ISOLATED HEMIHYPERTROPHY IN CHILD

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ABSTRACT

Hemihypertrophy or hemihyperplasia is a rare congenital condition, whose incidence is difficult to estimate, due to the fact that asymmetry is very mild, therefore remaining undiagnosed. Hemihyperplasia can be isolated or associated to certain genetic syndromes. We present the case of a 6-months-old female infant, in whom, during the neonatal period, was raised the suspicion of a congenital hemihypertrophy. She was admitted in our clinic due to the presence of a facial asymmetry. The clinical exam revealed also, besides the hemihyperplasia of the right hemiface more obvious at the level of the forehead, a hypertrophy of the right superior and inferior limbs. The laboratory tests identified a mild anemia, increased levels of transaminases and alfa-fetoprotein. The abdominal ultrasound revealed a mild hepatomegaly and the transfontanellar one discrete ventriculomegaly and frontal atrophy. The genetic test was negative, therefore the final diagnosis was of isolated hemihypertrophy. The further re-evaluations showed a decreasing level of alfa-fetoprotein, without other additional pathological elements. The particularity of the case consists in diagnosing an isolated hemohypertrophy in a 6-month-old female infant, with negative genetic test, in whom it was observed at the moment of birth a mild facial asymmetry, with afterwards favorable evolution, with progressive decrease of the alfa-fetoprotein level and normal abdominal ultrasound.

Keywords: isolated hemihypertrophy, isolated hemihyperplasia, infant, alfa-fetoprotein

INTRODUCTION

Hemihypertrophy represents a rare genetic condition characterized by the excessive growth of one half of the body completely or only of an area of the body, such as face, abdomen or one of the limbs (1-3). This excessive growth can be the result of the soft tissues hyperplasia, bones or both (4), leading to a body asymmetry that can be observed during inspections as part of any clinical exam performed routinely, by both the pediatrician and the general practitioner. Hemihypertrophy, or newly called hemihyperplasia can be isolated or it can be a part of certain genetic syndromes, such as: Beckwith-Wiedemann, Proteus, Russel-Silver, type 1 neurofibromatosis or Klippel-Trénaunay-Weber syndrome (2,3). If a hemihypertrphy is suspected, the pediatrician must solicit a genetic consult in order to exclude one of the above mentioned syndrome. Each of them presents associated with hemihyperplasia, other well-defined features that together will provide a different prognosis for every genetic syndrome. Therefore, the mortality rate, but also the monitoring protocols are different for each of these pathologies (5). Genetic tests with the assessment of karyotype will differentiate these syndromes by isolated hemihyperplasia.

Isolated hemihyperplasia is most of the times underdiagnosed, due to the fact that many forms are mild and the hemihypertrophy is difficult to identify, thus these cases will not be noticed. Therefore, the incidence of this condition is very difficult to estimate in the general population. Nevertheless, the estimated prevalence of isolated hemihypertrophy is of approximately 1 in 13,200 live newborns (6).

Isolated hemihypertrophy, especially of one limb, inferior or superior must always be differentiated by hemiatrophy that is characterized by a decrease in size and volume of certain cells that be-

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long to a certain tissue as a consequence of several conditions, such as: ischemia, hormonal modifications or malnutrition (7). The patients diagnosed with hemihypertrophy present an increased risk for developing tumors during their lives, especially embryonal ones (4). Therefore, the management guides for a case of hemihypertrophy recommends the following: any child suspected with isolated hemihypertrophy must be referred for a genetic consult, performing an abdominal ultrasound every 3 months until the age of 7 years, determining the level of alfa-fetoprotein every 3 months until the age of 4 years, but also training the care-givers/parents to examine the child's abdomen daily or as often as possible.

CASE PRESENTATION

We present the case of a 6-months-old female infant that was admitted in our clinic due to the presence of a facial asymmetry. The family history did not reveal any significant pathological elements. The personal history underlined the fact that the patient came from a second pregnancy, affirmatively physiological and monitored. She was born at term, without ante- or perinatal complications, with a BW of 3,400 grams and unknown APGAR score, being noticed a mild facial asymmetry after birth, which initially was interpreted in context of labor, but anyway, a further pediatric consult was recommended. The care-givers omitted these recommendation, therefore in the context of a respiratory intercurrence, the general practitioner noticed, at the clinical exam, the persistence of the facial asymmetry, associated with the hypertrophy of the superior and inferior right limbs, referring the patient for admission in our clinic in order to perform supplementary investigations.

The pathological elements identified at the clinical exam performed at the moment of admission were the following: mild facial asymmetry with the hypertrophy of the right hemiface, more obvious at the level of the forehead, the hypertrophy of the right superior and inferior limbs, pale skin, distended abdomen, liver at 1 cm under the right costal rib. The CBC count performed on the day of admission pointed out microcytic hypochromic anemia (Hemoglobin 11.6 g/dl, Hematocrit 33.5%, medium erythrocyte volume 77.5 fL). We performed biochemical tests that showed increased levels of transaminases (aspartate aminotransferase 40.8 U/L, alanine aminotransferase 33.7 U/L), without other pathological modifications. The serology for TORCH (T-Toxoplasma, O-Others, R-Rubella, C-Cytomegalovirus, H-Herpes) syndrome was also negative. The abdominal ultrasound revealed mild hepatomegaly (78.4/30.4 mm) and the transfontanellar one showed discrete ventriculomegaly (biventricular diameter 38.4 mm) and also mild frontal atrophy. Due to the identification of right hemihypertrophy, we raised the suspicion of Beckwith-Wiedemann syndrome. Thus, we determined the level of alfa-fetoprotein that was much above the superior normal limit, namely 30.7 UI/ml (normal values <6.7 UI/nl) and we solicited the genetic consult in order to perform the karyotype from the peripheral blood. The cytogenetic tests did not point out any numerical or structural chromosomal anomalies, the karyotype being 46,XX. Therefore, we established the diagnosis of isolated hemihypertrophy, discharging the patient with the following recommendations: liver protecting medications for a month, clinical and paraclinical with abdominal ultrasound after approximately 3 months.

The laboratory tests, after approximately 3 months, revealed a mildly increased level of aspartate aminotransferase (AST 36 U/l), without other pathological modifications. The determination of alfa-fetoprotein pointed out its decrease of approximately half of the initial value, namely 15.9 UI/ml. The abdominal ultrasound was without pathological modifications. Due to the decrease of alfa-fetoprotein and to the lack of pathological modifications at abdominal ultrasound, we recommended the patient's re-evaluation after approximately 6 months.

Therefore, at the age of 1 year and 4 months, after approximately 6 months from the previous evaluation, the patient was admitted again in our clinic in order to repeat the laboratory tests and to perform an abdominal ultrasound. The clinical exam did not point out any additional pathological elements in comparison to the previous one. The CBC count performed at the moment of admission revealed microcytic hypochromic anemia (hemoglobin 9.4 g/dl, hematocrit 30.3%, medium erythrocyte volume 62.7 fL, medium erythrocyte hemoglobin 19.5 pg). The biochemical tests showed the persistence of the mildly increased level of aspartate aminotransferase (AST 37.3 U/L), but also a decreased level of iron (Iron 3.66 µmol/l). Determining the level of alfa-fetoprotein, we noticed that it continued to decrease, the value being 7.8 UI/ml, approximately a half of the previous value. The abdominal ultrasound performed at this age was without pathological modifications, with normal sizes of the intraabdominal organs for the actual age. Due to iron deficiency anemia revealed by the labo-

ratory tests, we recommended a diet rich in iron (yolk, chicken meat, chicken liver, fresh fruits and vegetables, and oral iron supplementation for 6-8 weeks, with afterwards CBC count repetition. Also, in the context of the underlying pathology, we recommended the dosing of alfa-fetoprotein and an abdominal ultrasound after approximately 6 months.

The particularity of the case consists in diagnosing an isolated hemihypertrophy in a 6-months-old female infant, with negative genetic test, in whom it was observed, at the moment of birth, a mild facial asymmetry, with afterwards favorable evolution, with progressive decrease of the alfa-fetoprotein level and normal abdominal ultrasound.

DISCUSSIONS

Hemihyperplasia, or previously called hemihypertrophy, is a genetic rare condition, whose incidence is difficult to estimate in the general population, being most of the times underdiagnosed. The specialty literature reports a prevalence of hemihypertrophy of approximately 1 in 13,200 live newborns (6), but this estimation is not accurate, because it includes both the isolated cases of hemihypertrophy and those associated to different genetic syndromes (5). Thus, a large study, performed on 860,000 cases, identified a number of 10 cases of congenital body asymmetry, suggesting a prevalence of approximately 1 in 86,000 live newborns (8). Nevertheless, of the 10 patients identified with hemihypertrophy, some of them presented also other suggestive features for a genetic syndrome, such as Beckiwth-Wiedemann (8). Another study performed on 14,430 newborns in a hospital from Tokyo identified a single case of hemihyperplasia (9). Due to the fact that these are the only studies performed in the literature regarding this topic, the real prevalence of this condition in general population remains difficult to estimate (5). Most of the cases of genetic syndromes that include hemihypertrophy as feature are sporadic and with decreased recurrence risk (5). Nevertheless, there were described cases of Beckwith-Wiedemann syndrome in the specialty literature with familial aggregation (10). As in the case of Beckwith-Wiedemann syndrome, isolated hemihypertrophy also appears most often sporadically, but Heilstedt reported 4 members of a family diagnosed with isolated hemihypertrophy (5). In the case of the patient presented above, we did not identify other family members afflicted by this condition.

The highest risk in case of patients diagnosed with isolated hemihyperplasia, with a major impact on the mortality and morbidity rates, is represented by tumor development during life. This fact is based on multiple case presentations published in the specialty literature, but also on the prospective study performed by Hoyme on 160 children with isolated hemihypertrophy, who, during 10 years, identified 10 tumors in 9 individuals (11). Of the 10 diagnosed neoplastic conditions, 6 were Wilms tumors, a hepatoblastoma, 2 adrenal carcinomas and a leiomyosarcoma of the short bowel, leading to an incidence of tumor development of 5.9% (11). In a review on the same topic, Lapunzina noticed that tumors that appear in case of patients with isolated hemihypertrophy are similar to those identified in case of Beckwith-Wiedemann syndrome, but not identical (12). Therefore, even though 94% of the tumors are intraabdominal, like in the cases of patients diagnosed with Beckwith-Wiedemann syndrome, in patients with isolated hemohyperplasia, extra-abdominal tumors can also appear, affecting the brain, testis, lung, uterus and bone marrow (12). In the case presented above, we did not identify, until the present age, any type of tumor.

There are also other non-neoplastic pathologies that can appear in case of patients with isolated hemihypertrophy, such as: carpal tunnel syndrome (13), hemihypertrichosis (14), focal nodular hyperplasia of liver (15), upper airways obstruction (16), hearing loss or deafness (16), Lenarduzzi-Cachi-Richi disease or sponge-like kidney (17). We did not identify any of the above mentioned associations in case of our patient. Nevertheless, obstruction of upper airways associated with hearing loss or deafness is described in case of patients with facial hemihypertrophy. Our patient even though presented with right hemiface hypertrophy, did not develop until the present moment any of these two complications.

CONCLUSIONS

Isolated hemihypertrophy must be suspected in case of identifing a hypertrophy of one side of the body, completely or only an area of the body, such as the face, abdomen or limbs. The genetic consult is mandatory in order to exclude the genetic syndromes that can associate, in their clinical picture, hemihypertrophy. The patients diagnosed with isolated hemihyperplasia must be submitted periodically to an abdominal ultrasound and alfa-fetoprotein determination in order to early diagnose a potential tumor.

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