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DOWN SYNDROME WITH CONGENITAL HYDROCEPHALUS

Case report

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ABSTRACT - Down syndrome is the most frequent genetic cause of mental retardation. Although usually presenting dysmorphic features and organ malformations, it is rarely associated with congenital hydrocephalus. The case of male neonate whose hydrocephalus was detected since the pregnancy and was discovered to have the syndrome at birth is reported. Chromosomal analysis confirmed the genetic disorder, and hydrocephalus was treated with ventriculoperitoneal shunt because of abnormal increase of head circumference. The patient has been accompanied and his development is considered normal when compared to the expected for those affected by the syndrome.

KEY WORDS: Down syndrome, hydrocephalus, malformation.

Síndrome de Down associada a hidrocefalia congênita: relato de caso

RESUMO - A síndrome de Down é a causa genética mais freqüente de retardo mental. Embora comumente apresentando dismorfias e malformações de órgãos, raramente está associada à hidrocefalia congênita. O caso de um recém-nascido masculino cuja hidrocefalia foi detectada desde a gravidez e que se descobriu ser portadora da síndrome ao nascimento é relatado. O cariótipo confirmou a anormalidade genética, e a hidrocefalia foi tratada com derivação ventriculoperitoneal devido ao aumento anormal do perímetro cefálico. O paciente está sendo acompanhado e seu desenvolvimento é considerado normal quando comparado ao esperado para os portadores da síndrome.

PALAVRAS-CHAVE: síndrome de Down, hidrocefalia, malformações.

Down syndrome (DS) represents the most common genetic cause of mental retardation[1]. The syndrome is characterized by several minor malformations and mental retardation caused most commonly by the full trisomy of chromosome 21. Occasional cases result from triplication of just the distal part of the long arm of chromosome 21 or from the presence of trisomy 21 / diploid mosaicism[1]. Besides the several dysmorphic features, DS is also associated with organ malformations, especially in the heart and gastrointestinal tract, and constitutes a major risk factor for leukemia and precocious Alzheimer disease during the adult age. However, it is rarely associated with congenital hydrocephalus. Hydrocephalus is a serious condition characterized by an exceeding accumulation of cerebrospinal fluid (CSF) inside the brain ventricles. Its occurrence in the first months of life (infantile hydrocephalus) brings a considerable risk of subsequent developmental neuroimpairments, such as cerebral palsy, mental retardation, epilepsy and severe visual deficit[2-5], especially in pre-terms[4].

The present study describes the case of male neonate with DS associated with congenital hydrocephalus treated with ventriculoperitoneal shunt (VPS).

CASE

A 29-year-old white woman has become pregnant for the first time and started obstetric accompaniment. At 22

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weeks of pregnancy a moderate enlargement of fetal lateral brain ventricles was detected by a routine fetal ultrasonography. Since then neurological advice was commenced. An investigation was performed for common causes of hydrocephalus, like congenital infections, but the tests rendered normal results. She was a nondiabetic mother. Subsequent ultrasonographies demonstrated stable hydrocephalus. Pregnancy was interrupted at 34 weeks through cesarean delivery because of acute antepartum fetal distress detected by Doppler velocimetry. The fetus was in pelvic presentation, had clear amniotic fluid and the membranes were torn at the delivery. Later histological examination of the placenta revealed areas of villus stromal fibrosis.

A male neonate was born in good clinical conditions, with normal fontanelles. His gestational age was calculated as 34 weeks by the Capurro method. His head circumference was 29.0 cm, a point on the line corresponding to minus two standard deviations (–2 SD) of the population normal range. The other anthropometric measures were the following: 1.740 g of weight (between –1 SD and –2 SD); 40.5 cm of length (below –2 SD); 26.0 cm of thoracic circumference (on –1 SD). His Apgar score at the first minute was 4, and 7 at the fifth. His blood type was B+. The physical examination revealed characteristic features of DS: oblique (upslanting) palpebral fissures; flat nasal bridge; open mouth; protruding tongue; transverse palmar creases; hypotonia; poor Moro reflex; hyperflexibility; short stature; loose skin on nape of neck; flat facial profile; epicanthic folds; short broad hands; clinodactyly of fifth finger; gap between the first and second toes. The chromosomal analysis was undertaken and in a few days the full trisomy of chromosome 21 was confirmed. Echocardiography and screening for inborn errors of metabolism, both with normal results. He developed transient neonatal tachypnea and jaundice, reaching 13.7 mg/dL of total serum bilirubin (TB), mainly of indirect type (IB=13.0 mg/dL). Phototherapy was accomplished and TB fell to 6.8 mg/dL in a few days (IB=6.2 mg/dL). Cranial ultrasonography and computed tomography (CT scan) undertaken in the first week of life exhibited moderate increase of both lateral ventricles, especially in the posterior regions (occipital horns).

At 20 days after delivery he was discharged from the hospital and a close follow-up started. At 8 weeks of life the head circumference reached 37.0 cm (on +2 SD) and the anterior fontanelle became enlarged and a little bulgy. The patient seemed otherwise healthy, without symptoms of intracranial hypertension like vomiting or drowsiness. At that time a new cranial CT scan confirmed an additional increase not only of the lateral ventricles but also of the third one. The patient was then successfully submitted to VPS, with an immediate normalization of the fontanelle's aspect. Five days after that he was discharged from the hospital.

The child is 1.5 years-old at present and has been regularly accompanied. His head circumference is enlarging in the normal range, and his development is considered adequate to the expected for those affected by the syndrome. Except for mental retardation and muscular hypotonia, both normal in DS, there is no other neurological perturbation. The patient was evaluated for the possibility of malformations in other organs (heart, gastrointestinal tract) but no abnormality was found.

The family was refered to genetic counselling and the mother is now pregnant again, with normal development until the present.

DISCUSSION

DS (trisomy of chromosome 21) is the most common and best known of all malformation syndromes[6]. The birth prevalence of trisomy 21 is usually stated to be 1/650 live births, but is known to vary in different populations from 1/600 to 1/1.200 live births[7]. Although the syndrome occurs in offspring of mothers of all ages, the risk increases with maternal age[1].

In approximately 95% of all cases the syndrome results from nondisjunction (full trisomy) that may occur during the first or the second meiotic division in either female or male parent. Unbalanced translocation may be the cause in 3% to 4% of all cases, either arising *de novo* or being transmitted from the parents[8]. Detectable mosaicism is found in approximately 1% to 2% of DS cases[8]. The diagnosis is clinically suspected due to the dysmorphic features (phenotype), which are distinctive. Conditions that are clinically confused with DS include congenital hypothyroidism, XXXXY, penta-X syndrome, and Zellweger syndrome. Therefore, chromosomal analysis is necessary to confirm all cases[6].

The recurrence risk of a DS pregnancy after the birth of an affected child is approximately 1% to 2%[9], and studies have shown that while the majority of second DS pregnancies may be the result of chance alone[10], cytogenetic analysis is necessary to exclude parental translocation or mosaicism[11]. In these cases, the parents have a higher recurrence risk[1,11].

DS patients are generally microcephalic and have characteristic facies, hypotonia, and short stature. Although this phenotype is easily recognized, mental retardation of varying degrees is the most consistent feature of DS, ranging from mild (Intelligence Quotient=IQ: 50-70) to moderate (IQ: 35-50), and only occasionally to severe (IQ: 20-35)[8]. Another common late-onset complication that occurs in the adult stage is Alzheimer disease. Congenital malformations are generally related to the heart (particularly endocardial cushion defects) and gastrointestinal tract (especially duodenal atresia and Hirschsprung disease)[1], while the presence of major brain abnormalities is extremely rare. In fact, Källén et al. studied 5581 cases of DS and found no association with anencephaly, spina bifida, cephalocele, or hydrocephalus[12].

Only a few cases of hydrocephalus associated with

DS were published in the literature[13-17]. Fabia and Drolette collected 4 cases in 2421 patients[14]. Jayaraman and col. published the case of a newborn who had hydrocephalus, aqueductal stenosis, and partial agenesis of the corpus callosum[15]. Zadikoff reported another patient born with hydrocephalus and a left posterior porencephalic cyst[16]. There is also a case of an infant with DS but whose hydrocephalus was attributed to congenital toxoplasmosis[17]. Differently from the last forementioned cases, our patient did not present other brain malformations or diseases except from hydrocephalus. It lacks an adequate explanation for the occurrence of hydrocephalus in DS patients besides just the coincidence. A current hypothesis proposes that some mothers of infants with DS have abnormal intake or metabolism of folate, or even mutations in folate genes, features that are also seen in neural-tube defects (NTD), including hydrocephalus[18]. Though a study had suggested a link between DS and NTD in some families[18], a recent population and familial survey did not find an association between families at risk of NTD and those at risk of DS[19].

Infantile hydrocephalus is characterized by the expansion of brain ventricles due to elevated intraventricular pressure and an increased amount of intraventricular CSF manifested during the first year of life[20]. There are several etiologies that can be grouped in four categories: prenatal (congenital), perinatal, postnatal, and unclassifiable[14]. In preterm newborns the main cause is intraventricular heamorrhage usually occuring in the first days of life[3,21], while in infants born at term the most common is brain maldevelopment[3].

The clinical manifestations depend on the age of the patient and speed of onset. In infants an excessive increase of head circumference, seizures, headache, drowsiness, vomiting, bulgy and enlarged fontanelles may take place. The diagnosis is commonly confirmed by cranial ultrasound, CT scan, or magnetic resonance imaging (MRI). Treatment is essentially surgical, and two main approaches are currently performed: the ventriculoperitoneal shunt and the endoscopic third-ventriculostomy (ETV), the latter possible if the third ventricle is also enlarged. In the present case we did not perform the ETV because an appropriate endoscopic probe for infants was not available. In the past the head binding was used[16], but nowadays more efficient surgical techniques that ameliorate the prognosis are accomplished[2].

The role of folic acid in preventing NTD is clearly established[22]. In the present case the mother was advised to take 5 mg of folic acid supplement daily before and during the first trimester of the next pregnancies, a recommendation adopted by the couple in the current one.

In summary, DS is a common genetic disorder which is rarely associated with congenital hydrocephalus. There is no proved explanation for this association, and the management of the hydrocephalus in such situation is not different from the usual.

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