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SCIENTIFIC ARTICLE - CASE REPORT

ROBINOW SYNDROME: CASE REPORT

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ABSTRACT

Robinow Syndrome is a rare genetic disease, autosomal dominant or recessive, due to mutations in the WNT5A and ROR 2 genes with short stature, genitourinary changes, facial changes and important musculoskeletal abnormalities, such as mesomelic or acromelic shortening of limbs, brachydactyly, clinodactyly, vertebral anomalies such as hemivertebrae with fusion of thoracic vertebrae and short stature. The objective of this paper is to report a rare case of Robinow Syndrome.

Keywords: Robinow syndrome; musculoskeletal abnormalities.

INTRODUCTION

Robinow syndrome, also known as "fetal face syndrome," is a rare genetic disorder with autosomal dominant or recessive variants, due to mutations in the WNT5A and ROR 2 genes, respectively, mostly linked to consanguineous marriages. This disease is characterized by symptoms and signs such as short stature, genitourinary abnormalities, facial alterations, and significant musculoskeletal abnormalities [1-5].

The skeletal abnormalities of Robinow syndrome tend to be severe. The main orthopedic changes found in patients with this syndrome are mesomelic or acromelic limb shortening, brachydactyly, clinodactyly, vertebral anomalies such as hemivertebrae with fusion of thoracic vertebrae, and short stature. At the request of the Medical Genetics team, due to skeletal alterations, the orthopedic team was requested to follow up with the patient. It is important for the orthopedic team to be familiar with Robinow syndrome and thus be able to manage the musculoskeletal alterations in these patients [1-5].

The objective of this study is to report a rare case of Robinow syndrome, describing the characteristics of the musculoskeletal alterations.

CASE REPORT

Patient, 9 years old, male, son of a consanguineous couple with a sibling who is healthy. At birth, he presented with omphalocele, cryptorchidism on the right side, gingival hypertrophy, and septated hydrocele. On physical examination: hypertelorism, exophthalmos, anteverted nares, short nasolabial filter, thick lips, tented upper lip, gingival hypertrophy, clinodactyly and camptodactyly of the 5th fingers of the hands, pectus excavatum, and bilateral painless flexible flat feet.

X-rays of the hands demonstrating hypoplasia of the middle phalanx of the 5th digits (Figure 1), x-rays of the feet showing widened metatarsals and phalanges bilaterally, also noting bilateral fallen arches with flexible flat feet (Figure 2), and x-ray of the spine showing mild scoliosis (Figure 3). Bone densitometry revealing bone mass adequate for age but at the lower limit (Figure 4).

Figure 1 - Anteroposterior radiograph of hands demonstrating hypoplasia of the middle phalanx of the 5th digits.

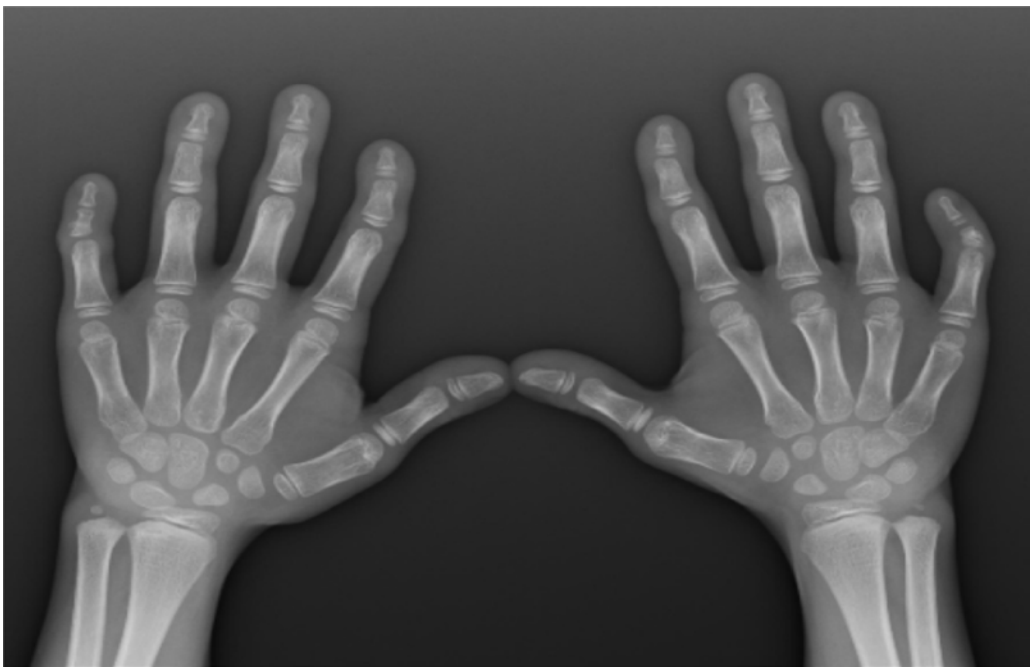


Figure 2 - Weight-bearing foot radiograph showing bilateral widening of the metatarsals and phalanges, with bilateral flat feet and dropped arches.

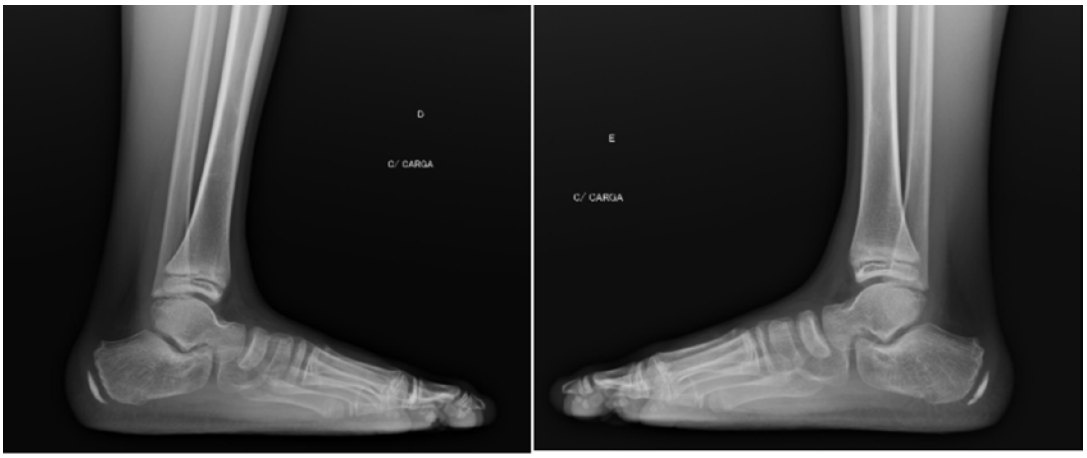


Figure 3 - Dorsolumbar spine radiograph showing mild scoliosis.

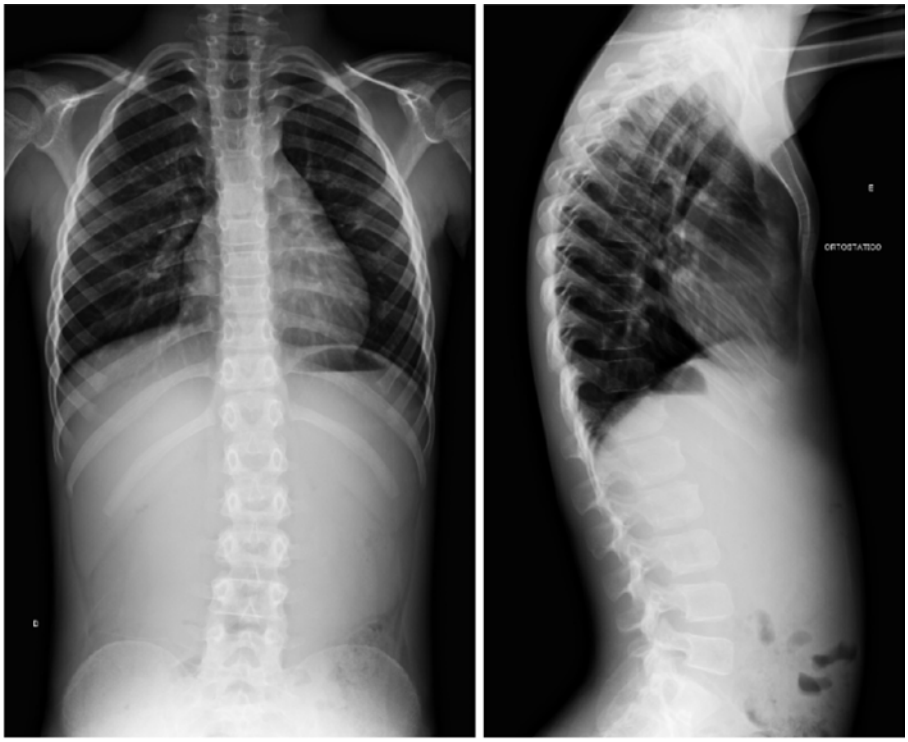
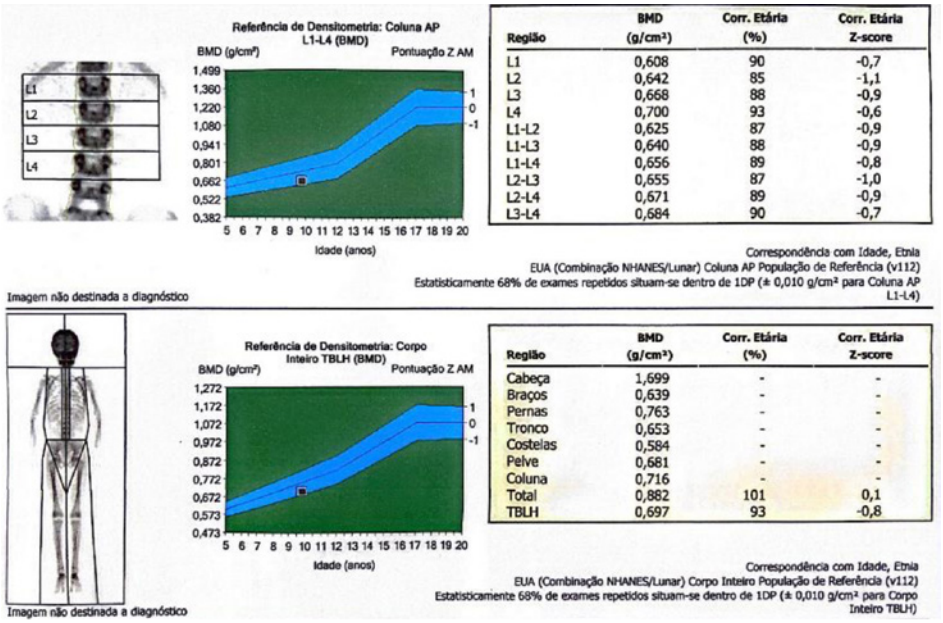


Figure 4 - Bone densitometry with normal bone mass at the lower limit.



Região	BMD (g/cm²)	Corr. Etária (%)	Corr. Etária Z-score
L1	0,608	90	-0,7
L2	0,642	85	-1,1
L3	0,668	88	-0,9
L4	0,700	93	-0,6
L1-L2	0,625	87	-0,9
L1-L3	0,640	88	-0,9
L1-L4	0,656	89	-0,8
L2-L3	0,655	87	-1,0
L2-L4	0,671	89	-0,9
L3-L4	0,684	90	-0,7

Região	BMD (g/cm²)	Corr. Etária (%)	Corr. Etária Z-score
Cabeça	1,699	-	-
Braços	0,639	-	-
Pernas	0,763	-	-
Tronco	0,653	-	-
Costelas	0,584	-	-
Pelve	0,681	-	-
Coluna	0,716	-	-
Total	0,882	101	0,1
TBLH	0,697	93	-0,8

DISCUSSION

Robinow syndrome, first described in 1969 by Meinhard Robinow, is a rare genetic disorder characterized by short stature, mesomelic limb shortening, external genitalia hypoplasia, gingival hyperplasia, and typical facial features (hypertelorism, midface hypoplasia, large nasal bridge, short upturned nose, and anteverted nostrils). With fewer than 200 reported cases, it is of autosomal origin, both dominant and recessive, with the latter being the more severe form [1].

Serum hormone levels showed a growth hormone (GH) deficiency and low basal levels of testosterone during sexual development and differentiation, which normalize during puberty. Additionally, a partial insensitivity of Leydig cells to human chorionic gonadotropin and a defect in the feedback mechanism of sex hormones were observed [2].

The autosomal recessive variant is characterized by skeletal abnormalities: shortening of long bones of the major limbs, especially forearms, brachydactyly, abnormal curvature of the spine due to bone deformities in the spine, short stature, and fused or absent ribs in certain areas. Additionally, defects in vertebral segmentation are common but more severe in the recessive form: hemivertebrae and scoliosis [3].

The recessive variant of Robinow Syndrome originates from mutations in the ROR2 gene (9q22), which result in premature stop codons, leading to non-functional proteins. Mutations in this gene prevent the production of any functional ROR2 protein, which plays a critical role in the formation of the skeleton, heart, and genitals. This interruption in development before birth triggers the characteristic symptoms of the syndrome [4].

The dominant form, on the other hand, presents more severe intraoral characteristics (wide retromolar ridge, deformation of the alveolar ridge, malocclusion, gingival enlargement, dental crowding, and hypodontia) than the recessive form. Autosomal dominant Robinow Syndrome has a heterogeneous genetic origin, being associated with mutations in the WNT5A gene (3p14), DVL1, DVL3 [5].

The diagnosis of Robinow Syndrome is mostly clinical and is made by identifying characteristic anomalies. Radiological exams are performed as a complement to confirm the presence of skeletal malformations. Additionally, molecular genetic tests can identify a heterozygous pathogenic variant in DVL1, DVL3, or WNT5A [1-5].

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