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CLINICAL CASE

Multifocal hepatic hemangioendothelioma

Hemangioendotelioma hepático infantil multifocal

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Abstract

Introduction: Hepatic hemangioendothelioma is a rare benign tumor in children, which frequently occurs in the first year of life. The clinical presentation is variable and the diagnosis is based on clinical suspicion, and laboratory and imaging studies. The objective was to describe a case of multifocal hepatic hemangioendothelioma. **Clinical report:** 3-month-old girl who presented hepatomegaly without elements of hepatic or heart failure. Abdominal ultrasound and CT scan were used to diagnose hepatic hemangioendothelioma, which was confirmed by CT abdominal angiography. The patient received glucocorticoid treatment at high doses for a prolonged period. A year and a half after treatment, there was evidence of tumor remission. She had side effects from the established treatment. **Conclusions:** In asymptomatic patients with isolated hepatomegaly, it should be considered a probable tumor pathology, considering the clinic and imaging studies. Possible complications and treatments risks must always be assessed. In this case, the tumor extension and its probable complications justified the use of prolonged corticosteroid therapy at high doses despite its adverse effects.

Keywords:
Hepatomegaly;
hemangioendothelioma;
child;
liver tumor

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Introduction

Infantile hepatic hemangioendothelioma (IHH) is a vascular tumor of mesenchymal origin, histologically benign[1,2]. This is a rare pathology in children, its incidence is higher in the first two years of life, most of them (more than 80%) occur before 6 months of age[1,3,4]. The multifocal presentation is observed in 45% of the cases[1].

Clinical presentation varies from asymptomatic hepatomegaly to heart failure, the latter has a high mortality[1,4,5]. It may appear with thrombocytopenia due to splenic sequestration and liver failure. Hemangiomas can be associated with other areas, especially skin[1].

Diagnosis is made based on clinical suspicion, laboratory, and imaging studies[2]. Histological confirmation is not always performed given the risks of the procedure[4].

In a high percentage of cases, it returns spontaneously around 12-18 months after the diagnosis has been made, without the need for treatment[1,2]. If required, there are different medical or interventional treatments depending on the tumor, including the use of corticosteroids, propranolol, chemotherapy, arterial embolization, partial hepatectomy, and liver transplantation[2-5,7-9].

The objective of this article is to describe the clinical and imaging presentation, therapeutic options, and evolution of a multifocal IHH case in a 3-month-old infant.

Clinical case

3-month-old female newborn, coming from a rural area in Uruguay, is admitted to the *Hospital Regional de Tacuarembó*, due to poor weight gain.

The seventh daughter of pregnancy without follow-up. Vaginal delivery, 40 weeks of estimated gestational age, birth weight 3220 g, appropriate for gestational age, height 49 cm, head circumference 34 cm, vigorous. Normal neonatal examination, discharge weight 3000 g. She was exclusively breastfed before turning one month old, then continued with whole cow's milk without adding sugar. The patient doesn't get vitamin D. Normal psychomotor development. Updated immunizations. Negative maternal screening for syphilis, hepatitis B virus, and human immunodeficiency virus (HIV).

Weight at admission 4480 g (lower than 3rd percentile), height 58 cm (15th percentile). Features in the examination: vigil, reactive, without fever or breathing problems. Skin and mucous membranes without paleness or lesions. Diminished fatty layer. At abdominal level, upper liver limit in 5th right intercostal space, lower edge 4 cm from the rib rim of normal consistency, painless. No splenomegaly. There are no other abdominal or lymph node tumors. Normal pleuropulmonary and cardiovascular examination.

Liver tests (serum aminotransferase levels, bilirubin, alkaline phosphatase, gamma-glutamyl transferase), and coagulation tests (prothrombin time, partial thromboplastin time) were requested and their results were normal. Abdominal ultrasound showed enlarged liver, heterogeneous echostructure with small hypoechoic diffuse images in right and left lobes.

Abdominal and pelvic CT scan with and without contrast (figure 1): marked heterogeneous density hepatomegaly due to multiple hypodense nodular lesions covering both lobes between 2 and 18 mm in size. After administering intravenous contrast medium, enhancing in the arterial phase and persisting with greater density than the hepatic parenchyma in the portal phase. There were no evidence of adenomegaly, abdominal or pelvic tumors. Rest of the study was normal.

It was suggested probable multifocal IHH, abdominal magnetic resonance angiography (MRA) was requested that showed diffuse hepatomegaly, the hepatic parenchyma is replaced by small rounded focal lesions between 5 and 11 mm in size and in large numbers; they are well defined, hypointense on T1, hyperintense on T2, and with intense enhancement with gadolinium administration, with centripetal filling. (Figure 2) The images are compatible with multifocal IHH.

It was decided to start the treatment with corticosteroids (prednisolone) at a dose of 3 mg/kg/day orally for 6 months, with a subsequent gradual decrease in dose, continuing each year with oral hydrocortisone at physiological doses. Clinical outpatient follow-up (oncologist, cardiologist, and pediatrician) and ultrasound follow-up were performed every three months. The patient was monitored with new MRA one and a half years after treatment, showing remission of liver lesions (Figure 3). She presented complications due to corticotherapy in high doses for a long time: adrenal insufficiency, Cushing's syndrome, and short stature. There were no other complications.

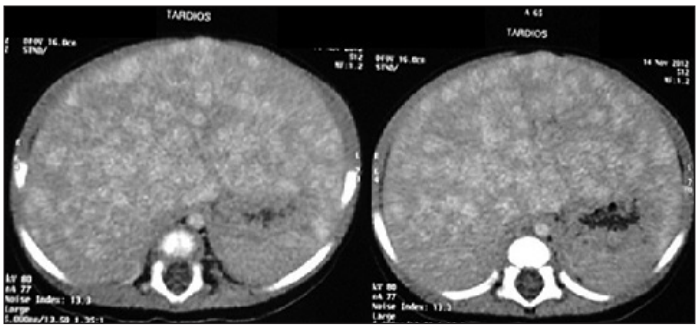

Figure 1. Abdominal Tomography: multiple hypodense nodules throughout the hepatic parenchyma.

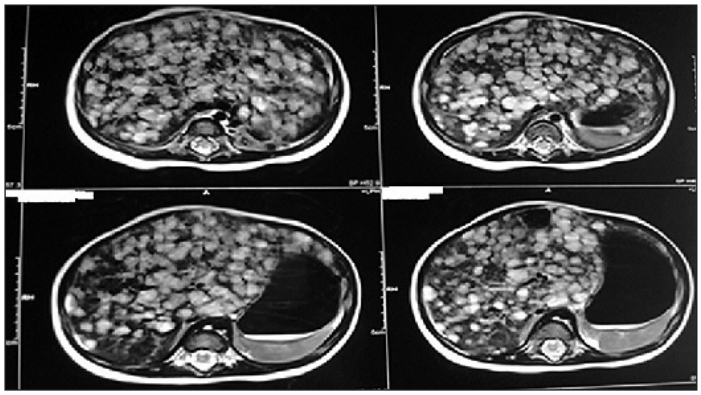

Figure 2. Abdominal Resonance with angiography: Hepatomegaly and focal lesions that enhance with gadolinium.

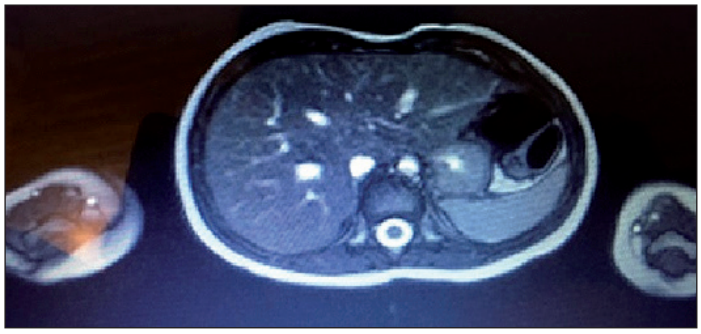

Figure 3. Abdominal Resonance with angiography 18 months after treatment. Decrease in the number and size of injuries.

Discussion

Malnutrition in the first trimester of the patient's life, which motivated hospital admission, was classified as exogenous because she received hypocaloric food and the weight curve improved with the correction of dietary intake. This made it possible to avoid the possibility of a pathology that associated growth failure with the hepatomegaly found in the physical examination. In this case, the hepatomegaly was painless and of normal consistency and there were no alterations in the physical examination or other associated symptoms. In the case of an infant with isolated hepatomegaly, the causes may be diverse: inflammation (infections, toxins), deposition (glycogenosis, Gaucher disease, Niemann-Pick disease, alpha 1 antitrypsin deficiency), infiltration (benign and malignant liver tumors, extrahepatic metastases), vascular congestion (veno-occlusive disease, Budd-Chiari syndrome, congestive heart failure), and biliary obstruction (biliary atresia, choledochal cyst)[10]. Due to the frequency and severity, the first etiologies to rule out are infectious diseases, metabolic deposition diseases, and cystic fibrosis[11].

This patient presented asymptomatic and isolated hepatomegaly, without elements of lesion or hepatic dysfunction. Based on serology for hepatitis B virus and HIV negative and normal neonatal screening, in the absence of clinical elements that would allow suspicion of other pathologies, it was a priority to rule out liver tumors. The most common liver tumors are metastases of neuroblastoma or nephroblastoma[1]. Primary tumors are less frequent, the most common are malignant tumors (60%) such as hepatoblastoma and hepatocellular carcinoma. Benign tumors such as hemangioendothelioma are rare and are diagnosed based on clinical features, analytical and imaging studies[2,11].

In this patient, the clinical findings that suggested the diagnosis of IHH are age (under 6 months), female sex, and presentation as isolated hepatomegaly[1-4]. 50% of cases of these tumors occur this way[3]. It is important to point out that other initial manifestations of this tumor are congestive heart failure, with a 70% mortality rate, thrombocytopenia due to splenic sequestration and, more rarely, liver failure[1]. Since these are also possible complications that emerge in evolution, they must be evaluated with a correct follow-up, for identification and eventual opportune treatment[2]. This patient did not present these manifestations either at the beginning or in the evolution.

Imaging studies are important in the evaluation of these types of cases. Abdominal ultrasound is a useful tool, which is the first imaging study to perform in case of any suspicion of liver tumor, given the low cost, safety, and good performance. However, in many cases, other radiological studies are needed, such as CT scan and MRA, to provide other more specific findings that help in the diagnostic orientation[12]. The patient, in this case, presented the characteristic images that allowed the IHH diagnosis. Although with any of the imaging techniques is possible to diagnose, the highest performance is the MRA. Most cases do not require histological confirmation[2,4]. In this patient, it was decided not to perform liver biopsy due to the high risk of bleeding[4] and the clear imaging findings.

There are no standardized international or national protocols for the treatment of this type of tumor[8]. Very few patients have been reported in the literature[3,9]. Therapeutic options depend on the characteristics of the tumor, whether it is isolated or multifocal, and the presence or absence of symptoms and/or complications[1-3,13]. Despite the fact that a high percentage of IHH cases spontaneously revert between 12 and 18 months after diagnosis[1], in this patient it was decided to initiate treatment due to the diffuse involvement of the liver parenchyma. In these cases, there is a risk that the lesions will quickly become symptomatic with the risk of complications that can cause death[2,4]. Most authors recommend corticotherapy in the proliferative phase, at doses of 2 to 3 mg/kg/day for around 5

months[4,5,14]. In this case, 6 months of full-dose prednisolone was administered and then the dose was gradually lowered until the year of treatment was completed. 30% have a total response, 40% a partial response, requiring additional treatment, and 30% do not respond[4]. In this patient, the response was very favorable, receiving only corticosteroids. Other therapeutic alternatives such as the use of propranolol, INF alpha, and vincristine[3,4,7,8,14] were proposed. When analyzing the risk-benefit balance of each of these treatments, it was considered that the best for this patient was the use of corticosteroids.

Interventional options include hepatic artery embolization, partial hepatectomy, and liver transplantation[3,4]. These options were not considered as first choice in this patient due to her age, the clinical characteristics of the tumor (multifocal), and the low experience in our sphere in the management of this type of tumor. In this case, surgical treatment was not considered, it should be considered in some isolated tumors[1,3].

The need to monitor and follow-up the possible complications of the tumor and those deriving from the treatment is evident. In the revised bibliography, although diagnostic and therapeutic algorithms are suggested[3,7,15], the form of follow-up and control of these patients is not protocolled. In this case, it was carried out quarterly evaluating clinical, analytical, and imaging studies. Monitoring the adverse effects of long-term high-dose corticotherapy was important. The intervention of a multidisciplinary team was essential to achieve better results[3,14].

Conclusions

The clinic and imaging allowed the diagnosis of a rare liver tumor, benign but that may have very severe complications. We should always suspect possible complications with the risks of the treatments. In this case, complete remission of the tumor would justify complications caused by long-term high-dose corticotherapy.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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