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Unique Roberts syndrome with bilateral congenital glaucoma: A case report

Almulhim A *et al.* Unique Roberts syndrome with congenital glaucoma

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Abstract

BACKGROUND

Congenital glaucoma associated with Roberts syndrome (RS) is an unusual and unique condition. No previous report describes this association. A multidisciplinary approach including molecular studies were conducted to reach the final diagnosis.

CASE SUMMARY

We present a rare case of a 1-wk-old male with RS associated with bilateral congenital glaucoma, left ectopic kidney, and left-hand rudimentary digits. A comprehensive approach was applied by which bilateral non-penetrating glaucoma surgery was performed with good control of intraocular pressure for more than 6 mo. Cytogenetic and molecular testing were conducted and revealed normal measurements.

CONCLUSION

This report described a case of a male baby with clinical features of RS but with a negative molecular analysis, presenting with left-hand rudimentary digits, bilateral congenital glaucoma, and left ectopic kidney. To the best of our knowledge, this is the first case reported with phocomelia, bilateral congenital glaucoma, and unilateral ectopic kidney.

Key Words: Roberts syndrome; Roberts-SC phocomelia syndrome; Phocomelia; Congenital glaucoma; Karyotype; Whole exome sequencing

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Core Tip: Roberts syndrome (RS) is an extremely rare disease characterized by a combination of deformities in the lower and/or upper extremities in association with other organ abnormalities. We provide here the first reported case of RS associated with bilateral congenital glaucoma. Bilateral non-penetrating glaucoma surgery was performed to control intraocular pressure and the outcome was excellent.

INTRODUCTION

Phocomelia with ocular and internal organ abnormalities are reported as part of Roberts syndrome (RS). RS (OMIM #268300; also known as Roberts-SC phocomelia syndrome) was reported by John Roberts in 1919 and is an autosomal recessive condition characterized by prenatal and postnatal growth retardation, skeletal malformation including tetraphocomelia or mesomelia, mental retardation, and craniofacial dysmorphic features^[1].

The clinical presentation is widely variable, from mild cases that can be difficult to confirm without a molecular test to the severe spectrum of diseases that present with a typical phenotype. Babies born with severe RS usually die *in utero* or shortly postpartum, while mildly affected people can survive to middle age^[2].

Herein, we report an unusual case of a male baby with clinical features of RS but with a negative molecular analysis, presenting with left-hand rudimentary digits, bilateral congenital glaucoma, and left ectopic kidney.

CASE PRESENTATION

Chief complaints

A 1-wk-old male baby was referred to our hospital in June 2021 with a picture of bilateral congenital glaucoma.

History of present illness

According to the parents, the deformed left hand with bilateral cloudy cornea were noticed immediately after birth.

Personal and family history

The baby was the second child of a healthy non-consanguineous couple and a product of an uneventful pregnancy with spontaneous vaginal delivery at 40 wk. Birth weight was 3 kg. There was neither a family history of similar conditions nor a prenatal history of exposure to any known teratogenic medication.

Physical examination

On physical examination, left-hand rudimentary digits were noticed (Figure 1). The child was active and sucking well. Examinations of the central nervous system, cardiovascular system, abdomen, and genitalia showed all to be normal.

An ocular examination was performed under general anesthesia and showed bilateral buphthalmos (Figure 2), significant corneal edema, and corneal diameter of 11 mm right/11.5 mm left. The patient was treated with travaprost and combined dorzolamide and timolol, and the intraocular pressure (IOP) was 25 mmHg right/39 mmHg left. Fundus examination showed a cup disc ratio of about 0.2 in both eyes. Central corneal thickness ranged between 900 microns and 930 microns in both eyes.

Imaging examination

Echocardiogram findings were normal. Abdominal ultrasound showed a left ectopic kidney located in the ipsilateral pelvic region and not in the lumbar area (Figure 3). Both kidneys appeared normal in size and echogenicity.

FURTHER DIAGNOSTIC WORK-UP

Based on the given detailed ophthalmological and medical assessment, we applied comprehensive genetic testing by performing karyotyping and chromosomal microarray analysis. Karyotype showed normal male (46, XY) with no evidence of clinically significant numerical or structural chromosome abnormalities. Moreover, we performed whole-exome sequencing (WES) that allowed us to screen the whole exome and to focus in particular on the *ESCO2* gene that is known to be linked with RS and other genes related to primary congenital glaucoma such as the *CYP1B1* and *LTBP2* genes. Despite our detailed review of the WES data, negative results were found, with no observed genetic variants or incidental findings.

Differential diagnoses

Thalidomide-induced phocomelia; Holt-Oram syndrome; Thrombocytopenia with absent radius syndrome; Sporadic phocomelia

FINAL DIAGNOSIS

Based on the clinical and diagnostic findings, the final diagnosis was RS with bilateral congenital glaucoma and left ectopic kidney.

TREATMENT

Bilateral non-penetrating deep sclerectomy plus mitomycin C was applied. The IOP was stable for more than 6 mo postoperatively.

Written informed consent was obtained from the parents of the baby. The Institutional Review Board reviewed and approved this study. Permission to publish photographs was also obtained.

OUTCOME AND FOLLOW-UP

At 6 mo, 9 mo, and 1 year postoperatively, the IOP was stable without anti-glaucoma medication.

DISCUSSION

RS is an extremely rare autosomal recessive condition that presents with widely variable prenatal and postnatal growth retardation, skeletal malformation, and mental retardation. It was first described by Roberts in 1919 in two children of consanguineous parents. The children presented with upper and lower limb anomalies, skull deformity, exophthalmos, cleft lip, and palate bilaterally^[3]. In 1969, Herrmann *et al*^[1] reported a syndrome with milder features and labeled it as SC phocomelia syndrome.

A systematic review and severity scoring system was published by Van Den Berg and Francke^[3] in 1993 that included 100 cases. Goh *et al*^[2] and Zhou *et al*^[4] conducted a review of the literature on RS in adult patients. None of the previously reported cases were associated with congenital glaucoma. Ocular manifestations reported in the literature to date have been hypertelorism in 86.7% of patients, exophthalmia in 69.4% of patients, cloudy cornea in 68.1% of patients, optic nerve cavernous hemangioma in 1 patient, and blue sclera with bilateral macular dysfunction in 1 patient. Renal abnormalities were reported in 50% of patients^[1-4].

Worldwide about 157 cases of RS have been reported, and the most recent case was published in October 2020 regarding a 30-wk gestation stillborn male who had the typical phenotype of RS with a normal molecular analysis^[5].

In our case, we applied comprehensive genetic testing by performing karyotyping and chromosomal microarray analysis. Chromosomal analysis revealed normal male (46, XY) without any detected abnormalities. WES revealed no abnormalities in the *ESCO2* gene (linked to RS) or the *CYP11B1* and *LTBP2* genes (linked to primary congenital glaucoma). Although this patient had normal molecular study findings, the diagnosis of RS can be established based on the phenotype because RS cases without any molecular abnormality have been reported in the literature^[5].

CONCLUSION

This report describes a case of a male baby with clinical features of RS but with a negative molecular analysis. He presented with left-hand rudimentary digits, bilateral congenital glaucoma, and left ectopic kidney. To the best of our knowledge, this is the first reported case of RS with a combination of phocomelia, congenital glaucoma, and ectopic kidney without any detected molecular abnormality.

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PRIMARY SOURCES

1

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