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CASE REPORT Open Access

Orthopaedic interventions in occipital horn syndrome: a rare case of mutation in *ATP7A* gene

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Abstract

Background: Occipital horn syndrome is a rare, X-linked recessive, connective tissue disorder caused by abnormal copper transporter proteins coded by the *ATP7A* gene. 32 cases have been reported worldwide to date. Clinically, patients typically present with inguinal hernia, exostosis, cutis laxa, and bladder diverticula. Orthopaedic problems often include exostosis of the elbows, thoracolumbar scoliosis, thoracic cavity deformities, and joint hypermobility due to joint laxity.

Case presentation: An 18-year-old presented with occipital horn syndrome and was treated for flat-valgus foot and posterior dislocation of the elbow joints. Due to collagen structure abnormalities, vulnerability to joint deformation makes treating patients with occipital horn syndrome challenging as they need complex orthopaedic intervention.

Conclusion: There is no effective causal therapy for this condition. Surgical procedures can help patients improve their physical condition and maintain adequate joint range of motion.

Keywords: Occipital horn syndrome, Connective tissue disorder, Exostosis, Joint hypermobility

Background

Type IX Ehlers-Danlos syndrome, also called Occipital horn syndrome (OHS), is an X-linked recessive connective tissue disorder stemming from an allele variant of Menkes [1]. About 32 OHS cases have been reported in the literature [2]. It is caused by pathogenic variants of the *ATP7A* gene, encoding a copper transporter (80–70% of *ATP7A* mRNA transcripts are incorrectly processed due to leaky splice junction mutations [3]). Copper accumulates in cellular cytosol to toxic levels. The result is deficient activity of lysyl oxidase, a copper-requiring enzyme which normally deaminates lysine and hydroxylysine in the first step of collagen crosslink formation, which produces connective tissue abnormalities [3, 4]. The pathognomonic sign of OHS is a wedge-shaped calcification within the tendinous insertions of the sternocleidomastoid and trapezius muscles at their attachments to the occipital bone [2]. These malformations are typically seen at 5–10 years and progress with age [5]. The related characteristic X-ray finding is exostosis around the elbow joint with possible radioulnar proximal fusion. Tendon calcifications and multiple exostosis are most likely caused by improper membranous bone formation resulting in abnormal facial features which include: elongated oval shape, large ears, down- slanting eyes, and unusually coarse hair [1]. Other clinical findings common in OHS are: recurrent urinary tract infections due to bladder diverticula, inguinal, umbilical, and hiatal hernias, varicose veins, and arterial aneurysms [6].

This paper will focus on the abnormalities of the musculoskeletal system of OHS as these disorders limit normal daily function and can be markedly improved with surgical treatment.

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Thoracic deformity such as pectus carinatum can cause difficulty in breathing. Combinations of movement-limiting deformities such as deformation of the humerus, dislocation of the head of the radius, deformation of the ulna, hammer-shaped claviculate, scoliosis, genu valgum, and coxa valga can be seen in most patients [5]. Low mineral bone density, which often leads to osteoporosis, can be observed at a young age [7]. Early diagnosis and multidisciplinary intervention results in the best outcome for patients with OHS.

Case presentation

An 18-year-old male was treated in various departments due to multiple abnormalities connected with OHS. He was born in the 39th week of pregnancy by caesarian section due to no progress in delivery with Apgar scores of 9 and 10 at 1 and 5 min. Molecular genetic analysis in the *ATP7A* gene was performed, and a novel base substitution c.2927 + 5 was detected. T to G intron 13 of the *ATP7A* gene in patient's DNA and is the disease-causing defect in this patient, confirming the diagnosis of OHS. At age 3, a bladder diverticula limited his outflow of urine and was corrected surgically. The patient also underwent Meckel's diverticulum resection and bilateral inguinal hernia repair. At age 4, his serum ceruloplasmin and copper were found to be 11 mg/dl 115 ug/dl, respectively. He subsequently underwent intramuscular copper histidine treatment but, due to pain, adhesions, and lack of apparent effects seen by the patient's family, the therapy was discontinued after 3 months.

Physically, the patient presented with abnormal proportions; short limbs relative to his body. An X-ray of both lower limbs in a standing position showed a mechanical lateral distal-femoral angle of 88.1° (normal range: 85°–90°) on both sides and a mechanical medial proximal tibial angle of 97.2° on the right 96.3° on the left (normal range: 85°–90°). Fragmented, deformed bones of the lower leg on both sides were visible. X-rays of the feet showed an increased angle of the longitudinal arch of the foot and reduced calcaneal inclination angle on both sides. Flat-valgus feet were also noted. Bilateral subluxation in the humero-radial joints caused visible deformation of the elbows. Deformity of both elbow joints with a prominent end of the proximal radial bone was observed. The densitometry of the spine and femur revealed Z-score lower than − 2, which indicated osteoporosis. He had a pigeon chest which impaired the expansion of both lungs and also presented with thoracolumbar junction kyphosis without possible active correction. Left-sided thoracolumbar scoliosis was diagnosed with a 24° Cobb angle.

The patient received care at a rehabilitation clinic since he was a 1-year-old. His premature fatigue, joint pain, and reduced mobility were explained by the patient's hyperlaxity and hypermobility. The patient was diagnosed with a type II atrial septal defect (ASD), and delayed weight gain was observed in his childhood. Diminished exercise tolerance was also observed along with low blood pressure causing dizziness and near-syncope when standing up. These symptoms may indicate chronic autonomic failure due to partial deficiency of dopamine-beta-hydroxylase; another copper-dependent enzyme.

To improve the patient's quality of life, surgical intervention was required for the above-mentioned abnormalities. On the right lower limb, percutaneous epiphysiodesis of the medial distal growing cartilage of the tibia was performed with an 8-plate. A fibula osteotomy and corrective tibia osteotomy were performed on the left. Surgeons performed an ankle arthrodesis and extra-articular tarsal arthrodesis according to the Grice procedure. Surgical correction of the metatarsophalangeal joint was also performed by stabilizing it with a locking plate and 2 Blount staples (Fig. 1). One and a half months later, another operation was performed on the left upper extremity. The patient was placed in a supine position, and the Esmarch band was put on. The skin was incised on the posterolateral surface of the left elbow along the proximal end of the radius, and the subperiosteal fragment of the radial bone was exposed. The course of the radial nerve that surrounds the head of the radial bone was preserved. The proximal end of the radius was dissected subperiosteally and obliquely resected. The junction of the radius with the ulna was left alone. The cut bone was secured with a hemostatic sponge, and the periosteum was sutured above the stump of the radius. Then, the Esmarch band was removed, and hemostasis was checked. Temporary paralysis of the radial nerve was observed after the operation. The paralysis was relieved after few days of rehabilitation. The patient was positively assessed with the applied treatment. The current condition shows minimal impediment to the patient's physical or mental function (Fig. 2). The deformation of the chest wall was corrected using the classical method with 8-plate sternum stabilisation. Laryngeal treatment included bilateral coagulation of the nasal conchae and adenotomy.

Discussion

OHS is an exceedingly rare disease (only 32 reported cases worldwide). Consequently, its associated clinical aspects have not been extensively documented in scientific studies. While reviewing the literature, the authors did not find a description of the orthopaedic treatment undertaken in these patients. The list of surgical procedures with their description is a novelty of this paper. The basis of diagnosis is a genetic test which shows

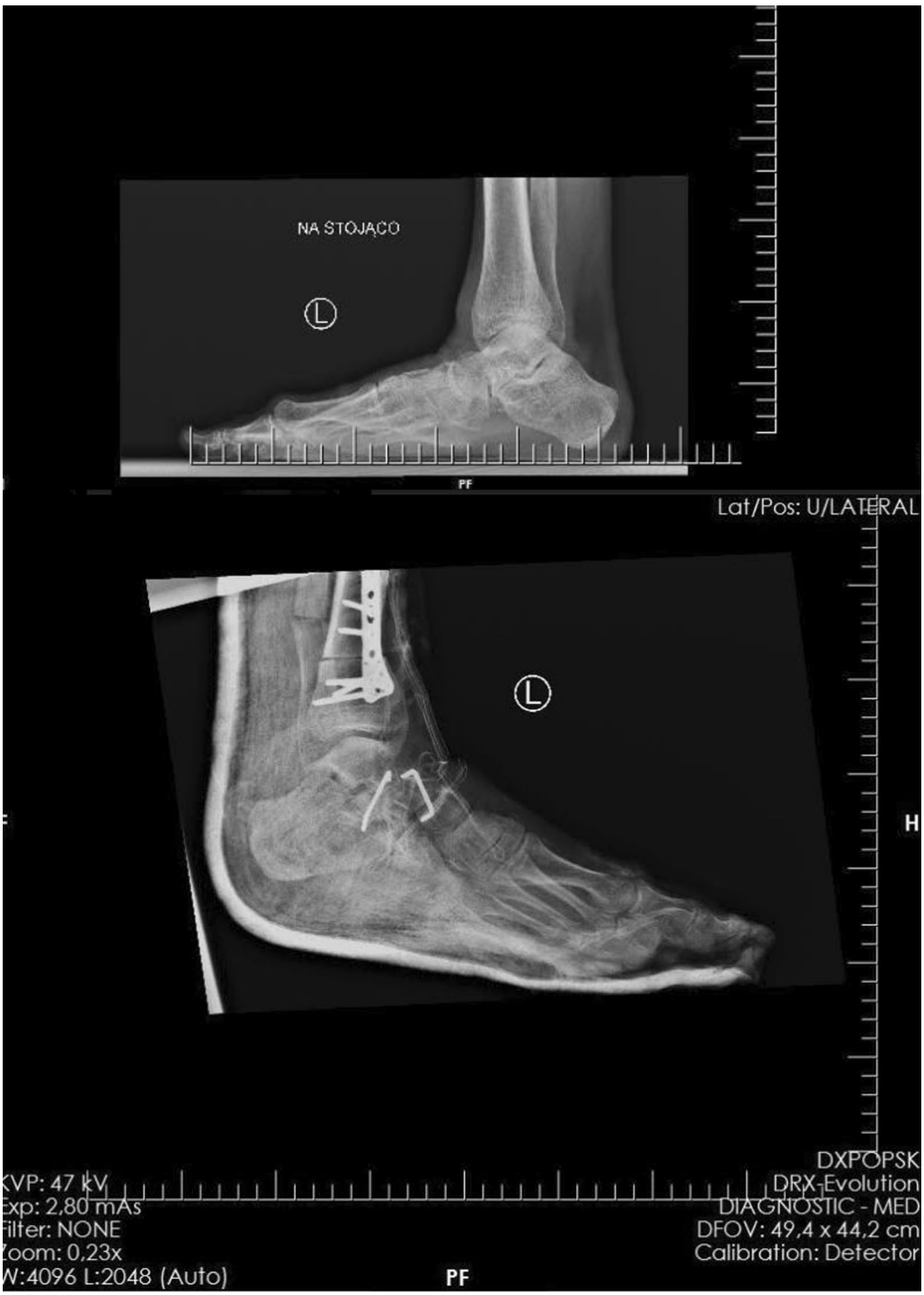

Fig. 1 X-rays of the left lower limb before and after surgical correction

mutation in the *ATP7A* gene. This variant is responsible for a copper-transporting ATPase and was detected in the presented patient [1]. He presented with most of the features characteristic for OHS (i.e. changes in bone structure and density). The patient had to be operated on due to hernias and diverticula of the bladder. Fortunately, no developmental delay was observed [2, 7].

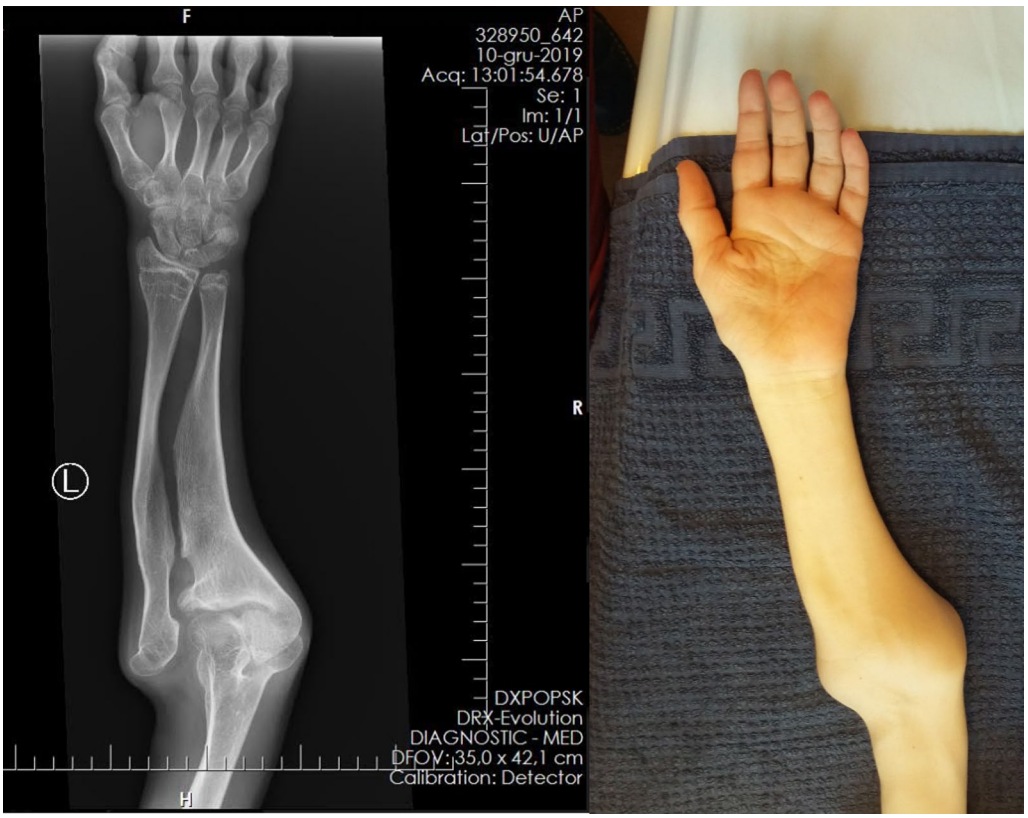

Fig. 2 Photograph and X-ray of the left upper limb before surgery

Conclusion

In order to determine the best medical management for patients with OHS, an interdisciplinary approach is needed. Careful follow-up of such unique patients is also necessary.

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Declarations

Ethics approval and consent to participate
Patient know and agree for the publication. There is no photograph of the face of the patient. We removed the patient's personal data from the X-rays.

Consent for publication
Patient signed the consent for publication.

Competing interests
The authors declare that they have no competing interests.

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