Rothmund-Thomson syndrome and ophthalmologic alterations: a case report in childhood

Síndrome de Rothmund-Thomson e alterações oftalmológicas: relato de caso na infância

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ABSTRACT

Rothmund-Thomson Syndrome (RTS) is a rare congenital disorder with fewer than 300 cases reported in the literature, characterized by dermatological, skeletal, and ophthalmological abnormalities, as well as a predisposition to osteosarcoma. This study describes the ophthalmological findings of an 11-year-old patient diagnosed with RTS who was referred to the ophthalmology service due to decreased visual acuity. Based on a review of the scientific literature and analysis of the patient's medical records, the case highlights the ocular manifestations associated with RTS and reinforces the importance of multidisciplinary follow-up to ensure early diagnosis, appropriate management, and improved visual outcomes.

RESUMO

A Síndrome de Rothmund-Thomson (SRT) é uma condição congênita rara, com menos de 300 casos descritos na literatura, caracterizada por alterações dermatológicas, esqueléticas e oftalmológicas, além de predisposição ao osteossarcoma. Este estudo descreve os achados oftalmológicos em uma paciente de 11 anos diagnosticada com SRT, encaminhada ao serviço de oftalmologia devido a redução da acuidade visual. Com base em revisão da literatura científica e análise dos prontuários médicos, o caso destaca as manifestações oculares associadas à síndrome e reforça a importância do acompanhamento multidisciplinar para garantir diagnóstico precoce, manejo adequado e melhores desfechos visuais.

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INTRODUCTION

Rothmund-Thomson Syndrome (RTS) is a rare congenital disorder with autosomal recessive inheritance, and only a few cases have been described in the literature to date.[1] The main clinical features observed in individuals with RTS include: cutaneous erythema progressing to poikiloderma, short stature, sparse hair, eyelashes and/or eyebrows, as well as skeletal, dental, ophthalmologic, and hematologic abnormalities, and a predisposition to neoplasms, depending on the genetic variant involved.[1]

We report the case of a child with RTS, followed by a multidisciplinary team, presenting with bilateral cataracts and other ophthalmological abnormalities, in association with characteristic systemic clinical features.

This study was conducted through a review of the published scientific literature and a review of the medical records of a patient treated at a specialized service. The literature search was carried out using the PubMed®, SciELO, and GeneReviews platforms, with the keywords "Rothmund-Thomson syndrome", "ocular manifestations", "juvenile cataract" and "ophthalmology". Articles addressing the ophthalmological manifestations of RTS, as well as genetic and clinical aspects relevant to the reported case, were included. The analysis of the patient's medical records allowed for the collection of clinical, ophthalmological, and systemic data, contributing to the phenotypic characterization of the case and to the correlation with findings reported in the literature.

This study was approved by a Research Ethics Committee under the protocol number CAAE 83667924.7.0000.5102.

CASE REPORT

An 11-year-old brown-haired girl with a genetic diagnosis of RTS, under multidisciplinary follow-up, presented to the ophthalmology team due to progressive decreased visual acuity in both eyes. She had normal neurocognitive and neuropsychomotor development. She was under endocrinological follow-up for short stature, with a height of 1.26 m at age 11 (below the third percentile for age), and bone age consistent with 9 years. In the first months of life, she developed cutaneous erythema affecting the flexor and extensor surfaces of all four limbs, as well as the hands, trunk, and back, progressing to hyperpigmented lesions with poikiloderma characteristics (Figures 1 and 2). No dental, scalp hair, or eyebrow abnormalities were observed.

In February 2020, she was evaluated for progressive bilateral visual impairment. On examination, her visual acuity was hand motion in both eyes. External ocular examination revealed bilateral ptosis, preserved extraocular motility, and esotropia. Slit-lamp examination of both eyes showed intense photophobia, sparse eyelashes (Figure 3), clear conjunctiva, transparent cornea with peripheral neovascularization and signs of limbal stem cell deficiency, trophic iris, deep anterior chamber, and total white cataract in both eyes. Intraocular pressure was within normal limits in both eyes. An ocular ultrasound was performed, showing attached retina in both eyes. The patient underwent lensectomy with implantation of a rigid three-piece intraocular lens in both eyes, with no complications. In the immediate postoperative period, her visual acuity improved to 20/25 in both eyes. Fundus examination revealed well-defined and stained optic discs, normal macula and vessels, and attached retina in the posterior pole of both eyes. Regarding esotropia (Figure 4), after surgery, she presented with 1+/4+ underaction of the lateral rectus muscle (LR) and 1+/4+ overaction of the medial rectus muscle (MR) in both eyes. The cover test revealed an esotropia (ET') of 25 prism diopters (PD) at distance and 30 PD at near, with fixation preference for the left eye (OS), with no indication for strabismus surgery at that time. The patient continues to be monitored with routine ophthalmologic follow-up.

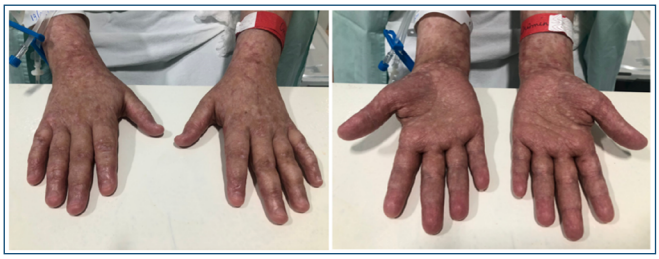

Figure 1. Presence of hyperchromic skin lesions on the hands, characteristic of poikiloderma.

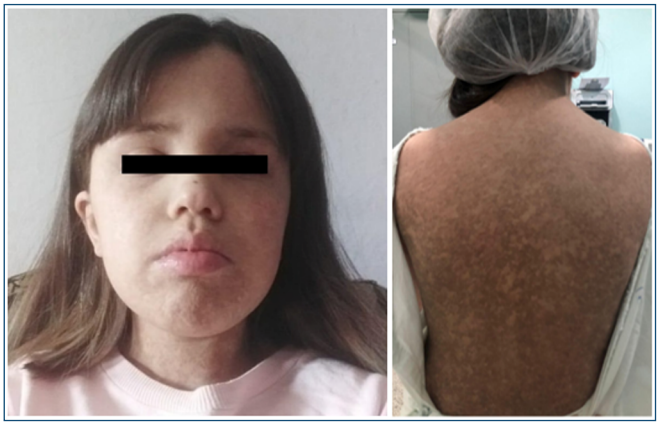

Figure 2. Presence of hyperchromic skin lesions on the face and back, characteristic of poikiloderma.

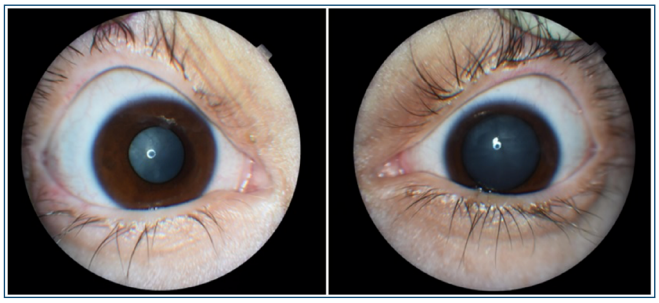

Figure 3. Patient's eyes showing sparse eyelashes and cataracts.

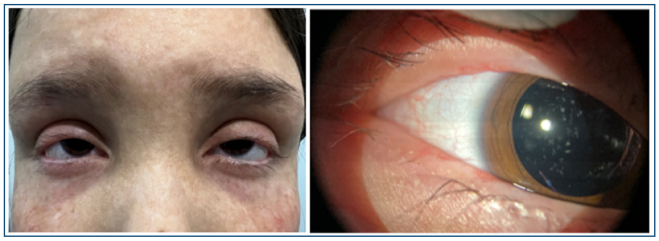

Figure 4. Patient's face indicating hyperchromic skin lesions, eyelid ptosis and esotropia. Right eye with sparse eyelashes and centered intraocular lens.

DISCUSSION

Rothmund-Thomson syndrome is a rare congenital disease with few cases reported in the literature[1,2]. It was first described in Austria in 1868 by Auguste Rothmund[1]. The condition is inherited in an autosomal recessive pattern and is attributed to mutations in the ANAPC1 or RECQL4 genes[3,4]. The prevalence of RTS in the general population and the carrier frequency remain unknown, and there are no reports indicating a higher or lower predisposition to the syndrome among specific ethnic groups[3].

The diagnosis of RTS can be established based on characteristic clinical manifestations and/or the identification of pathogenic variants through molecular genetic testing, specifically in the ANAPC1 or RECQL4 genes[3]. Dermatologists are often the first to identify the syndrome, as the skin, hair, nails, and teeth are frequently the initial sites affected[1]. The hallmark clinical feature is cutaneous erythema, which typically appears between six months and three years of age. It begins with swelling and, occasionally, blistering on the face, later spreading to the buttocks and extremities. The skin lesions become chronic, developing reticulated hypo- and hyperpigmentation, telangiectasias, and punctate atrophy – collectively referred to as poikiloderma[1,3].

There are two clinical subtypes of RTS. Type 1, associated with pathogenic variants in ANAPC1, is characterized by poikiloderma, ectodermal dysplasia, and juvenile cataracts. Type 2, linked to RECQL4 mutations, is marked by poikiloderma, congenital bone abnormalities, a high risk of osteosarcoma during childhood, and skin cancer in adulthood[1,4]. The overall cancer prevalence in adults with RTS is not yet known; however, in a clinical cohort study of 41 patients with RTS, 32% developed osteosarcoma. The estimated prevalence of skin cancer in individuals with RTS is around 5%, including basal cell carcinoma, squamous cell carcinoma, and melanoma[3,4]. Additionally, an independent cohort study reported that RTS is typically diagnosed at an average age of 10 years[4].

Most reports of early-onset bilateral juvenile cataracts are associated with pathogenic variants in ANAPC1 (Type 1 RTS)[3]. This condition usually progresses rapidly and may be accompanied by other ocular abnormalities previously described in RTS, such as absence of eyelashes, exophthalmos, corneal atrophy, strabismus, photophobia, symblepharon, microphthalmia, keratoconus, scleralization and pigment deposits in the cornea and conjunctiva, iris and retinal coloboma, chorioretinal atrophy, congenital glaucoma, and tilted optic discs[2]. Due to the rarity of the syndrome, data on the incidence of these ophthalmological findings are lacking in the literature[1,2].

The differential diagnosis of RTS includes other causes of poikiloderma that are clinically distinct, such as Bloom syndrome, Werner syndrome, Ataxia-telangiectasia, Fanconi anemia, Xeroderma pigmentosum, Kindler syndrome, Dyskeratosis congenita, Poikiloderma with neutropenia, and Hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis[1,3].

Most individuals with RTS have normal neuropsychological development, and in the absence of malignancies, life expectancy is likely to be normal[3]. However, long-term follow-up data in the literature remain limited. Genetic counseling is recommended for relatives of affected individuals, as RTS follows an autosomal recessive inheritance pattern. At conception, each sibling of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Carrier testing for at-risk family members, prenatal testing for pregnancies at increased risk, and preimplantation genetic diagnosis are possible if the family-specific ANAPC1 or RECQL4 pathogenic variants are known[3].

We report the case of a rare syndrome, with ophthalmological manifestations and indication for surgical intervention to seek visual improvement. Visual symptoms are considered minor diagnostic signs, although juvenile cataracts may be present in up to 50% of patients[1,2]. The

patient must be followed by a multidisciplinary medical team due to the described systemic alterations[1].

AUTHORS' CONTRIBUTION

Priscila Helena Araújo Oliveira contributed to the study's conception and design, as well as to data analysis and interpretation, drafting, and critical revision of the manuscript. Bárbara de Cássia Vilela collaborated in the analysis and interpretation of data and contributed to drafting and critically reviewing the manuscript content. Eduardo Nogueira Lima Sousa was involved in the study's conception and planning, drafting, and critical revision of the manuscript. All authors approved the final version and take full responsibility for the work, ensuring its accuracy and integrity.

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