Case Study

CLINICAL DILEMMA OF ROBINOW SYNDROME: A CASE SERIES

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Received on: 10-Jul-2024 Accepted for Publication: 03-Dec-2024

Introduction

Robinow syndrome (RS) is a rare genetic condition [01], having an incidence of one in every 500,000 people. (02). Initially reported by Robinow et al. in 2004, RS can exhibit a broad variety of clinical manifestations. Its primary features are small stature, coarse facial features and mesomelic limb dwarfism, anomalies of the head and external genitalia, and skeletal deformities of the vertebrae and other limbs. While mutations in the ROR2 gene (9q22) generate autosomal recessive disease, the WNT5A gene (3p14.3) mutation is typically linked to the autosomal dominant phenotype, which is observed in less than 10% of cases. Three patients with "Robinow syndrome" are described here; two of the patients belonged to the same family.

Case Presentation

CASE 01

A 04-year-old girl presented with a complaint of not gaining height, although developmentally, she was appropriate for her age. Her height was 68cm [SDS -8.83], and her weight was 09 kg. Her arm span to height difference was (-13), and her upper to lower segment ratio was (1.6). She had coarse facies and mesomelic limbs. A skeletal survey showed multiple vertebral (scoliosis, hemivertebrae, butterfly vertebrae) and rib anomalies (crowding ribs, fork ribs). Echo showed a large membranous VSD. Her thyroid profile was within the standard limit. [Fig 1.0 A B & C]

CASE 02

Four-month-old baby girl sister of case 1 had similar coarse facies and mesomelic limb shortening as her elder sister. Her length was 44 cm (SDS = -5.64), and her weight was 2.8Kg. Arm span to length difference was (-8), and upper to lower segment ratio was (1.5). The skeletal survey showed multiple vertebral anomalies, underdeveloped paranasal sinuses, partial agenesis of the sacrococcygeal segment, and an absent proximal radial head. Unlike case 1, her Echo and thyroid profile were unremarkable. [Fig 2.0 A & B]

CASE 03

A 4-month-old baby boy presented with complaints of a chest infection and failure to thrive. He had short arms and legs compared to other children. His length was 53cm (SDS = -3.44) and his weight was 3.5Kg. His arm span to length difference was (-14cm), and upper to lower segment ratio was (1.2). He had similar facies, and the oral cavity showed a tongue-tie. Genital examination showed a buried penis and right undescended testis. A skeletal survey was advised, which showed mesomelic limb shortening and vertebral anomalies. Clinodactyly and syndactyly of feet were also evident on radiographs. Echo and thyroid profile were normal. [Fig 2.0 A & B]

Figure 1.A

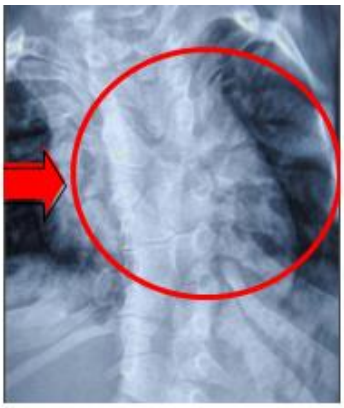

Figure 1.B Vertebrae

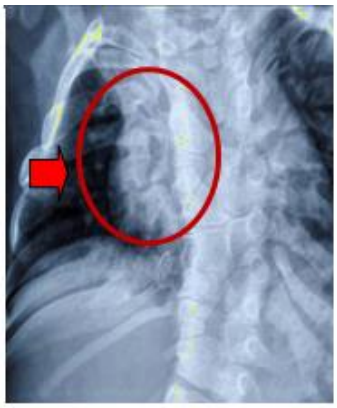

Figure 1.C Ribs anomaly

Figure 2.A.

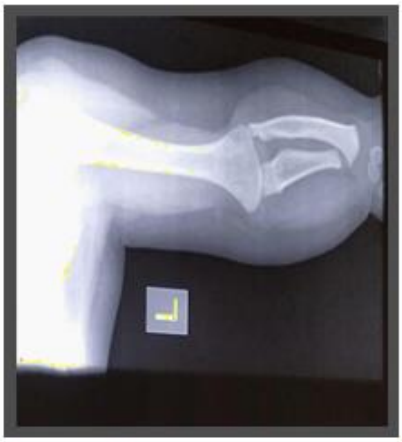

Figure 2.B. Absent radial head

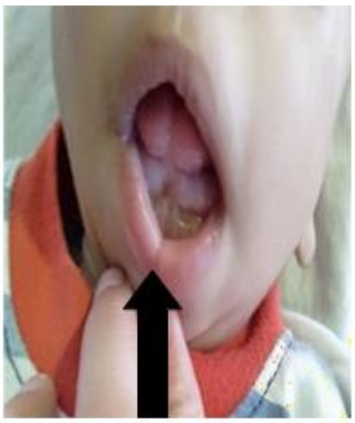

Figure 4.A. Tongue tie

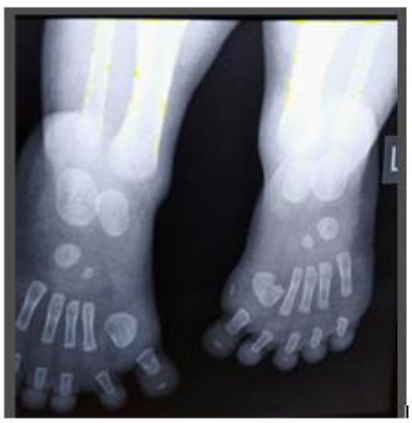

Figure 3. B. Syndactyly

DISCUSSION

Robinow syndrome, additionally known as mesomelic dwarfism-small genitalia syndrome, fetal face syndrome, or Robinow-Silverman-Smith syndrome, is a rare illness that weakens the development of numerous body parts, mostly the skeleton. In addition to anomalies in the head, face, and external genitalia, it is typified by short-limbed dwarfism and spinal segmentation. Robinow et al. (1) reported hemivertebrae, genital hypoplasia, and mesomelic limb shortening associated with this dwarfing disease. The phrase "fetal facies" was used by him to characterize the similarity between a developing fetus's facial features. The intensity of each type's symptoms, indications, and inheritance pattern can be used to identify it.

The skeletal anomalies associated with autosomal recessive Robinow syndrome include forearm brachymelia, brachydactyly, clinodactyly, abnormally small hands with broad thumbs, wrist madelung deformity, hemivertebrae, kyphoscoliosis, fused or missing ribs, and short stature. A small, upturned nose with anteverted nostrils, a depressed nasal bridge, low-set, posteriorly rotated ears, frontal bossing, midface hypoplasia, ocular hypertelorism, exophthalmos, and broad, downwardly slanting palpebral fissures are examples of characteristic defects. A wide, triangularly-shaped mouth that is downwardly oriented in some affected newborns may be accompanied with gingival hyperplasia, micrognathia, a short chin, and/or a long philtrum. Dental anomalies include crowded back teeth, delayed eruption of permanent teeth, misaligned teeth, and bifid uvula are frequently seen. While IQ is typical, 10 to 15 percent of persons have delayed development. (02)

The symptoms and indicators of the autosomal dominant variant are less severe than those of the autosomal recessive form. Short stature is less prominent, and abnormalities of the spine and ribs are uncommon. An additional feature of autosomal dominant Robinow syndrome is cranial osteosclerosis. Nowadays, over 100 cases have been published in medical journals, covering the majority of ethnic groups; nevertheless, reports of Afro-Caribbean or Japanese patients have been few. Clusters with the autosomal recessive variant have been documented from Turkey (06), Czechoslovakia (05), and Oman (06). This illustrates how closely related these populations are to one another. (03) Pakistan has not reported any cases at all.(01)

Gene mutations in DVL1, DVL2, WNT5A, and DVL3 have been linked to autosomal dominant Robinow syndrome (03). Mutations in the DVL1 gene cause the osteosclerotic type of the disease. There are certain individuals who exhibit the telltale signs and symptoms of Robinow syndrome without having a recognized gene mutation. In these instances, the condition's etiology is uncertain.

The majority of kids with Robinow syndrome have intellectual impairment, small stature, and growth and developmental abnormalities. Abnormalities of the skeleton (06, 07, 08) can include

The fingers and toes may have hypoplastic phalanges, or the terminal phalanges of the thumbs and great toes may be bifid. Scoliosis, hemivertebrae, fusion of certain vertebrae, limited elbow extension, dislocated hips, and aberrant fusion or absence of specific ribs are possible further problems. Robinow syndrome neonates typically

have ambiguous genitalia (08). Early infancy is usually the best time to establish gender. The clitoris and the outside, longer folds of the labia major may be undeveloped in females. Micropenis and cryptorchidism may be found in males. Males affected seldom may develop typical secondary sexual characteristics, with the exception of persistent micropenis, but may also exhibit partial primary hypogonadism. Females affected show normal fertility and gonadal function.

Physical anomalies such as kidney duplication, hydronephrosis, inguinal/umbilical hernia, or corpus callosum agenesis may also be present in individuals with Robinow syndrome. Furthermore, in newborns with Robinow syndrome, congenital cardiac abnormalities may affect about 13% of them. Pneumonia is a recurrent lung infection that can seldom befall newborns and children with Robinow syndrome. Pneumonia can occasionally cause severe cases that, if left untreated, could be fatal.[01]

Treatment is mainly supportive; however, some patients may have a concomitant growth hormone deficiency, and recombinant growth hormone therapy has shown significant improvement in growth rate (10). Prenatal diagnosis is also available and can be possible at the 19th week of gestation (11). Genetic testing is also available. The main objective is to highlighting this rare disorder in our society is that we can diagnose these cases in the future quickly and also, we can proceed with growth hormone trials to improve outcomes.

Robinow syndrome is typically diagnosed based on distinctive physical characteristics not long after birth. On the other hand, radiographic analysis is required to verify the existence of skeletal abnormalities. To confirm the diagnosis of autosomal recessive Robinow syndrome, molecular genetic testing for mutations in the ROR2 gene is available. The diagnosis of autosomal dominant Robinow syndrome can be verified by molecular genetic testing for mutations in the DVL1 and WNT5A genes.

Fetal ultrasonography can be used to diagnose pregnancies as early as the 19th week, although it can be challenging to determine the severity of the syndrome. In situations of AR, genetic testing may be done to confirm the diagnosis.[11]

A group of experts must work together in a coordinated manner to treat Robinow syndrome. A child's therapy may need to be carefully planned by pediatricians, orthopedists, surgeons, cardiologists, physical therapists, and/or other medical specialists. Bracing or surgical treatment are two methods of managing bone abnormalities. Children with the disease have received growth hormone injections to accelerate their growth.[12] It is advised that afflicted individuals and their families seek genetic counseling. The general approach to treating this illness is supportive and symptomatic.

CONCLUSION

The main objective is to highlight this extremely rare disorder in our society and get our clinicians familiar with it. In this way, individuals with this disorder will be diagnosed earlier, and associated conditions (like heart defects) will be picked at an earlier stage. Thus, initiating prompt treatment will impact the prognosis in the long run. Some patients can be found to have concomitant growth hormone deficiency and growth hormone therapy has shown significant improvement in growth rate. We can sensitize our clinicians to diagnose concomitant growth hormone deficiency and initiate growth hormone trials and monitor the response.

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