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Case Report

Neonatal Cholestasis Revealing Congenital Cytomegalovirus Infection Combined with Alagille Syndrome

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Abstract

Liver illnesses that run in families might start childhood with cholestatic jaundice and proceed to severe hepatic dysfunction. Although congenital cytomegalovirus (cCMV) infection can initially affect the liver in otherwise healthy hosts, chronic hepatitis is rare. We present an infant with cholestatic jaudnice evolving since birth and dysmorphic facies revealing alagille syndrome, the biological tests is revealing a biological cholestasis and a CMV serology positive. The patient was treated for 3 months.

Keywords: liver illness, congenital cytomegalovirus infection, cholestatic jaudnice, alagille syndrome, gancyclovir.

INTRODUCTION

Congenital cytomegalovirus infection is the most frequent congenital infection, with an estimated incidence of approximately 0.6–0.7% of livebirth [1]. However, 10% of newborns with CMV infection during pregnancy present clinical symptoms at birth that range greatly from moderate to severe multi-organ illness. The vast majority of neonates with CMV infection during pregnancy remain asymptomatic [2]. Low birth weight, microcephaly, chorioretinitis, thrombocytopenia, aberrant brain MRI, and sensorineural hearing loss are examples of clinical characteristics [3]. Hepatomegaly, newborn hepatitis, and cholestatic jaundice are only a few hepatic complications that could occur [4]. Alagille syndrome is an inherited multi-organ disease of variable severity [5].

CLINICAL OVERVIEW

It was an infant aged 40 days, from a consanguineous marriage, from a pregnancy estimated to be full term, with a history of low birth weight, admitted to the pediatric department at the Mohammed VI University Hospital of Marrakech for total and permanent cholestatic jaundice evolving since birth, with mucocutaneous jaundice, dark urine and discolored stools.

Physical examination was noted a dysmorphic facies with a flat nose and a pointed chin, hepatomegaly with a liver arrow at 8cm

To the biological check-up:

- Biological cholestasis; total/direct bilirubin: 206/186, GGT 176 (6-42), PAL 687 (0-449), TP 63.4% increased to 98% after administration of vitamine K
- Hepatic cytolysis: ASAT 694 (10-35) and ALAT 568 (7-33);
- In the etiological work-up: CMV serology type IgA and IgG positive and PCR-CMV positive at 758,000 IU/ml

On the spine X-ray a butterfly aspect. On the cardiac ultrasound: Pulmonary stenosis of the right branch, 3mm CIA, millimetric muscular IVC. Amino acid and organic chromatography, plasma protein electrophoresis were normal. In view of the low birth weight, chronic cholestasis, hepatic cytolysis and CMV serology as well as positive PCR, the patient was treated with Gancyclovir for 3 months. A liver biopsy was performed showing dystrophic and inflammatory changes of the liver parenchyma with portal tracts devoid of bile ducts and the presence of METAVIR stage I liver fibrosis, suggesting an alagille syndrome.

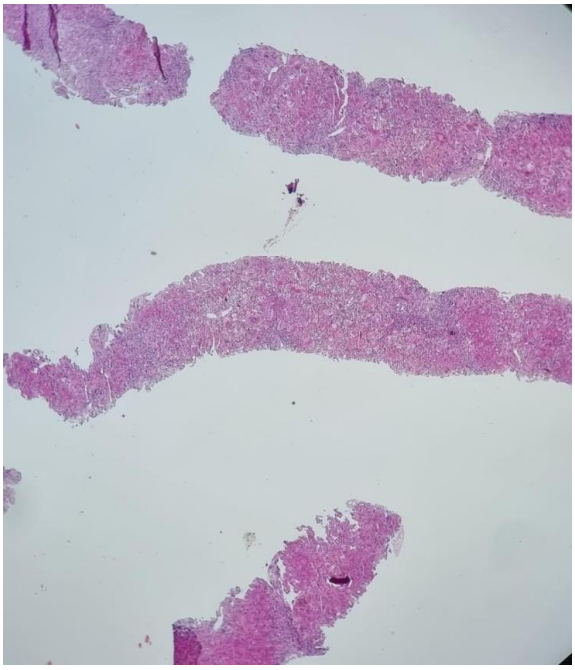

Figure 1: Histological examination of 3 biopsy cores measuring 0.2cm, 0.4cm and 0.5cm respectively

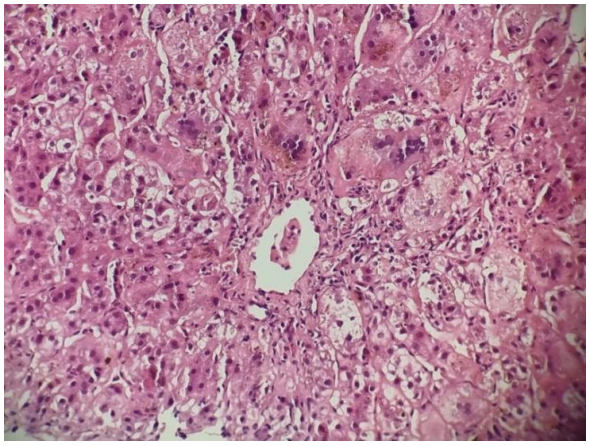

Figure 2: Hepatic parenchyma with minimal fibrosis and no septa, punctuated by rare mononuclear inflammatory elements; the spaces are devoid of bile ducts. Hepatocytes have a trabecular architecture and are the site of degenerative lesions: giant cells, ballooning, etc…Their cytoplasm contains biliary pigments

The patient's progress was marked by stabilization, after 6 months of follow-up, he showed little weight gain (2kg over 6 months), a decrease in biological cholestasis: total/direct bilirubin: 150/126, GGT /PAL: 116/601 and hepatic cytolysis: ASAT/ALAT: 504/410, CMV seology type IgA, IgG is always positive and PCR-CMV positive at 690,000 IU/ml. The patient was treated with vitamin therapy.

DISCUSSION

Only a few publications exist on the management of concurrent cCMV infection in these individuals, despite the fact that the course and outcomes of these genetic illnesses are widely reported in the literature. The liver might be involved in cCMV infection clinically in the form of newborn hepatitis or cholestasis. Other organs can also be affected. Clinical studies have revealed that cCMV (39-83%) can cause a variety of hepatic involvements, such as increased liver enzymes, direct hyperbilirubinemia, jaundice, and hepatosplenomegaly [6]. The majority of cCMV-induced hepatic illness cases fully recover with no persistent hepatic dysfunction.

A patient had Alagille syndrom, a multisystem autosomal dominant illness. Chronic cholestasis caused by a lack of intrahepatic bile ducts and peripheral arterial disease are the key clinical and pathological characteristics. The presence of dysplastic kidneys, pulmonary artery stenosis, vertebral abnormalities, distinctive faces, posterior embryotoxon, and pigmentary retinopathy. In 95% of cases, the liver illness associated with this syndrom manifests as chronic cholestasis and most frequently manifests as jaundice brought on by conjugated hyperbilirubinemia during infancy or the first three months of life [7].

Unprecedented comorbidity between PFIC (progressive familial intrahepatic cholestasis) and cCMV infection poses a problem when determining the necessity and length of antiviral treatment. In the first instance, a liver biopsy revealed no evidence of CMV-related damage. Nevertheless, the biopsy was carried out while the patient was receiving valganciclovir medication, which may have corrected CMV-induced hepatitis and confused the histology results. Valganciclovir withdrawal caused CMV reactivation, which was followed by a decline in clinical status and a worsening of hepatitis. Therefore, we suggest that cCMV infection significantly contributes to the severe course of the hereditary primary disease, perhaps causing further decline in liver function [8].

Having cholestasis and having hereditary liver conditions identified (Götze *et al.*, 2015) offered a thorough work-up method and a clinically oriented summary of potential differential diagnosis of newborn cholestasis in their review. Since cCMV infection testing is crucial to this workup, we tried to change the suggested diagnostic strategy to reflect our suggested method for evaluating newborn cholestasis [9].

Questions about the length of treatment, particularly the necessity for suppressive antiviral therapy after the treatment, are raised after cCMV is detected in individuals with an underlying hereditary liver disease mandated time frame following symptomatic cCMV diagnosis. There is a dearth of clinical and scientific data to address these issues. In order to improve chances of survival while awaiting transplant, we recommend treating patients with suppressive medication if they have a quickly progressing hepatic illness or are about to experience

liver failure. Patients with slowly progressing or stable illness may have valganciclovir treatment for symptomatic cCMV for 6–12 months after delivery, and after stopping antiviral therapy, they will be watched for signs of reactivation [8].

CONCLUSION

Screening for cCMV infection is crucial when dealing with patients who are being assessed for newborn cholestasis and discovered to have inherited liver illnesses because therapy may change the clinical course. When these patients have an immediate decline in liver function, CMV reactivation should be suspected. To determine whether suppressive Ganciclovir medication can help these patients hepatic function from further deteriorating, more research is required.

Conflict of interest

The authors have no conflicts of interest to declare.

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