, Shah SA. The Spine in Patients with Osteogenesis Imperfecta. J Am Acad Orthop Surg. 2017; 25: 100-109.

14. Liu G, Chen J, Zhou Y, et al. The genetic implication of scoliosis in osteogenesis imperfecta: a review. J Spine Surg. 2017; 3: 666-678.
15. Aström E, Jorulf H, Söderhäll S. Intravenous pamidronate treatment of infants with severe osteogenesis imperfecta. Arch Dis Child. 2007; 92: 332-338.
16. Anissipour AK, Hammerberg KW, Caudill A, et al. Behavior of scoliosis during growth in children with osteogenesis imperfecta. J Bone Joint Surg Am. 2014; 96: 237-243.
17. Sato A, Ouellet J, Muneta T, et al. Scoliosis in osteogenesis imperfecta caused by COL1A1/COL1A2 mutations - genotype-phenotype correlations and effect of bisphosphonate treatment. Bone. 2016; 86: 53-57.
18. Ranjan R, Sud A, Adhikary D, et al. Incidence and risk factors for iatrogenic distal tibia/fibula fracture during Ponseti technique of clubfoot treatment. J Pediatr Orthop B. 2019; 28: 572-578.
19. Franzone JM, Wallace MJ, Rogers KJ, et al. Multicenter Series of Deformity Correction Using Guided Growth in the Setting of Osteogenesis Imperfecta. J Pediatr Orthop. 2022; 42: e656-e660.