A CASE OF RWANDAN PATIENT WITH RING CHROMOSOME 15 SYNDROME

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ABSTRACT

Ring chromosome 15 is a rare disorder. The mechanism of ring chromosome formation is usually associated with loss of genetic material. Its clinical features are nonspecific with a wide spectrum ranging from a near normal phenotype to multiple malformations. We are herein reporting a first case of a Rwandan patient who was a 30 month-old female child with ring chromosome 15 syndrome. He presented with a growth delay and café-au-lait spots among other common features found in this syndrome. The diagnosis was confirmed by karyotype.

Key word: Ring chromosome 15 - growth retardation - Rwandan patient.

RESUME

Le chromosome 15 en anneau est une anomalie rare. Le mécanisme de formation des chromosomes en anneau résulte en perte du matériel génétique. Les patients affectés par ce syndrome présentent un spectre large et non-spécifique de manifestations cliniques pouvant aller du phénotype presque normal à plusieurs malformations. Nous rapportons ici le premier cas d'une patiente Rwandaise âgée de 30 mois ayant un chromosome 15 en anneau. Elle présentait des signes cliniques retrouvés dans ce syndrome tel qu'un retard de croissance et des taches café-au-lait. Le diagnostic a été confirmé par le caryotype.

Mots-clés: : Chromosome 15 en anneau - retard de croissance - patiente Rwandais

INTRODUCTION

Ring chromosome 15 is a rare abnormality. It has been described for the first time by Jacobsen in 1966 and up to now about 40 patients have been reported [1,2]. Ring chromosomes are uncommon disorders and they have been reported for all chromosomes [2,3]. Ring chromosomes usually result from two terminal breaks in both chromosome arms, followed by fusion of the broken ends or from the union of a broken chromosome end with the opposite telomere region, leading to the loss of genetic material. The alternative mode of formation is telomere-to-telomere fusion, with telomeric and subtelomeric sequences being retained, resulting in complete ring chromosomes with, in principle, no genetic material loss [2,3].

Patients with r(15) syndrome present a wide spectrum of clinical manifestations encompassing a near normal phenotype to multiple malformations [1]. The phenotype variability depends on the extent of the deletion and the stability of the ring chromosome in post-zygotic mitosis [1-5]. Common findings in reported cases include pre and postnatal growth delay, low birth weight and birth length, microcephaly, mental retardation, triangular face, hypertelorism, broad nasal bridge, brachydactyly, speech delay, and multiple hyperpigmented or depigmented spots. Congenital heart defects and renal anomalies have been observed in severe phenotype [1,2,4].

We herein report the first case of a Rwandan patient with ring chromosome 15.

CASE PRESENTATION

A 30 month-old-girl born at term by normal delivery with 2,300 kg from non-consanguineous parents is presented. She consulted our clinical genetic department at the Kigali University Teaching Hospital for global development delay because she sat at one year and walked around two years. Her weight was 8 kg (< 3rd percentile), height 69 cm (< 3rd percentile) and head circumference 45 cm (< 3rd percentile). Her clinical features were characterized by microcephaly, hypertelorism, strabismus, hypoplastic alae nasi, short philtrum (Figure 1), disseminated café-au-lait spots on the abdomen and on the back. She also presented clubfeet (Figure 2).

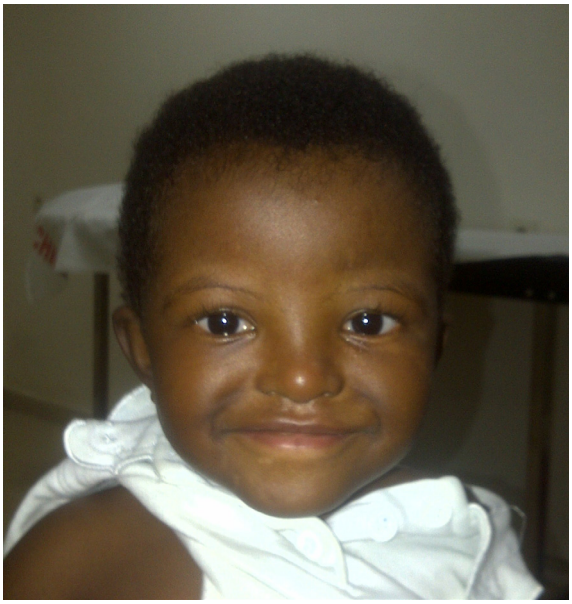

Figure 1: Patient with ring chromosome 15. Note facial dysmorphic features characterized by hypertelorism, strabismus, hypoplastic alae nasi, and short philtrum.

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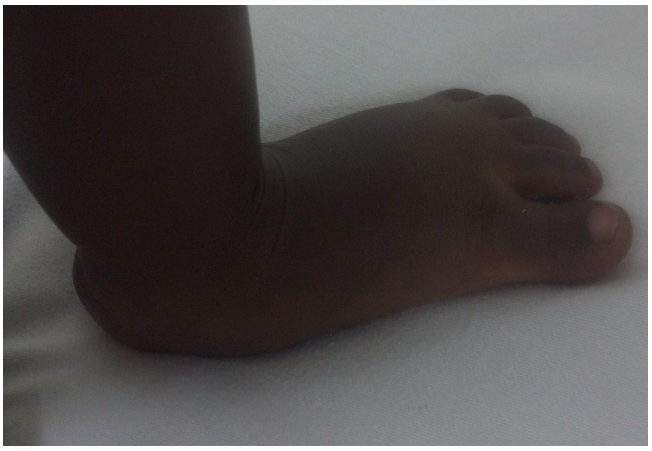

Figure 2: Clubfoot in patient with r(15).

CYTOGENETIC ANALYSIS AND RESULTS

Blood sample from the patient was drawn in heparin tube. Chromosome preparations were made from 72-h peripheral blood lymphocytes' culture and routinely stained with Quinacrin. Chromosomes were analyzed with a resolution of 550 bands according to ISCN (2011). Results showed a conventional karyotype of 46, XX, r (15) in all 20 analyzed mitoses (Figure 3). The analysis of parent's karyotypes was normal.

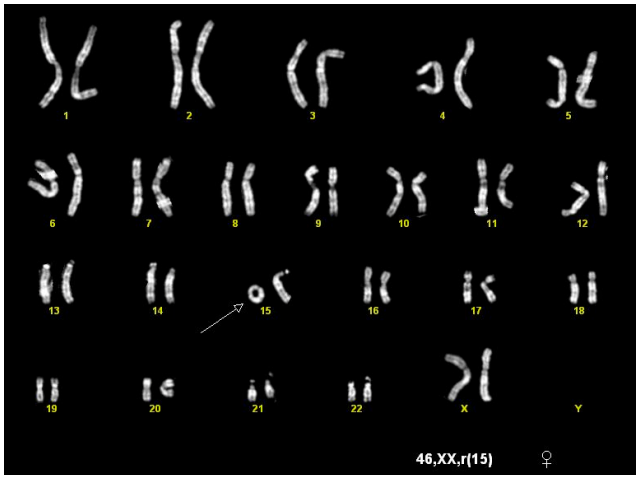

Figure 3: Karyotypes of the proband. The arrow shows ring chromosome 15.

DISCUSSION

Ring chromosomes usually result from two terminal breaks in both chromosome arms, followed by fusion of the broken ends or from the union of a broken chromosome end with the opposite telomere region, leading to the loss of genetic material.

In the presented report, we described a case of 30 month-old-girl presenting a ring chromosome 15. This patient presented some typical clinical features described in this syndrome such as global development delay, facial dysmorphic features, microcephaly, disseminated café-au-lait spots on the abdomen and on the back [2,6]. Thus, clinical findings in our patient suggest that the first mechanism was involved in the ring formation with loss of genetic material however it is not possible to elucidate with the routine karyotyping technique used in our facilities. Some of the features observed in patients with r(15) are the same in patients with 15q terminal deletion and growth delay commonly observed in these patients is suspected to mainly result from loss of the IGF1R gene located at 15q26.3, which is required in normal embryonic and postnatal growth [1,2,7]. Low birth weight, post natal growth retardation, microcephaly, hypertelorism, and café-au-lait spots found in our patient are typically characteristic for distal deletion15q26, and club foot is not a new finding in patients with r(15) syndrome [1,8].

There are also several disease conditions that have been reported so far to be related to r(15); these include congenital diaphragmatic hernia, Russell-Silver syndrome, Prader-Willi syndrome (PWS) and autism [2,5,9-11].

In conclusion, we report the first case of Rwandan patient affected by ring chromosome 15. The combination of above described clinical features with or without other findings like congenital heart or renal anomalies should raise suspicion of ring chromosome 15 syndrome among other differential diagnosis. Both genetic diagnosis and counseling are helpful and the majority of these cases are de novo.

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