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OLGU SUNUMU *Pediatri*

Osteogenesis imperfecta associated with partial trisomy 20p: Case report

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SUMMARY

Osteogenesis imperfecta (OI), a secondary cause of osteoporosis, principally manifests as bone fragility. It is an inherited disorder of connective tissue integrity, and affects up to one in 10 000 persons. Diagnosis of moderate OI is challenging due to its variable phenotypic expression and inconsistent course. Here we report a patient suffering from OI showing a moderate form of increased bone fragility and skeletal deformities, mental retardation and partial trisomy 20p.

Key words: *Osteogenesis imperfecta, partial trisomy 20p, mental retardation*

ÖZET

Osteogenezis İmperfekta ile Parsiyel Trizomi 20p Birlikteliği: Olgu Sunumu

Kemik frajilitesi olarak genelikle gösterilen osteogenesis imperfekta (OI) osteoporozisin sekonder bir nedenidir. 10000'de bir kişiyi etkiler. Orta OI'nın tanısı çeşitli fenotipitk ekspresyon ve devamsız gidiş ile ilgilidir. Burada orta düzeyde artmış kemik frajilitesi ve iskelet deformitesi, mental retardasyon ve parsiyel trizomi 20p gösteren OI'lı bir hasta sunduk.

Anahtar kelimeler: *Osteogenezis imperfekta, parsiyel trizomi 20p, mental retardasyon*

Osteogenesis imperfecta (OI), a secondary cause of osteoporosis, principally manifests as bone fragility. It is an inherited disorder of connective tissue integrity; it aff ects up to one in 10 000 persons [1,2]. Osteogenesis imperfecta results from mutations in genes encoding for type I collagen. Collagen is the major structural protein in bone, ligaments, tendons, skin, sclera, and dentin [3,4]. Mutant expression produces non-functional collagen (severe OI) or insufficient quantities of collagen (mild OI). The parient presented with OI type 1A and partial trisomy 20p syndrome.

CASE REPORT

The case was 10- year-old boy of Turkish origin suffering from OI. During childhood he suffered several fractures of the upper and lower extremities leading to distinct deformities of the legs and arms. The patient was the first child of non-consanguineous parents, aged 41 (father) and 30 (mother). On examination, the patient was 140 cm tall and weighed 23 kg. He was noted to have growth deficiency, attrition teeth, high arched palate, micrognathia, large ears, joint contractures, and mental retardation (Fig. 1). The patient had low bone mass, increased bone fragility and skeletal deformities on X ray examination. Osteoporosis was suspected, and dual-energy x-ray absorptiometry assessment of bone mineral density confirmed mild disease in the lumbar spine. The patient had renal pelvic stone and hydronephrosis on ultrasound examination. Cytogenetic study showed that the patient's karyotype was 46, XY, der (5), t(5;20) (p15.3; p11.2) pat (Fig. 2); partial trisomy for 20p11.2 → pter resulting from the balanced translocation of the father. His father carried a balanced translocation: 46, XY, t (5p+; 20p-) (p15.3; p11.2) (Fig. 3), but his mother had normal a karyotype. The family history was unremarkable.

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The hospital Ethical Committee approved the human study. We obtained written informed consent from the parents of the patient. Because the patient presented as a child with relatively minor symptoms, diagnosis of Type IA OI (the mildest form) was established.

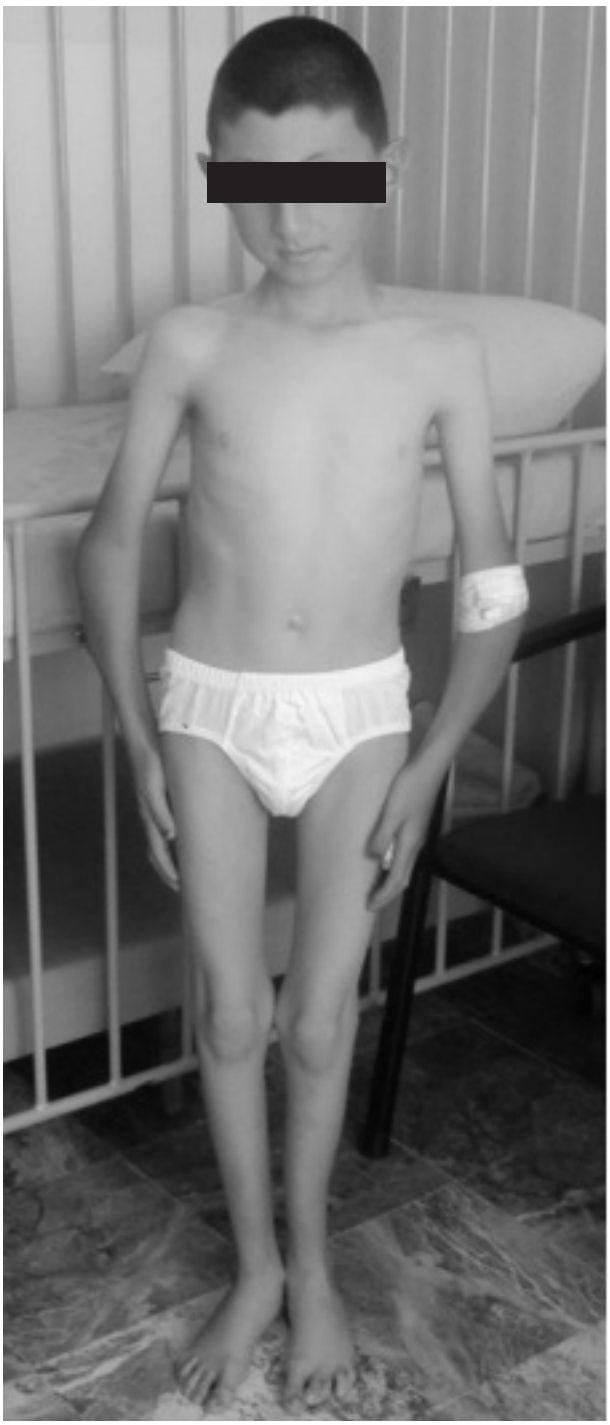

Figure 1. Clinical appearance of the patient with osteogenesis imperfecta and parsiyel trizomi 20p.

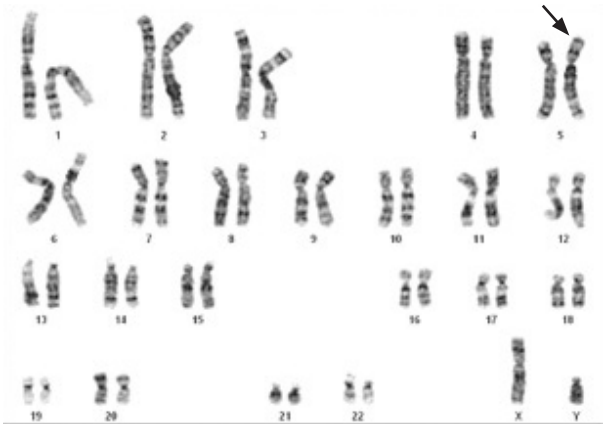

Figure 2. The patient karyotype by GTG banding 46, XY, der (5), t(5;20) (p15.3; p11.2) pat (partial trisomy 20p). Arrow indicate the translocation.

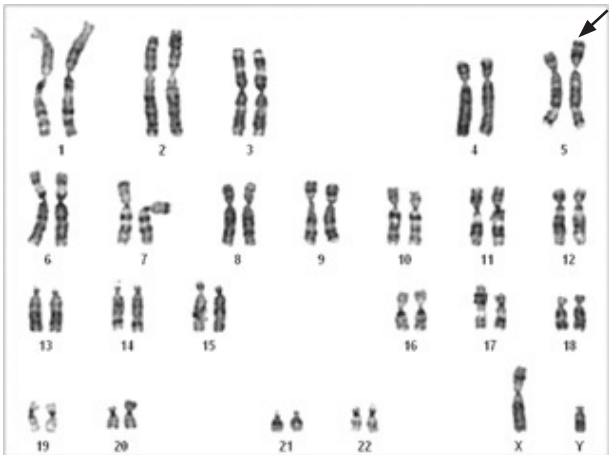

Figure 3. Father of the patient karyotype by GTG banding [46, XY, t(5p+;20p-) (p15.3; p11.2)]. Arrows indicate the breakpoint and the translocation.

DISCUSSION

Osteogenesis imperfecta is a disorder leading to bone fragility. This disorder is most commonly caused by a mutation in 1 of the 2 genes coding for type 1 collagen [1,2,4,5]; which is the most abundant structural component of skin, bone, cartilage, tendons, and ligaments. This structural collagen defect leads to bone fragility and pathological fractures. Osteogenesis imperfecta is a well-characterized heritable disorder in humans and can vary in severity 5. In humans, there are several distinct clinical variants of the disease, with greater than 90 % of the cases caused by autosomal dominant mutations in the genes coding for type 1 collagen [1,2,4,5]. All types are characterized by fragile bones that shatter spontane-

ously or secondarily when exposed to minimal trauma [1,2,4]. Onset of clinical disease is most common in puppies and kittens between 10 and 18 weeks of age [1,2,4,6,8].

Mutant expression produces non-functional collagen (severe OI) or insufficient quantities of collagen (mild OI). There are seven subtypes of OI varying in severity, age of presentation, and clinical features [5-7,9]. Type IA OI is the most prevalent and mildest form and it is genetically transmitted in an autosomal dominant or sporadic-mutation fashion1 [3,10].

Our patient had growth deficiency, long nose, high arched palate, attrition teeth, micrognathia, large ears, joint contractures, and mild mental retardation. The patient had low bone mass, increased bone fragility and skeletal deformities on X ray examination. Osteoporosis was suspected, and dual-energy x-ray absorptiometry assessment of bone mineral density confirmed mild disease in the lumbar spine. The patient had renal pelvic stone and hydronephrosis on ultrasound examination. The family history was unremarkable. Because the patient presented as an adult with relatively minor symptoms, diagnosis of Type IA OI (the mildest form) was established. Cytogenetic study showed that the patient's karyotype was 46, XY, der(5), t (5;20) (p15.3; p11.2) pat; partial trisomy for 20p 11.2 → pter resulting from the balanced translocation of the father. His father carried a balanced translocation: 46, XY, t (5p+; 20p-) (p15.3; p11.2). His mother had normal karyotype. The child had an unbalanced form of the translocation with partial trisomy for 20p. Mental retardation of the patient is believed to be related to an unbalanced trisomy 20p condition.

Trisomy 20p syndrome is usually characterized by mild mental retardation, brachycephaly, micrognathia, round face, and mongoloid slant. In a recent study, Brenk CH [11] reported three patients with partial trisomy p20. First case had a long face, strabismus, a broad nose, a thin upper lip, hydrocephaly, inguinal herni, psychomotor retardation, muscular hypotonia, ataxia and tetraparasis, epilepsy, and growth deficiency. Second case had hydrocephaly, brain atrophy, hemiparasis, epilepsy, mental-motor retardation, and growth deficiency. Third case had a flat round face, periorbital fullness, hypertelorism, ptosis, a short nose, micrognathia, renal dysplasia, tetralogy of Fallot, and growth deficiency. Similarly, in early studies, some authors reported several cases [12-14]. Our patient had growth deficiency, high arched palate, thin upper lip, attrition teeth, micrognathia, large ears, joint contractures, and mild mental retardation.

In practice, diagnosis of OI is by exclusion, fortified by consistent clinical presentation, family history, and low bone mineral density scores. Specialized investigations, although rarely warranted, include serum quantification of low levels of type I procollagen peptide, bone biopsy demonstrating high osteocyte levels with low bone turnover, direct collagen analysis from fibroblast culture through skin biopsy, and confirmation of mutation by DNA extraction from white blood cells [1,15].

Type IA OI does not affect longevity of life but influences morbidity due to recurrent fractures and related complications. Other clinical characteristics of Type IA OI can include blue-gray sclera and sensorineural hear ing loss beginning in early adulthood. Neurologic sequelae result from basilar invagination and cervical spinal cord compression syndromes presenting as paresthesias, peripheral weakness, incontinence, central sleep apnea, and upper motor neuron signs [9]. Cardiac complications include aortic and mitral valve insufficiency as well as increased aortic root diameter predisposing to dissection [16,17]. Restrictive lung disease secondary to spinal deformity and rib fractures [18], hypermetabolism with nephrolithiasis and vascular fragility can also occur [4,10]. Systemic screening for disease complications includes an echocardiogram, pulmonary function tests, an audiogram, and consultation with a geneticist. Family physicians must maintain a high index of suspicion, as diagnosis, along with proper follow up and counseling, can prevent many complications of this disorder.

This report is presented with the intention to describe a rarely encountered case of osteogenesis imperfecta syndrome with trisomy 20p.

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