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CLINICAL CASE

Importance of prenatally diagnosed portosystemic vascular shunts in clinical outcomes

Importancia de las derivaciones vasculares portosistémicas de diagnóstico prenatal en la evolución clínica

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What do we know about the subject matter of this study?

Portosystemic shunts are rare malformations that are mostly asymptomatic and can be associated with different syndromes and malformations of other systems. When there are symptoms, they are non-specific, difficulting and delaying their diagnosis and management.

What does this study contribute to what is already known?

We emphasize that prenatal suspicion allows early study and the multidisciplinary management required by the patient. In addition, we mention the possible clinical manifestations in the pediatric age, which can guide us to establish the diagnostic suspicion.

Abstract

Portosystemic venous shunts (PSVS) are malformations that result from abnormal communications between the portal and hepatic veins or inferior vena cava. Prenatal diagnosis is made by evaluating the fetal venous circulation and it is classified as intrahepatic and extrahepatic, with different evolution and complications. **Objective**: To report two cases of prenatal diagnosis of portosystemic vascular shunts and review the importance of this rare pathology in its neonatal and pediatric evolution. **Clinical Cases**: Case 1: pregnancy with fetal growth restriction, 2nd percentile, polyhydramnios, without fetal malformations and abnormal patterns on fetal Doppler. Abnormal blood flow through the ductus venous and abnormal venous communication in the liver were identified. Normal genetic study. Male newborn (NB) delivered at 36 weeks, because of severe fetal growth restriction, by emergency cesarean section. He evolved asymptomatic, with normal liver function, and did not continue follow-up. Case 2: pregnancy with fetal growth restriction < percentile 1. Agenesis of the ductus venous and abnormal communication between the portal vein and the left suprahepatic vein were identified with no other malformations or signs of heart failure. Severe SGA newborn was de-

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livered by induction of labor at 35 weeks. He evolved asymptomatic. Normal complementary study. A home check-up at 2 months showed persistent vascular anomaly without systemic involvement. **Conclusions**: Even though in the cases presented there were no neonatal complications, this kind of malformations require a high index of suspicion in cases with fetal growth restriction, as well as a long-term multidisciplinary follow-up.

Introduction

Portosystemic shunts are rare malformations with an overall prevalence estimated at 1:30000 to 1:50000 newborns. They result from abnormal communications between the portal veins and hepatic veins, or the inferior vena cava system caused by a lack of complete involution of the vitelline veins during fetal development[1,2].

They can be extrahepatic, which are classified into two types according to the presence or absence of intrahepatic portal flow, with intrahepatic shunts as the most frequent which are classified into 5 types (Figures 1,2, and 3)[1,3-5].

Under normal conditions, about 30% of the umbilical venous flow is diverted to the ductus venosus and the rest is directed to the liver, in order to carry highly oxygenated blood contributing to normal fetal development[6-9].

In the context of fetal growth restriction, flow through the ductus venosus may increase to ensure perfusion of vital organs with highly oxygenated blood, decreasing blood flow to the liver[10]. In the presence of an intrahepatic portosystemic shunt, the distribution of nutrient- and oxygen-rich blood flow may be altered, creating a kind of flow sequestration compromising the blood supply mainly to the left lobe of the liver and the blood flow through the ductus venosus, thus affecting normal fetal development and growth, and therefore constituting a possible explanation for the abnormalities detected in the ductus venosus flow on Doppler ultrasound evaluation[6,11].

In addition to fetal growth restriction, which may be present in 15-50% of these cases, the natural history of extrahepatic portosystemic shunts involves complications such as hepatic encephalopathy, pulmonary hypertension, and hepatopulmonary syndrome[1,5].

The objective of this study is to report two cases of prenatal diagnosis of portosystemic shunts and to review the importance of this rare pathology in its neonatal and pediatric evolution.

Clinical Cases

Case 1

36-week preterm newborn, son of a 34-year-old woman, referred to the Maternal-Fetal Medicine Unit of the *Hospital San Borja Arriarán* at 27+4 weeks for evaluation due to obstetric history of recurrent miscarriage. An ultrasound showed severe fetal growth restriction with estimated fetal weight in the 2nd percentile, polyhydramnios, without fetal malformations. In the Doppler ultrasound evaluation, the pulsatility index of the uterine arteries and the umbilical artery were in normal range, but the middle cerebral artery was vasodilated and there was also a ductus venosus with a reverse wave (Figure 4). When evaluating the fetal venous circulation, in the intra-abdominal trajectory of the umbilical vein, an additional accessory vessel was observed with direction to the left (anterolateral wall of the stomach) that after making a "loop" continues through the anterior wall of the stomach towards the inferior vena cava at the level of the entrance to the right atrium (Figure 5). Evaluation of fetal cardiac structure and function was normal. The patient was hospitalized for administration of prenatal corticosteroids, etiological study, and strict ultrasonographic follow-up. Amniocentesis was performed for genetic study (FISH for trisomies 13,18, and 21) in amniotic fluid which was normal, and congenital infections were ruled out. At follow-up, the fetal weight estimate remained below the 3rd percentile, the middle cerebral artery Doppler ultrasound normalized and the ductus venosus persisted with an intermittent reverse wave. At 31 weeks, it was decided to continue the fo-

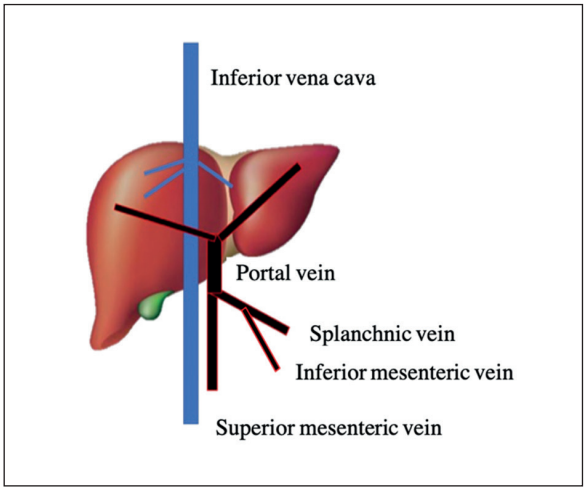

Figure 1. Normal hepatic portal system:

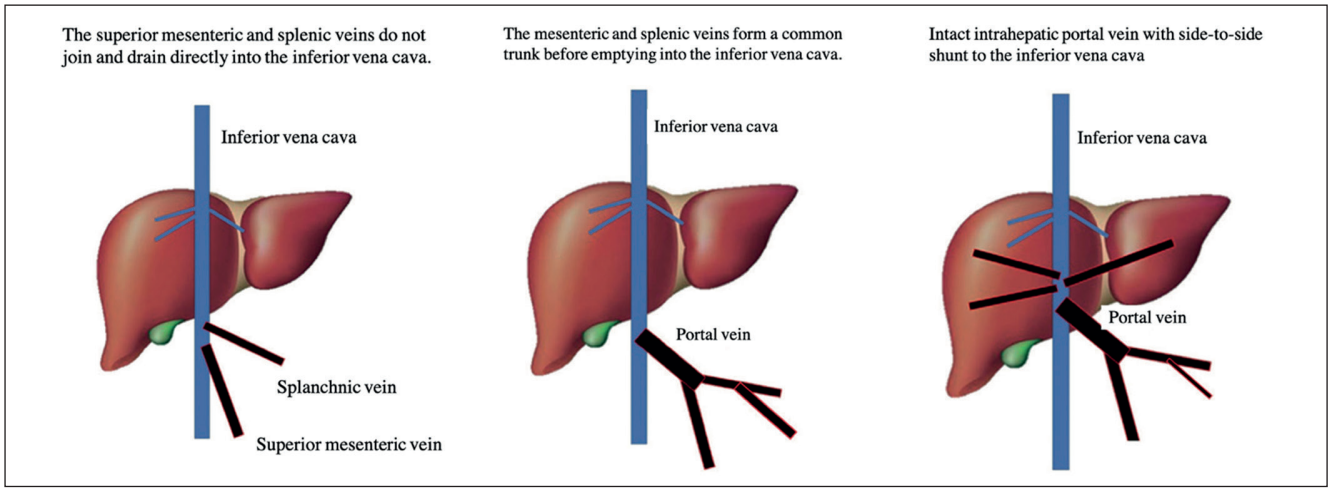

Figure 2. Extrahepatic portosystemic shunts:

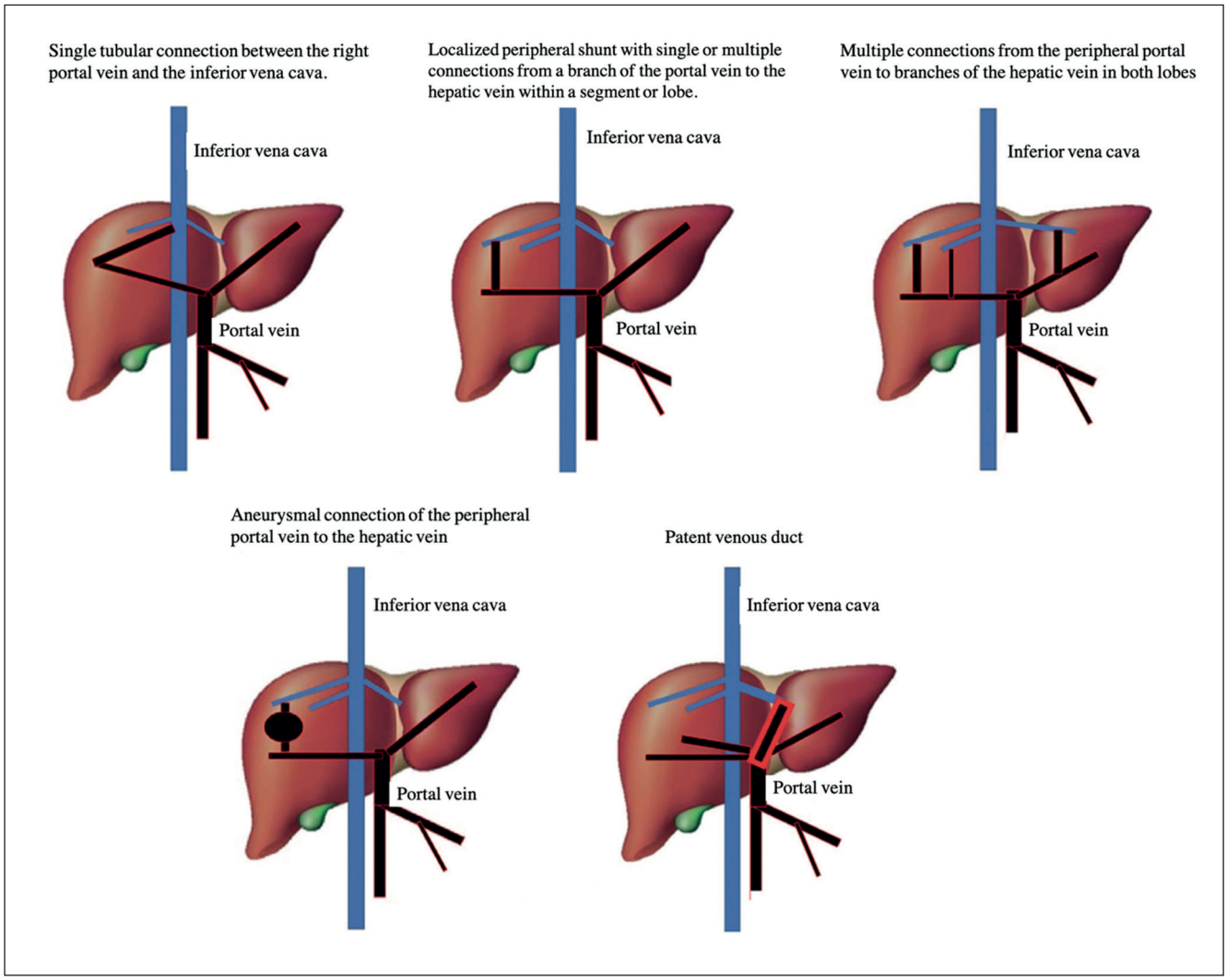

Figure 3. Intrahepatic portosystemic shunts:

llow-up with biweekly outpatient check-ups, in which the previously described ultrasound findings were maintained. Due to fetal growth restriction below the 3rd percentile, it was decided to interrupt the pregnancy by induction at 36+6 weeks, but due to an altered intrapartum fetal monitoring, an emergency cesarean section was performed. The newborn was male, birth weight 2,190 grams (percentile 3), birth length 42 cm, head circumference 32.5 cm, and Apgar score 8-8.

In the postnatal evaluation, an abdominal ultrasound showed an aberrant vessel in the left hepatic lobe communicating the left portal vein with a branch of the suprahepatic vein, with normal main portal vein, which confirmed the diagnosis of an intrahepatic portosystemic shunt. The complementary study with liver function tests, ammonia levels, echocardiography, and cerebral ultrasound was normal. The newborn was evaluated by the pediatric gastroenterology team, who indicated an ultrasound check-up in 6 months to evaluate the persistence of this anomalous venous communication or its possible spontaneous closure. Given his favorable clinical evolution, with good enteral tolerance and weight gain, the newborn was discharged without complications. He attended the first outpatient check-up without undergoing the requested abdominal ultrasound and then did not attend any more check-ups, losing the follow-up.

Case 2

35-week preterm newborn of 35 weeks, daughter of a 26-year-old woman who was referred to the Maternal Fetal Medicine Unit of the *Hospital Clínico San Borja Arriarán* at 33+3 weeks due to fetal growth restriction. On ultrasound, she presented fetal growth restriction below the 1st percentile, with normal pulsatility index in the umbilical artery and signs of vasodilatation in the middle cerebral artery. However, the ductus venosus could not be identified and an anomalous umbilical vein was observed, which also presented an anomalous vessel directed towards the left hepatic lobe and then towards the right to flow into the infundibulum of the inferior vena cava arrival to the right atrium (Figure 6). No other malformations were identified on directed anatomical evaluation and no signs of heart failure were identified. The pregnant woman was hospitalized for corticosteroid administration and strict ultrasonographic follow-up. Ultrasound evaluation at 34+6 weeks showed vasodilatation of the middle cerebral artery with an altered cerebroplacental ratio. It was indicated to interrupt the pregnancy at 35 weeks, and labor induction was performed, resulting in a vaginal delivery without incidents. The newborn was female, birth weight 1,660 g (0 percentile), birth length 41 cm, and head circumference 31 cm.

In the postnatal evaluation, an abdominal ultrasound was performed, which confirmed the agenesis of the ductus venosus and evidenced the presence of a communication between the left branch of the portal vein and the left suprahepatic vein, with both vessels dilated and a thick, high-caliber vessel shunt. This image was found in the left lobe of the liver, consistent with an intrahepatic portosystemic shunt. The complementary study with liver function tests, ammonia levels, echocardiography, and cerebral MR angiography were normal. In addition, an abdominal CT angiography

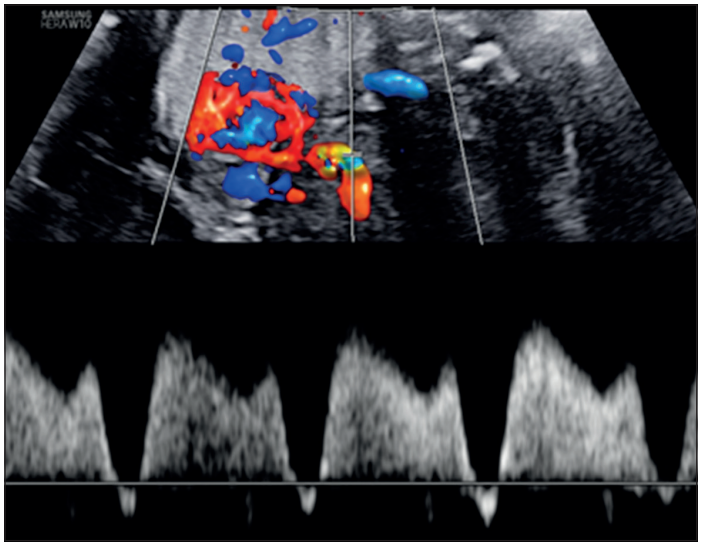

Figure 4. Ductus venosus with reverse wave. Constant antegrade flow is normally observed, without the reverse component seen in the a wave (during atrial contraction). In this case, the reverse wave in the ductus venosus is not secondary to hypoxia. The theory is that in the presence of this vascular malformation there would be a shunt flow diversion and less flow through the ductus venosus would produce an increase in return in the right atrium, producing a volume overload of it, generating retrograde flow towards the ductus venosus. in atrial contraction manifesting as a reverse wave.

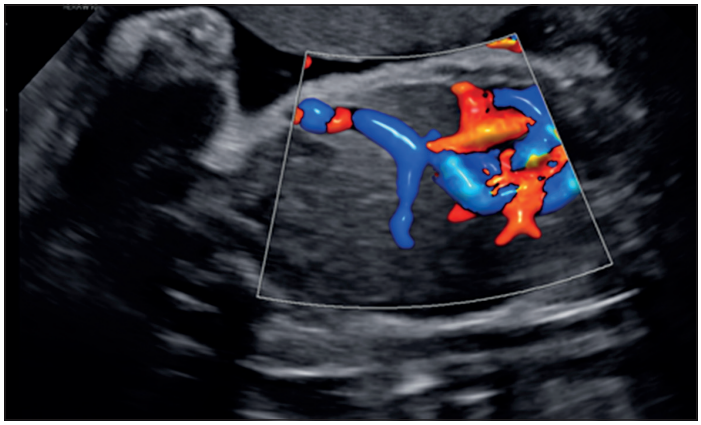

Figure 5. Additional accessory vein directed to the left (anterolateral wall of the stomach) that after making a "loop" continues along the anterior wall of the stomach towards the inferior vena cava at the level of the entrance to the right atrium.

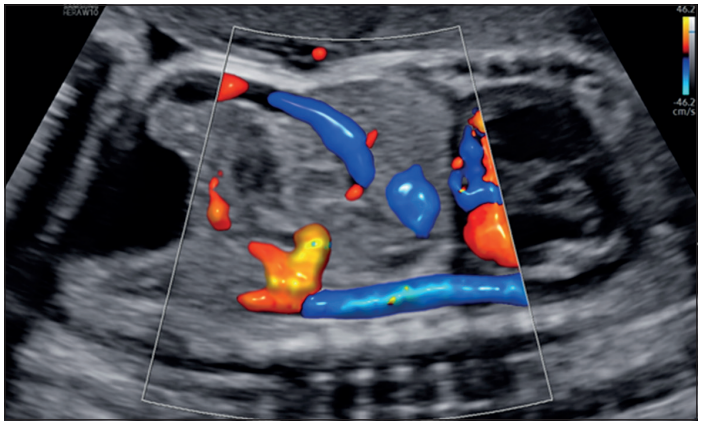

Figure 6. Umbilical vein with an anomalous course, which also presents an anomalous vessel directed towards the left hepatic lobe and then towards the right to empty into the infundibulum of the arrival of the inferior vena cava to the right atrium. (This image only shows the agenesis of the ductus venosus, the anomalous vessel does not appear).

was performed, which ruled out portal hypertension and reported a porto-suprahepatic veno-venous shunt. The pediatric gastroenterology team indicated ultrasound to evaluate the persistence of this anomalous venous communication or its possible spontaneous closure. Given the favorable evolution, the patient was discharged with outpatient check-ups in pediatric gastroenterology. In the outpatient follow-up, she remained asymptomatic, with normal liver function, and an ultrasound at 2 months of chronological age showed persistence of the porto-suprahepatic veno-venous shunt.

Discussion

The two cases presented were asymptomatic in the neonatal period and had no malformations or alterations detected, except for intrauterine growth restriction. It is important to know the associations and complications of this rare malformation, which requires follow-up evaluating spontaneous closure, the need for surgical closure, and hepatic complications[1-3,5].

Portosystemic shunts are rare, and their diagnosis is often made incidentally in prenatal ultrasound evaluations[2,3]. Intrahepatic shunts, as were the cases presented, are naturally smaller in size and blood flow and, therefore, are expected to have fewer complications and better chances of spontaneous closure, usually within 1 to 2 years[4]. However, complications such as cholestasis, hypoglycemia, and persistence of the shunt may occur, justifying follow-up[12]. Multisystem effects of portal venous blood shunting around the liver can lead to encephalopathy, hepatopulmonary syndrome, and pulmonary hypertension[13].

In a retrospective cohort of 19 fetuses with portosystemic shunts, the diagnosis was made at 33.8 ± .5 (range 25-40) weeks of gestational age. 63% had a single shunt of the left branch of the portal vein and the concomitant findings coincided with those reported in the literature such as fetal growth restriction in 47% and congenital heart disease in 21% of cases[4]. Other congenital malformations are more frequently found in patients with extrahepatic portosystemic shunts, with cardiac malformations being more frequent[5]. Their association with Turner syndrome, Down syndrome, Noonan syndrome, and other RASopathies has also been reported[2,12].

In a cohort of 16 patients with prenatal diagnosis of this pathology and symptoms in the neonatal period, all presented jaundice, only one had transient acholic stools, and two had upper gastrointestinal bleeding[14]. In addition, neonatal seizures were observed in two patients who responded to anticonvulsant therapy. 12 patients (75 %) presented congenital anomalies such as cardiopathies, abdominal malformations, genetic syndromes, orthopedic anomalies, urogenital malformations, and cerebrovascular malformations. Laboratory alterations included hyperammonemia, neonatal cholestasis, elevated liver enzymes, hypoglycemia, thrombocytopenia, and coagulopathy[14].

Badahori et al. mention the complex endocrine role of the liver which, in the presence of a portosystemic shunt, causes various pathologies such as tall stature, hyperinsulinemia, and hyperandrogenism[2]. It has been described that tall stature could be related to abnormal growth hormone metabolism with the absence of the hepatic first-pass effect and its degradation, with a consequent altered secretion of insulin-like growth factor[2]. Hyperinsulinemia in patients with portosystemic shunts would be related to several mechanisms such as absence of hepatic insulin metabolism after its secretion in the mesenteric and portal system, excessive insulin secretion in response to peripheral hyperglycemia due to the absence of the hepatic first-pass effect, and insulin resistance due to negative feedback of hyperinsulinemia on insulin receptor binding proteins[2]. Hyperandrogenism with precocious puberty may also occur due to the proportional decrease in hepatic dehydroepiandrosterone sulfate[2].

The most frequent laboratory finding in affected children, as in the neonatal period, was hyperammonemia and hypergalactosemia, the latter could occur due to the absence of the hepatic first-pass of ingested milk, despite normal galactose-1-phosphate uridyltransferase activity 1 leading to false positive neonatal screening for galactosemia in up to 13-30% of portosystemic shunts[2]. Neurological alterations such as cognitive deficits, attention and hyperactivity disorders and behavioral problems, seizures, Parkinson-like

syndromes, or hepatic myelopathy have been described in school-aged patients. Relevant findings include hyperammonemia and the characteristic sign of hepatic encephalopathy on MRI with hyperintense T1 signal of the globus pallidus[2].

Radiological manifestations include a prominent hepatic vein, abnormal tubular structure, and a pulsatile triphasic spectral pattern in the porto-mesenteric venous system. To evaluate the anatomy of the shunt, portal vein patency, the presence of hepatic nodules, and associated abnormalities, it is advisable to perform an abdominal CT or MRI scan with cross-sections. Annual liver imaging is recommended in patients with portosystemic shunts. When liver nodules are identified, liver biopsy should be considered[12,14,15].

Most hepatic nodules related to portosystemic shunts, mainly extrahepatic, are benign, but there are reports of hepatocellular carcinoma and hepatoblastoma[15]. Their origin would be related to abnormal hepatic vasculature that can result in alternating hypoxia and/or hyperoxia with altered balance of micronutrients and waste products, resulting in tissue acidosis. Liver lesions include focal nodular hyperplasia, regenerative nodules/nodular regenerative hyperplasia, hepatic adenomas, hemangiomas, and hepatocellular carcinoma[15]. Normal liver enzymes with absence of signs of advanced fibrosis or cirrhosis in liver biopsies rule out hepatic inflammation as a predisposing factor for its development[12,15]. Regression of hepatic nodules following shunt closure has been demonstrated[15,18,20].

In 2022, an article was published on a retrospective cohort of 29 patients with portosystemic shunts from the Boston Children's Hospital, of which 15 corresponded to intrahepatic and 14 to extrahepatic shunts [5]. Spontaneous shunt closure occurred in 8 patients (28%); all of whom had intrahepatic shunts and less than 12 months of age. Shunt closure was performed in 10 patients (34%), in 3 by interventional radiology (median age 1.9 years), 5 by laparotomy (median age 7.6 years), and in 2 patients both procedures were performed. The indications for treatment were large-caliber bypass, portal hypertension, hepatopulmonary syndrome, hepatic tumor, recurrent hypoglycemia, heart failure, and encephalopathy. In 8 patients, there was clinical improvement with resolution of symptoms, normalization of liver functions, and permanent closure of the shunt in the ultrasound follow-up. In the remaining patients, follow-up was maintained. No patient required liver transplantation, a procedure that is considered when there is no portal vein, and patients with innumerable liver masses at a higher risk of hepatocarcinoma[5,12].

According to the available evidence, portosystemic shunts remain stable or decrease in size over time and only a small percentage require surgical treatment, depending fundamentally on their location and size. Spontaneous closure is more frequent in multiple and distal intrahepatic shunts, so in these cases and asymptomatic patients, it is advisable to maintain expectant management with adequate follow-up. Management should be individualized considering that, in symptomatic cases, early diagnosis and closure of the portosystemic shunt according to the experience of each center improves the prognosis of the patients[5, 15-20]. In some cases, depending on the size of the shunt and the presence of portal hypertension, it is necessary to perform its closure in 2 stages[5, 15-20].

Unfortunately, the patients presented were lost to follow-up, but because of their location and characteristics, spontaneous closure of the vascular shunts without major complications should be expected.

Conclusions

We present two cases of neonates with antenatal diagnosis of portosystemic shunts. Although both had intrauterine growth restriction as the only clinical manifestation, the study was completed at birth due to the risk of complications, which were ruled out. Prenatal ultrasound is an effective tool for early diagnosis, improving follow-up, management, and prognosis considering that the onset of symptoms can be nonspecific and late. Most are asymptomatic at the time of diagnosis and only a small percentage require surgical treatment.

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.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

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