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Fulminant Hepatitis Due to Father-to-Newborn Transmission of Herpes Simplex Virus type 1

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Abstract: We describe a case of a severe neonatal infection by herpes simplex virus (HSV) type 1 acquired postnatally from his father. The delivery and the first days of life were normal. He developed liver failure and disseminated intravascular coagulation when he was 19 days old. He was treated with intravenous acyclovir and the outcome was favorable. This case underlines that prevention of post-natal transmission of HSV merits to be considered in educational pregnancy programs directed at mothers and fathers.

Keywords: *E. coli*, HSV1, infection, transmission.

INTRODUCTION

Human herpes simplex virus (HSV) causes lifelong infections, a vast majority of which do not manifest clinically. Neonatal HSV infection can be acquired in utero (transplacental hematogenic transmission), at delivery (the most frequent route *via* direct contact of the baby with infected vaginal secretions) or postnatally (indirect transmission), and cause significant morbidity and mortality [1,2]. HSV infections in newborns are classified into three patterns, occurring with equal frequency, disseminated disease involving multiple visceral organs, central nervous system disease, and disease limited to the skin, eyes, and mouth [3]. Postnatally acquired HSV infections are rarely reported and the source of infection remains poorly documented. We report here one case for which extensive investigations were conducted to document it to the best of our possibilities.

CASE REPORT

A 8-day old male newborn was admitted to the emergency ward for abdominal pain with 39°C fever. *Escherichia coli* pyelonephritis was laboratory-documented on the urine sample. At this time, except for an elevated inflammatory marker (CRP = 15 mg / l), liver function tests, blood cell count and hemostasis markers were normal. He was transferred to pediatric unit to receive intravenous antibiotics. Eleven days later, his condition suddenly deteriorated with jaundice, abdominal collateral circulation, hepatosplenomegaly, and diarrhea in a febrile context (39.5°C) suggesting splenic hypertension; he was transferred to the neonatal intensive care unit. Biologic analyses showed a severe hepatic failure (prothrombin ratio at 25%, fibrinogen at 0.19g/L) with severe cytolytic hepatitis (AST = 2,720 IU/L, ALT = 1,353 IU/L, normal range = 6-40 IU/L), moderate cholestasis (total bilirubin at 119 µmol/L), severe thrombocytopenia (13g/L) and disseminated intravascular coagulation (fibrin monomer at 50 µg/mL, activated coagulation time at 58 sec). He was transfused with platelet, plasma and fibrinogen units. An empirical treatment by aciclovir was started. Bacterial sepsis was ruled out since blood and CSF cultures were negative. Other conditions such as metabolic disease, macrophage activation syndrome and hemochromatosis were negative (myelogram, iron status). Hepatotropic viruses (hepatitis A-E viruses, Cytomegalovirus, Herpes simplex virus (HSV), varicella-zoster virus, and Epstein-Barr virus) were tested *via* serology and PCR or RT-PCR-based genome amplification, but were negative except for HSV for which acute serum contained IgM, and HSV PCR was positive in whole blood and in the liver biopsy [4]. HSV type 1 (HSV-1) infection was confirmed using PCR based typing [5]. Histologic analysis of the liver biopsy showed a severe disseminated cytolysis. Thorough clinical examination of the patient did not find either mucocutaneous vesicles or encephalitis signs. Before this episode and apart from the pyelonephritis, the first 3 weeks of life were associated with normal weight gain. The treatment by intravenously acyclovir was prolonged during 21 days. The clinical and biological examinations progressively improved and the newborn was discharged after one month.

DISCUSSION

Mother-to-newborn transmission at the delivery time is unlikely due to the following facts and regarding the related

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data in the literature: (i) There was an absence of genital lesions [6]. (ii) The serological profile of the mother (HSV IgG-positive / HSV IgM-negative / HSV real-time PCR negative) indicated a past immunity against HSV and the absence of reactivation. (iii) The newborn developed normally with normal weight gain in the first 3 weeks of life. (iv) The hepatitis signs and symptoms were developed 11 days post admission, i.e. 19 days after birth. The long delay between birth and HSV-1 signs is strong evidence against the per-delivery infection due to active virus shedding in an asymptomatic mother (v) The post natal transmission is almost always due to HSV-1 [7].

Assuming post-natal transmission of HSV-1, the father-to-infant transmission is much more likely than the mother-to-infant transmission because upon interview (i) the father reported a lesion highly suggestive of oro-labial herpes when the newborn was first hospitalized, (ii) he recalled and spontaneously reported to have repeatedly kissed his son while he was symptomatic, (iii) he declared that he often presented recurring oro-labial herpes lesions.

The *E. coli* infection seems to be an intercurrent infection that has played no role other that provoking the hospitalization. Although there is no undisputable evidence, according to the aforementioned array of data, the HSV-1 infection of the newborn is much more likely to have been acquired from his father than from his mother.

In Light's comprehensive review of postnatal acquired HSV infection in newborn infants (less than 28 day-old), there is no report of father-to-infant transmission between 1959 and 1977 [8]. A thorough bibliographic search retrieved only two cases where father-to-newborn transmission was reported [9,10]. In our case, the issue was excellent; however it is likely that the 3-week acyclovir treatment has played a major role in the favorable outcome.

Because, the etiological quest of severe sepsis in newborn is difficult and that delayed therapy jeopardizes the outcome, it is recommended to start empiric acyclovir treatment when cytolytic hepatitis is diagnosed [8, 11]. In addition, the risks and means of prevention of post-natal transmission of HSV should be considered in educational programs associated with pregnancy.

AUTHORS CONTRIBUTION

Laboratory tests: Zandotti C, Ninove L.

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Supervision: Zandotti C, Charrel RN.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Declared none.

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