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CASE REPORT

Diencephalic Syndrome (Russell Syndrome): A Clinical Case Report

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Abstract

Diencephalic syndrome, or Russell syndrome, is characterized by extreme weight loss without subcutaneous adipose tissue associated with symptoms such as vomiting, hyperkinesia, euphoria, irritability, nystagmus, optic atrophy, and pallor without anemia. Although rare, diencephalic syndrome should be considered in children with developmental delay and preservation of linear growth. We present below a clinical case report of a child with Russell syndrome.

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INTRODUCTION

In 1951, Russell described a syndrome marked by extreme weight loss and absence of subcutaneous adipose tissue, despite adequate caloric intake, associated with vomiting, hyperkinesia, euphoria, irritability, nystagmus, optic atrophy and pallor without anemia[1].

When faced with these symptoms, pediatricians investigate various causes of weight loss, such as inborn errors of metabolism, cystic fibrosis, celiac disease, Kwashiorkor and gastrointestinal problems, with the hypothesis of a tumor involving the hypothalamus being rarely raised[2].

As a result, patients face a significant delay in diagnosis. Although rare, diencephalic syndrome should be considered in children with developmental delays, which is unexplained by other causes, and with linear growth preservation[3].

In order to draw attention to Russell syndrome as a differential diagnosis, we present below a clinical case of an infant with diencephalic syndrome.

CLINICAL CASE

A.N.D.S., 9 months old, male, born in Rio de Janeiro/RJ, started experiencing weight loss and postprandial emesis at 6 months of age. After approximately 3 months of this condition, he went to the healthcare service close to his residence, with altered anthropometric measures, weighing 5,700 kg (Z score below -3), despite his height being within normal limits for his age.

His clinical evaluation revealed, intense visible weight loss, muscular hypotrophy, with loss of Bichart's fat pad, subcutaneous cellular tissue reduction and adipose panniculus, especially in the buttocks, without edema or visceromegaly. The infant was active, without irritability, with a preserved appetite, as well as unaltered diuresis and bowel movements.

He was admitted to the hospital to investigate severe malnutrition of the marasmus type (weight below Z-3) and immediately began the procedure recommended by the Hospital's Care Manual for Children with Severe Malnutrition[4], he was administered metronidazole 40 mg intravenously every 8 hours for 7 days, mebendazole 5 ml orally every 12 hours for 3 days and sulfamethoxazole + trimethoprim 35 mg + 7 mg intravenously every 12 hours for 7 days. In addition to treatment with antibiotics and anthelmintics, the hospital nutrition team followed the Ministry of Health's food preparation protocol for rapid growth[5] with 100 Kcal and 2.9 g per 100 ml with a target of 130 ml/kg daily. However, despite the measures adopted, our patient was unsuccessful in gaining weight.

Having classified the case as failure to thrive[5] – developmental delay or growth failure when the child's anthropometric parameters are well below expected values –, some diagnostic hypotheses were raised, such as celiac disease, allergy to cow's milk protein, tuberculosis Russell syndrome. Mother and patient started a diet restricting cow's milk protein and extensively hydrolyzed milk formula without lactose was introduced. During the hospitalization period, he did not present emesis, remained afebrile, with good acceptance of the diet offered and the mother's breast.

In the previous history, the infant was regularly seen by a pediatrician from the Family Health Program (FHP), maintained adequate neuropsychomotor development, reaching all the milestones stipulated by the Brazilian Society of Pediatrics[6] within predetermined periods. Weight, height and head circumference within the expected percentile for age (between Z0 and Z-2). No comorbidities or use of medications. Updated vaccination calendar.

Inadequate dietary history, with exclusive breastfeeding until 2 months of age, with cow's milk being introduced. At 4 months, he started dairy products and flour products, and, at 6 months, he was introduced savory porridge, which was always well accepted. During this period, her mother kept breast feeding on demand. At 7 months, she decided to add polymeric formula to his diet due to significant weight loss.

In the gestational history, the mother underwent complete prenatal care, GIIPIAI; the child was born vaginally, at 38 weeks and 2 days, 3440 g, 50 cm, AIG, Apgar 9/9, without complications during pregnancy, birth and neonatal period. Neonatal screenings showed no changes.

During the hospital stay, several laboratory tests were carried out with normal results, including: blood count, biochemistry, blood culture, TORCHS, anti-HIV, TSH and free T4, anti-endomysium IgA and IgG, anti-transglutaminase IgA and IgG, immunoglobulin A , total IgE, immunoglobulin M, immunoglobulin G, fecal parasitology, EAS, urine culture, as well as PPD. He was submitted to fundoscopy evaluation by an ophthalmology, with no signs of hypovitaminosis A or other changes.

Furthermore, he underwent diagnostic imaging investigation with chest X-ray and abdominal ultrasound (USG) without any changes. Transfontanella USG showed echogenic expansive formation in the projection of the third ventricle and ectasia of the lateral ventricles. A skull MRI was performed confirming the presence of an expansive hypothalamic-chiasmatic lesion, with infiltration of the intracranial portion of the optic nerves and the pituitary stalk, noticing an area of edema and infiltration along the optic tracts, bilaterally.

On the 20th day of hospitalization, based on the skull MRI findings, neurosurgery took over the case, continuing the investigation with a biopsy of the lesion. The histopathological result was compatible with optic pathway glioma. In this procedure, an external ventricular shunt (EVS) was placed, which remained for 30 days, evolving into Ventriculitis due to Staphylococcus aureus, treated with 20 days of vancomycin. After three negative CSF cultures, a ventriculoperitoneal shunt (VPS) was surgically placed.

The patient was discharged from hospital after 54 days to continue monitoring in the oncology, neurosurgery and gastroenterology clinics.

DISCUSSION

Russell syndrome has an insidious onset and the first symptoms generally appear before the first year of life, which can vary between 2 and 36 months, with a predominance in males[7]. The patient in our clinical case began to suffer at the age of 6 months, corresponding to the average found in the literature of 6.2 months[8].

The main characteristic of Russell syndrome is extreme weight loss with absence of subcutaneous adipose tissue and preserved linear growth[1], which also occurred with our patient, who had altered anthropometric landmarks (z score below -3) with a marked reduction in adipose tissue, mainly on the buttocks. Despite his visible weight loss, his height was within normal limits for his age.

The etiopathogenesis of extreme weight loss is not yet fully understood. The hypothesis that the presence of the tumor would be one of the causes is unlikely, as the involvement of the hypothalamic nuclei leads to reduced intake and, consequently, a decrease, but not absence, of adipose tissue[9]. However, this does not occur in the syndrome, which is characterized by preserved appetite with absence of adipose tissue[10], as presented by our patient, including loss of Bichart's fat pad.

Some other hypotheses are described in the literature. It is suggested that GH increase, which has a lipolytic action and is present in the majority of patients, is related to the pathophysiology of the syndrome. An increase in cortisol levels is also found, which would enhance the lipolytic action of GH, thus causing profound weight loss[11].

Other studies show that the tumor leads to the production of a lipolytic peptide, β-lipotrophin. It is also reported that there would be a hypersecretion of lipid-mobilizing hormone (LMH), which is under the control of the hypothalamus. These factors would explain the reduction in subcutaneous adipose tissue in these patients[12].

The neurological signs and symptoms of the syndrome, such as hyperkinesia, euphoria, irritability and nystagmus, are the most frequently encountered, while caused by compression of the tumor in the diencephalic region, such as vomiting, optic atrophy, papilledema, tremors, sweating, hyperthermia, convulsions and hydrocephalus, which are rarer[7,8].

Our patient presented postprandial emesis and euphoria, which are described in the syndrome[13]. It is also common to become startled and alert due to eyelid retraction (Collier's sign) and bilateral proptosis resulting from the diencephalic lesion[14].

Ophthalmological changes, such as nystagmus, decreased visual acuity and optical pallor, have been reported in 56-66% of patients in some studies[15]. Nystagmus, which is generally rotatory, would be the result of fixation deficiency due to low visual acuity resulting from compression of the optic nerves by the tumor.

Some neurovegetative manifestations are also found, such as sweating, hypotension and thermoregulation disorders (hypo or hyperthermia without apparent cause)[1]. The causes of thermoregulation disorders would be due to damage to the thermolysis center and thermogenesis carried by the tumor. These vegetative changes would also lead to pallor in the absence of anemia.

Regarding metabolism, there are no changes in protein levels, but hypoglycemia has been reported in some cases[1]. Regarding behavioral changes, it is hypothesized that they would result from the interruption of the fronto-thalamic-hypothalamic pathways, which would be equivalent to a prefrontal lobectomy.

Initially, the electroencephalogram (EEG) and fundus exam are normal. Diffuse EEG changes and optic atrophy related to intracranial hypertension may be found, as described in some cases[2]. Our patient did not undergo EEG and there was no change in the eye fundus examination.

The skull x-ray is generally unremarkable. As the disease progresses, signs of intracranial hypertension may be found. In some cases, cerebrospinal fluid diversion may be necessary.

In the case of our patient, a transfontanella USG was performed, which showed ectasia of the lateral ventricles and echogenic expansive formation in the projection of the third ventricle. A skull MRI was performed, which confirmed an expansive process in the third ventricle, as in most cases published in the specialized literature[12].

The tumors involved in Russell syndrome are usually gliomas, within which astrocytoma is the most frequently found. However, ependymomas, gangliogliomas and dysgerminomas are also described[8]. Our patient's histopathological findings were compatible with optic pathway glioma. It is worth noting that Central Nervous System tumors are the second most common cause of pediatric neoplasms after leukemia, and their incidence is estimated at around 2.8 per 100,000 children per year[16]. Russell syndrome tumors are rarer, with few cases reported in the literature[1,2,7,8,10].

The prognosis for these patients is not good. In general, life expectancy is only until the second or third years of life[6]. There are, however, reports of survival up to 12 years[17].

Regarding treatment, there are divergences in the literature on the subject. In most cases, due to delay in diagnosis, tumor volume and anatomical location, total resection is impossible. Therefore, some authors advocate only radiotherapy and chemotherapy. Others already consider radiotherapy and chemotherapy to be ineffective[7,8]. It is important to highlight that radiotherapy is contraindicated until the age of 3[18].

A case analysis showed that the average survival of patients without treatment was 12.3 months. With surgical treatment, survival was longer, reaching 20 months, and treatment with radiotherapy alone had a result of 25 months. The association of surgery with radiotherapy increased the average survival rate to 29 months[8].

Our patient is currently being monitored by the oncology service with a proposal to undergo chemotherapy. There was no resection of the tumor due to the difficult anatomical location for a surgical approach. The patient is now 1 year and 1 month old and has not yet gained weight. He continues to be monitored by the neurosurgery and gastroenterology clinics.

In short, although it is rare, diencephalic syndrome should be considered as a differential diagnosis in pediatric patients with developmental delay and who present normal linear growth.

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