ONE GENE, TWO DİSEASES: OSTEOGENESİS İMPERFECTA, OR BRUCK SYNDROME?

Hasan Arı[1], Semra Çetinkaya[1], Naz Güleray Lafcı[1], Merve Şakar[1], Gülin Karacan Küçükali [1], Melikşah Keskin[1], Nursel Muratoğlu Şahin[1], Şenay Savaş Erdeve[1]
Dr. Sami Ulus Gynecology, Obstetrics, and Child Health and Diseases Training and Research Hospital, Ankara, Turkey

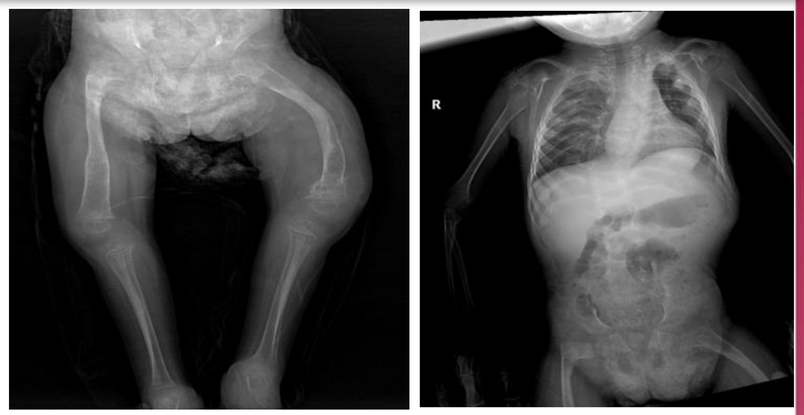
BACKGROUND

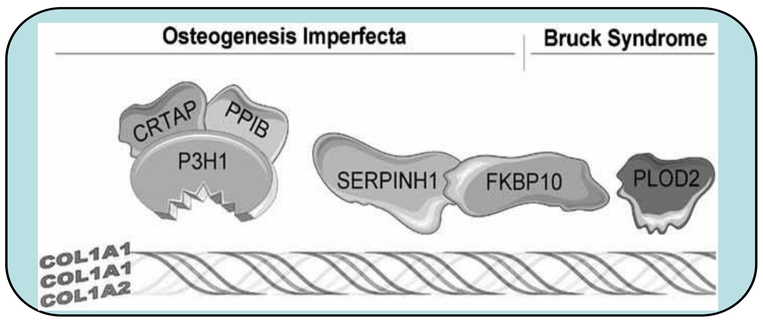
Osteogenesis imperfecta (OI) is a genetic disorder characterized by diffuse osteoporosis, recurrent fractures, and resulting deformities. Bruck syndrome (BS) is a rare autosomal recessive disease that manifests with many symptoms of OI. In addition to the deficiency of type I collagen in OI, congenital joint contractures also occur in BS. BS is caused by mutations of FKBP10 (BS type 1) and PLOD2 (BS type 2) genes encoding the chaperone-collagen complex. Here, we present a BS type 1 case with recurrent fractures and congenital joint contractures and discuss its genetic etiology.

CASE

A 3-year-and-5-month-old male patient, who had been born by cesarean section with a weight of 3000 grams at term, had multiple bone fractures (3 femoral, 1 humeral, multiple costal) from minor trauma. Due to congenital pes equinovarus, splint had been applied for six months, and then surgery had been performed. His parents were fourth-degree relatives.

At presentation, the patient had a height of 71 cm (-7.16 SDS) and a weight of 7 kg (-7.65 SDS). He had blue sclera, pectus excavatum, severe kyphoscoliosis, knee and elbow flexion contractures, and no dentinogenesis imperfecta or hearing loss. His calcium, phosphorus, alkaline phosphatase, 25-OH vitamin D, and parathyroid hormone serum levels were normal. A bone survey showed mild microcephaly, Wormian bones within the cranium, tubulation defect in all long bones, coxa vara in both femurs, bendings secondary to prior fracture at lower ends of the femur, bilateral rib fractures, sloped appearance of the clavicles, and severe osteoporosis in all skeletal structures. The patient's lumbar DEXA Z-score was -8, and genetic analysis revealed a homozygous deletion in exons 5-8 of the FKBP10 gene.





Genetic analysis revealed a homozygous deletion in exons 5-8 of the FKBP10 gene.

CONCLUSION

FKBP10 mutations can be detected in OI and BS type 1 and affect the endoplasmic reticulum chaperone complex, which is involved in post-translational modifications of type 1 procollagen. The physician should consider BS in cases presenting with findings resembling OI and congenital joint contractures. Genetic analysis and long-term follow-up of these cases are critical to elucidate the genotype-phenotype relationship.