CASE REPORT

Bannayan-Riley-Ruvalcaba syndrome with deforming lipomatous hamartomas in infant - Case report*

Síndrome de Bannayan-Riley-Ruvalcaba com hamartomas lipomatosos deformantes em lactente - Relato de caso

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Abstract: Bannayan-Riley-Ruvalcaba Syndrome is a rare condition caused by mutations in the PTEN gene. It displays association of multiple lipomas, macrocephaly, hemangiomas, hamartomatous intestinal polyposis, developmental delay and speckled pigmented maculae on the male genitalia. We report the case of a nine-month-old boy who had fast growing and progressive tumors for three months, macrocephaly and lentigines on the penis. Imaging tests showed extensive lipomatosis with invasion of paraspinal muscles, enlargement of the spinal canal and spinal cord compression; after surgical excision of the mass, the pathology was consistent with lipoma. Adipocyte culture karyotype demonstrated PTEN mutation. We present this case for its rarity and exuberance.
Keywords: Hamartoma; Hamartoma syndrome, multiple; Lipoma

Resumo: A síndrome de Bannayan-Riley-Ruvalcaba é afecção rara, causada por mutações no gene PTEN. Apresenta associação de múltiplos lipomas, macrocefalia, hemangiomas, polipose hamartomatosa intestinal, atraso do desenvolvimento e máculas salpicadas na genitália masculina. Relatamos o caso de um menino de nove meses com lesões tumorais de crescimento rápido e progressivo em três meses de evolução, macrocefalia e lentigos no pênis. Exames de imagem demonstraram extensa lipomatose com invasão da musculatura paraespinhal, alargamento do canal vertebral e compressão medular. Depois da excisão cirúrgica da massa, o anatomopatológico foi compatível com lipoma. A análise do cariótipo em cultura de adipócitos demonstrou mutação do PTEN. Apresentamos este caso por sua exuberância e raridade.
Palavras-chave: Hamartoma; Lipoma; Síndrome do hamartoma múltiplo

INTRODUCTION

Bannayan-Riley-Ruvalcaba Syndrome is a rare condition manifested with multiple lipomas, macrocephaly, hemangiomas, hamartomatous intestinal polyposis, developmental delay and speckled pigmented maculae on the male genitalia.[1,2]

CASE REPORT

We describe the case of a nine-month-old male child, who had fast growing and progressive lesions on the trunk and abdomen since the age of 6 months. A previous evaluation by a pediatrician diagnosed first degree malnutrition and absence of psychomotor development deficit. At the examination, the child was thinner, presented macrocephaly, voluminous abdomen with multiple masses of soft consistency, affecting also the back and thorax, the larger of the lesions being located on his right flank (Figure 1). He also presented brownish, round macules on the penis, measuring around three millimeters in diameter (Figure 2).

General physical examinations included lipid profile, without any alterations. Computerized tomography of the abdomen and pelvis revealed extensive lipomatosis in the right postero-lateral thorax-abdomen region at the T8 level, extending down-

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ward until the perineal region with signs of controlateral paraspinal muscle invasion starting at T12. Lesional infiltration of vertebral, retrodural and psoas muscle epidural regions of the spinal canal could also be bilaterally observed (Figure 3). Magnetic resonance of the thoracic column revealed lipomatous dorsal lesion associated with enlargement of the spinal canal and spinal cord compression in the low thoracic column, as well as nonenhanced lumbosacral medullary compression after contrast.

The child underwent surgery for partial removal of the larger lesion, thus avoiding progression of medullary compression and functional deficit; examination of the sample confirmed the lipoma diagnosis (Figure 4). After the surgery, growth of the other lesions was observed, although without functional deficit (Figure 5). In order to detect chromosomal alterations in the adipocytic lesion, DNA was extracted, followed by CGH array. Loss of approximately 1MB of the long arm of chromosome 10, the region where the PTEN gene is located, was revealed. The same alteration was confirmed in the peripheral blood of the patient.

The authors present this case because of its exuberance and rarity. The child should be followed for early detection of intestinal polyps and possible neoplasms.

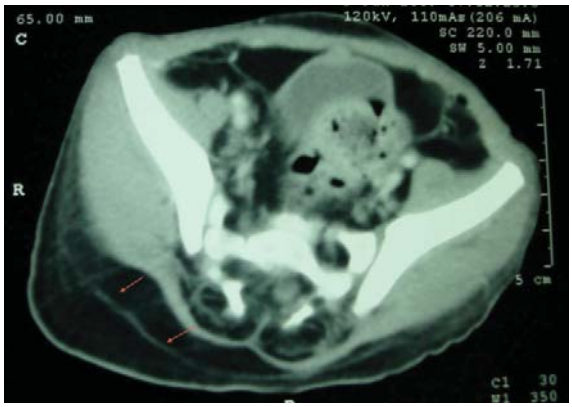

Figure 3: Computerized tomography of the pelvis showing large lipomatous hamartoma in the right postero-lateral region (arrows)

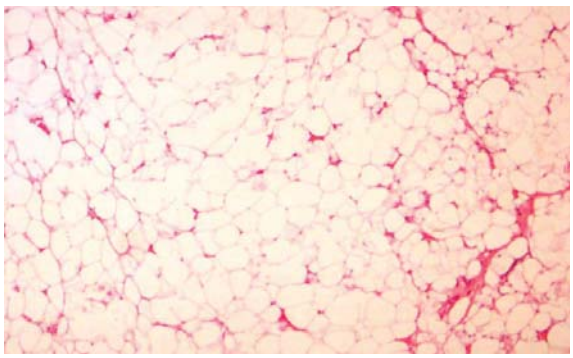

Figure 4: Anatomopathological examination: lipoma

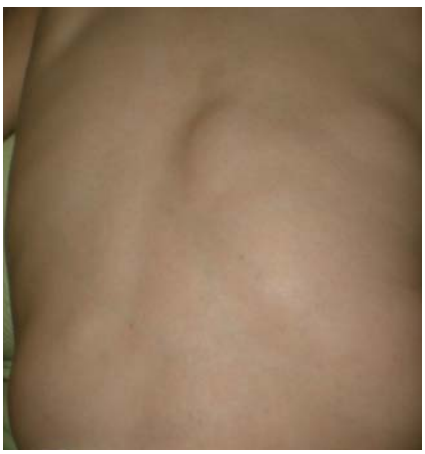

Figure 1: Multiple masses of soft consistency on the back and hips, larger on the right side

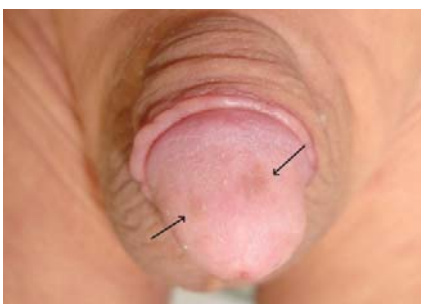

Figure 2: Brownish round maculae on the penis, measuring around three millimeters in diameter

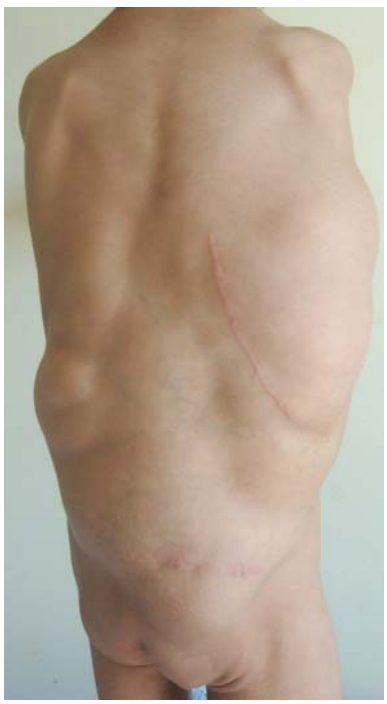

Figure 5: New growth of masses on the thorax and back, after excision of the larger lesion

DISCUSSION

Bannayan-Riley-Ruvalcaba Syndrome (BRRS) is a rare disorder, caused by mutations in the PTEN gene. It occurs both in an autosomal dominant and in a sporadic manner.[1,2] PTEN gene mutations are detected in 60% of the patients with SBRR.[3] It is manifested by the presence of multiple lipomas, hemangiomas, intestinal hamartomatous polyposis, arteriovenous malformations, developmental delay, macrocephaly and speckled pigmented maculae on the male genitalia.[2,4,5,6] Penile maculae are possibly the most marked and valuable characteristic for diagnosis of the syndrome; they may be present at birth or appear during infancy or puberty and persist in adulthood.[4] Some authors recommend investigation of PTEN mutations in children who present extreme macrocephaly with normal neurological images, specially when one of the parents has macrocephaly and also when older children present extreme macrocephaly and motor development delay or learning difficulties.[1]

Other characteristics of BRRS include thyroid abnormalities, high-arched palate, frontal bone protuberance, hypertelorism, strabismus, macrosomia, hypotonia, joint hyperextensibility, hypoglycemia, convulsions, café-au-lait spots, wide mouth and relative micrognathia.[2,7]

Marsh *et al* defined the clinical diagnosis of BRRS as the presence of three of four characteristics: macrocephaly, lipomatosis, hemangiomas and speckled pigmented maculae on the penis.[8] Parisi *et al* used less rigorous criteria, defining the syndrome as the presence of two of the three characteristics: macrocephaly, hamartomas (including at least one lipoma, hemangioma or intestinal polyp) and maculae on the penis.[4]

Lipomas and vascular malformations are manifested as soft lesions on the trunk and extremities; they may grow fast and become painful, with aggressive local behavior, without tendency for spontaneous resolution.[7,9] Intestinal hamartomatous polyposis occurs in 35-45% of BRRS cases, but without association with a greater risk for malignancy.[9] The polyps may be located along the entire gastrointestinal tract, more frequently in the colon and rectum. During infancy, they may present with diarrhea, abdominal pain, painless rectal bleeding, anemia, intussusception and intestinal obstruction. Considering the fact that hamartomatous polyposis may not manifest before middle age, routine yearly hemoglobin and fecal occult blood test may be useful for early diagnosis.[7,9]

The PTEN (phosphatase and tensin homologue) is a tumor suppressor gene that has a significant role in the molecular pathway of cellular proliferation, migration and apoptosis. Mutations result in uncontrolled cellular proliferation and failure in programmed cellular death.[9] The main clinical consequence is the onset of hamartomas derived from all three germinative layers,[9] as well as increase in risk for certain types of tumors in adulthood.

Mutations of this gene cause Cowden Syndrome (CS), characterized by facial trichilemmomas, acral keratosis, papillomatous papules, benign hamartomas, macrocephalia and increased risk for breast, thyroid and endometrium cancer, colorectal adenocarcinoma, non-Hodgkin lymphoma and melanoma, among others.[2,9,10] These may occur also in a variant, Lhermitte–Duclos disease, characterized by dysplastic cerebellar gangliocytomas, which may evolve with hydrocephaly, ataxia and convulsions.[2]

Identical mutations were demonstrated in patients with BRRS.[2] There are common characteristics also in CS and BRRS, like hamartomas, macrocephaly and thyroid abnormalities[2,8] Families have reported that the same mutation is found in different individuals with phenotypes more consistent with CS or BRRS.[2]

Due to these clinically and genetically overlapping disorders, BRRS and CS are considered different phenotypical expressions of the same allelic syndrome, collectively named PTEN Hamartoma Tumor Syndrome (PHTS).[2,5,8,9] Screening, vigilance and prevention of possible malignancies are the base of treatment of patients with PHTS, particularly those with CS.[5] Such screening should be done in the following manner:[9]

Patients younger than 18 years of age: Annual thyroid ultrasound, dermatological, neurological and psychological examination

Patients older than 18 years of age: Annual thyroid ultrasound, annual mammography, biopsy of the endometrium or annual transvaginal ultrasound starting at 40 years of age, biannual colonoscopy, biannual renal ultrasound or MRI

Although an increased risk of malignancies in BRRS has not been documented, due to the clinical and genetic similarities between Cowden and Bannayan-Riley-Ruvalcaba Syndromes and because patients with PTEN mutations have increased risk for cancer, some authors recommend that BRRS patients be advised to comply with the same malignancy screening recommendations for patients with CS.[2,5,8,9] ❑

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