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Congenital syphilis and hepatic infarction, a not previously reported association. A pediatric case report

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ABSTRACT

Congenital syphilis is caused by *Treponema pallidum* infection of the fetus during pregnancy. Symptoms are variable. While endothelial damage is common, it is not usually present in congenital cases.

Here we report the case of a 42-day-old infant hospitalized due to an abdominal mass. Imaging studies confirmed the presence of an injury in the left lobe of the liver without mass effect. Biopsies showed changes compatible with infarction and neonatal hepatitis. The patient's and his mother's serologies confirmed the diagnosis of congenital syphilis, and he was treated with intravenous penicillin. The liver is protected from ischemic injury by its double irrigation, but the accumulation of harmful agents may have caused this unusual presentation.

Three months later, the patient was symptom-free, and the control MRI showed atrophy of the left lobe, while the rest of the parenchyma was unchanged.

Key words: *congenital syphilis; hepatic infarction; hepatic circulation; fetus.*

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INTRODUCTION

Syphilis, an infection caused by *Treponema pallidum*, may manifest in a myriad of ways and one of them is congenital, when the spirochetes pass from an infected mother to their unborn child. Symptoms usually include fever, rash, and low birth weight, but anemia, hepatomegaly with jaundice, periostitis, or mental retardation are frequent findings.

T. pallidum may damage the epithelial cells, particularly arterioles; in fact, cases of gangrene of the extremities have been described.

Here we describe the case of an infant diagnosed with localized hepatic infarction of the left lobe associated with neonatal hepatitis due to congenital syphilis.

CASE REPORT

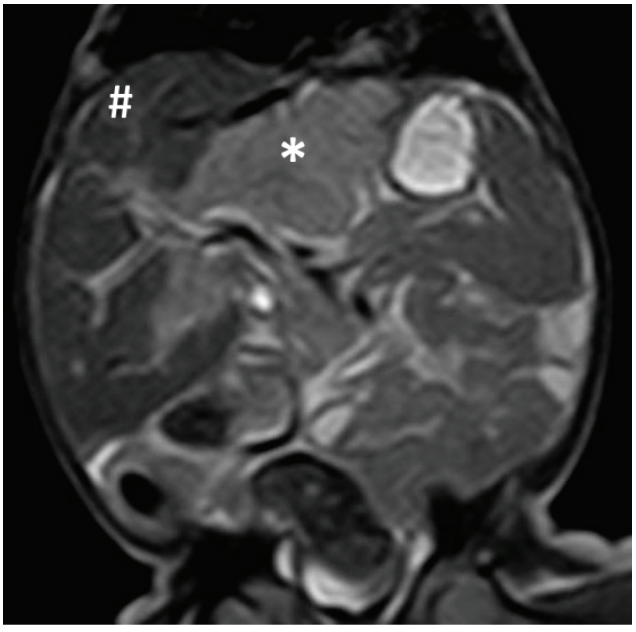
A 42-day-old infant, born in another facility, was transferred to our Department of Hepatology with a diagnosis of abdominal space-occupying mass. The baby had been born at term from an uncomplicated pregnancy; he was hospitalized in the neonatal intensive care unit for 24 hours due to perinatal cardiac arrest that resolved with basic resuscitation maneuvers. He was discharged 5 days after birth. Unfortunately, the specific details of this hospitalization could not be corroborated because the parents did not have a discharge report or the serological tests for the third trimester of pregnancy.

During history-taking, it was observed that the patient had a transient jaundice episode during the first week of life with recurrence before hospitalization, but he never presented with acholia, so, according to his parents' account, it was interpreted as physiological jaundice and no lab tests were performed. Again, this information could not be corroborated during hospitalization.

The physical examination found abdominal distension and the presence of a palpable mass in the right upper quadrant and epigastric region. The patient also had jaundice and macular lesions on the back. The patient's irritability during his physical examination and position changes was striking, which resolved when lying on the examination table. No dimorphisms were observed.

The ultrasound showed a hypoechoic area in segments II, III, and IV of the liver. The lab test results were hematocrit 18%, conjugated bilirubin 6.35 mg/dL, aspartate aminotransferase (AST) 141 IU/L, alanine aminotransferase (ALT) 47 IU/L, and gamma-glutamyltransferase (GGT) 62 IU/L. Although it is not part of the differential diagnosis of a liver space-occupying mass, serological tests were requested to look for possible infections, given the absence of an accurate prenatal history.

Figure 1. Liver MRI. T2 sequence showing a lesion involving most of the left and caudate lobes (*), without signs of a mass effect. The right lobe has a normal aspect (#)



An MRI of the liver revealed diffuse changes in the left lobe, hypointense signal in T1, and hyperintense signal in T2, without a mass effect, which was compatible with hepatic infarction. Diffusion sequences showed changes compatible with residual inflammatory activity and hypertrophy of the caudate lobe (*Figure 1*).

A needle biopsy of both lobes was performed: the left lobe showed total disruption of the architecture, absence of hepatocytes, and structures similar to portal tracts immersed in a lax fibrous tissue stroma ("*foie vide*") (*Figure 2*). The right side showed giant-cell transformation compatible with neonatal hepatitis (*Figure 3*).

At the same time, the nontreponemal tests (venereal disease research laboratory, VDRL) were positive for both the patient and his mother, confirming the diagnosis of congenital syphilis.

Figure 2. Histology of the left lobe of the liver. Abundant fibrous tissue can be seen replacing the normal architecture. No evidence of inflammatory reaction and no normal structure is recognized. H&E stain 250x

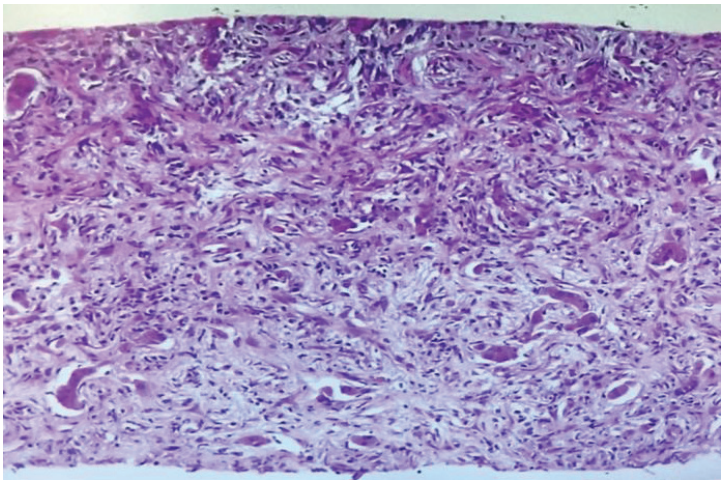
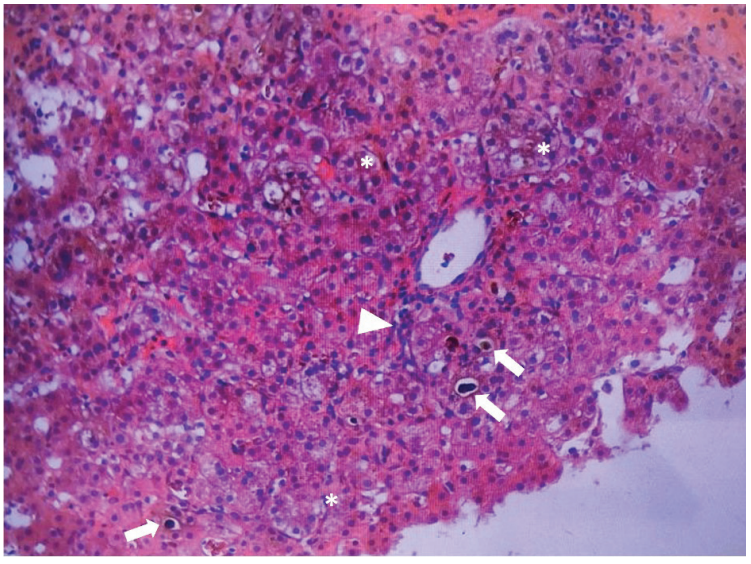


Figure 3. Histology of the right lobe of the liver. Giant hepatocytes and rosette formation (hepatocytes grouped and separated from the rest) observed throughout the specimen (*). Ductular reaction (arrowhead) and the presence of evident bile plugs (arrows). Isolated remnants of normal structures. H&E stain 250x



The VDRL test in cerebrospinal fluid was positive, so treatment with intravenous penicillin was started according to the protocols established by the Argentine Ministry of Health. Treponemal tests (FTA-ABS) were also positive. Finally, during the follow-up after hospital discharge, the mother submitted the pregnancy serological tests, and the VDRL test was positive in the third trimester. However, she reported that she was never informed of these results and was never given any treatment.

The patient's lab test results normalized rapidly, with a negative VDRL test and the control MRI 3 months later showed only residual atrophy of the left lobe with no signs of inflammatory activity.

DISCUSSION

Congenital syphilis is the result of *T. pallidum* infection of the fetus during pregnancy. Therefore, a serologic screening should be routinely performed in all pregnant women given that cases of prenatal infection are the result of poorly controlled pregnancies. It may manifest in a myriad of ways, hindering its recognition, but certain findings, such as low birth weight, rash, and fever are typical, and patients often develop rhinitis, hepatosplenomegaly with jaundice, and cytopenias. Without treatment, physical malformations become evident (nasal, frontal bone, or limb deformities) and patients are often described as irritable, especially when held in the arms, because of periostitis.[1–3]

Most of the typical manifestations of syphilis are secondary to endothelial damage by *T. pallidum*, but such lesion is rare in congenital cases.[3,4] However, peripheral artery disease and even gangrene of the extremities have been reported by other authors.[5–7]

Hypoxic-ischemic liver damages are exceptionally rare, and hepatic infarction even more so, even among critically ill patients or newborn infants with perinatal lesions. This is because the liver is normally protected from ischemic damage thanks to its double irrigation. In the physiological state, the portal vein supplies 75% of the blood, but only 30% of the oxygen required; the rest is provided by the hepatic artery. Although fasting or hypovolemia may alter this distribution, significant changes in one system are compensated for by the other. Such ability of the adult liver to maintain a constant blood flow, despite major changes in systemic circulation, is not fully developed in newborn infants,[8,9] particularly because fetal hepatic circulation has specific characteristics. During fetal life, oxygenated blood comes from the placenta through the umbilical vein, enters the liver, and form anastomosis through the left portal vein to a relatively underdeveloped portal system. In addition, in the fetal liver, there is a communication with the inferior vena cava, the ductus venosus.[9,10] Haugen et al.[9] demonstrated that blood reaches the portal system and the inferior vena cava through the left branch of the portal vein in human fetuses.

Although rare, ischemic lesions may occur as a result of the sudden drop in blood flow at the time of umbilical vessel closure during birth, because the left portal vein is not sufficiently developed to supply blood to the left lobe. In addition, because the ductus venosus does not close immediately, some of the blood is shunted directly into the inferior vena cava instead of into the left portal system.[10–12]

In 1952, Emery[10] described a series of 110 necropsies, from stillbirths to subjects aged up to 8 weeks, and found liver changes, predominantly in the left lobe. These changes were present in those who died during the first 48 hours of life, but not in stillbirths. These findings are compatible with other reports where ischemic lesion is usually observed in the left lobe.[13]

A common feature of all these cases is that they had palpable liver masses and that imaging studies showed hypertrophy of the caudate lobe with hypotrophy of the left lobe, as in our case.[14,15] However, in our patient, the particular histological and imaging findings in each lobe must necessarily respond to different harmful agents, since neither hypoxic-ischemic injury nor congenital syphilis account for such differences. The characteristics of the right lobe are compatible with neonatal hepatitis, while the complete destruction of the hepatic parenchyma in the left lobe is compatible with hepatic infarction. In addition, the biochemical alterations of our patient are not compatible with a typical ischemic lesion.

Therefore, we suspect that our patient's liver was damaged by syphilitic hepatitis, an infection characterized by endothelial damage, sometimes severe, and that the hemodynamic changes after birth, in addition to the circulatory alteration at the time of cardiorespiratory arrest, caused the ischemic necrosis of the left lobe.

Although it is impossible for us to confirm

our hypothesis, the remarkable differences found between both lobes, the confirmation of congenital syphilis with resolution after antibiotic treatment and the perinatal history of our patient make our explanation at least appealing. We believe that our cases forces us to consider the possibility of congenital syphilis among the differential diagnoses of hepatic ischemia. ■

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