may result from septal deformities, which affect nasopulmonary and nasal reflexes.

Mcauliffe, *et al.* studied the sensitivity of the nasal cavities and the paranasal sinuses using mainly faradic stimulation and found that the lateral wall of the nasal cavity was much more sensitive than the septum [3]. Clinical studies show that the very severely impacted nasal septum can exert pressure on the more sensitive structure of the lateral nasal wall and cause referred trigeminal pain and chronic headache [4].

Thus, when a pediatric patient presents with such a history, appropriate radiological evaluation should be carried out and thorough nasal endoscopic examination has to be performed to reach the correct diagnosis and appropriate management of patient.

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Evolving Biliary Atresia with Cytomegalovirus

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Multiple studies have been conducted to demonstrate the role of viruses in causing biliary atresia. Although *cytomegalovirus* (CMV) is known to cause intrahepatic bile duct destruction, its role in biliary atresia is not proven. We report two cases of CMV infection, initially presenting with intrahepatic cholestasis, who subsequently developed biliary atresia.

Key words: *Biliary atresia, CMV, Liver biopsy*

Extrahepatic biliary atresia (EHBA) occurs in 1 in 10,000 live births, more commonly in Asians. 65-90% of EHBA cases are post-natal, and in these, a role for infectious agents in causing bile duct obliteration is suggested [1]. Although cytomegalovirus (CMV) is known to cause intrahepatic bile duct destruction and paucity, its role as a cause of EHBA has been a topic of much debate.

Over a period of 2 years, 32 EHBA cases were seen at our Pediatric Hepatobiliary Clinic. Out of the 13 who were tested for associated CMV infection, 11 tested positive for CMV either by positive CMV IgM or CMV PCR (Polymerase Chain Reaction) [2]. We present two cases of cholestatic jaundice, tested positive for CMV and had rising titres of CMV IgG on follow-up. Although the biliary tree was found to be patent at presentation, both children subsequently developed biliary atresia.

CASE REPORT

Case 1: A 5 months old infant, exclusively breastfed, immunized and well-developed for age, presented with jaundice since birth with high coloured urine without clay colored stools. On examination she had jaundice with

hepatosplenomegaly, ascites, umbilical hernia and corneal xerosis. Other examination and investigations are depicted in ***Table* I**. Liver biopsy could not be done due to uncorrectable coagulopathy and ascites. Since HIDA (Hepatobiliary Iminodiacetic acid) scan showed excretion of dye in the intestines, biliary atresia seemed unlikely. Due to a positive CMV IgM serology and decompensated liver disease, the child was treated with oral ganciclovir for 6 weeks along with antibiotics but liver functions remained deranged. Subsequently, stools became clay colored and an intraoperative cholangiogram showed no passage of dye in the intestines. A portojejunostomy was done but the child died postoperatively.

Case 2: A 3 months old child presented to a peripheral hospital with jaundice since day 15 of life and high coloured urine. She did not have clay coloured stools initially (***Table* I**). Her TORCH titres (IgM and IgG for Toxoplasma, Rubella, CMV and Herpes) demonstrated equivocal CMV IgM (0.96 IU/mL) and positive CMV IgG (6.58 IU/L). Other viral titres were negative. Ultrasound showed presence of gall bladder. HIDA scan showed decreased extraction of tracer by liver with non visualization of tracer after 24 hours. She was subsequently referred to us at 5 months. On presentation, her weight was 5 kg, length was 58 cm. She had jaundice and hepatosplenomegaly. Other systems were normal. A Magnetic Resonance (MR) cholangiogram showed patent biliary tract. Her hearing and ophthalmological evaluations were normal. Urine organic acids and reducing substances were negative. Blood CMV viral load was undetectable, but rising CMV IgG was seen. Her bilirubin had decreased to 4.2 mg/dL (direct = 3.06 mg/dL). She was started on valganciclovir (250mg/mm^2/day in 2 divided doses). However, after 15 days, she started passing persistent clay coloured stools. Liver biopsy showed features suggestive of biliary atresia without inclusion bodies. She underwent a Kasai portoenterostomy at 6 months. She continues to have jaundice post-operatively.

DISCUSSION

Landing suggested that neonatal hepatitis and EHBA represent two ends of a spectrum of a single disease process. Viruses have been proposed as a likely cause, CMV, reovirus and rotavirus among the probable agents [3]. The rarity of EHBA in neonates, the presence of inflammatory changes in the biliary tree soon after birth, and their persistence following portoenterostomy argue in favour of an infectious agent [4,5].

CMV infection has been found in a large number of EHBA cases. However, normal infants are also commonly infected with CMV, without developing overt disease. In a Canadian study of 12 children with biliary atresia, bile duct biopsy did not show CMV inclusions or DNA(4). On the other hand, a study from Sweden showed CMV DNA to be present in livers from 9 of 18 patients with EHBA [5]. In a study by Tarr, *et al*, CMV infection was documented in 5 of 21 i.e. 24% of patients with EHBA [7]. The study concluded that the establishment of CMV infection in infants with cholestasis should not deter the search for EHBA [7].

In both our cases, the presentation was classical of EHBA; full-term infants with jaundice and dark urine, with otherwise normal growth, who develop acholic stools over the first few weeks of life. Case 1 initially showed evidence of intrahepatic cholestasis without biliary atresia on HIDA scan, but subsequently developed EHBA, as evidenced by change in stool form and the intraoperative cholangiogram. Case 2, with evidence of recent CMV infection, showed patent biliary tracts on MR cholangiogram, but subsequently developed acholic stools and liver biopsy evidence of EHBA. In a similar case of CMV infection in a 2 month old, confirmed by PCR analysis of blood and urine, HIDA scan showed biliary atresia, and though urine samples turned negative with ganciclovir treatment, progressive damage of the liver continued with subsequent development of portal hypertension and hepatic coma [8].

In a Norwegian study on 10 patients of EHBA, 4 tested positive for CMV and 5 for EBV infection [6]. While 3 of these had positive CMV PCR on liver biopsy, serum or urine, only one had CMV IgM positive, thus indicating that newer PCR techniques can pick up viral disease which may otherwise be missed by serology [5]. Another interesting example is of two non-identical twins with CMV infection in utero, one of whom developed neonatal hepatitis while the other developed EHBA after birth [9].

In summary, infants with EHBA should be tested for viral antibodies, like CMV. The association of CMV infection with EHBA is too often seen to rule out its role as an etiological agent; and cases of CMV hepatitis must be monitored for subsequent development of biliary atresia.

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TABLE I PATIENT CHARACTERISTICS

History	Patient 1	Patient 2
Examination findings	Jaundice, ascitis, hepatosplenomegaly, umbilical hernia, corneal xerosis	Jaundice, hepatosplenomegaly
Investigations		
Bilirubin (mg/dL)	13.6	6.5
Direct bilirubin (mg/dL)	5.8	3.7
SGOT (IU/L)	350	390
SGPT (IU/L)	175	341
Total proteins (g/dL)	6	6.5
Albumin (gm/dL)	2.5	3.7
Prothrombin time (sec)	21.7	17
Partial thromboplastin time (sec)	39	40
Alkaline phosphatase (IU/L)	2467	1312
GGTP (IU/L)	10	629
Ultrasound abdomen	Hepatosplenomegaly + portal hypertension	Gall bladder seen
CMV IgM (IU/ml)	1.7	0.96
CMV IgG	247.6 (AU/ml)	6.58 IU/ml
CMV Viral load (copies/ml)	–	Undetectable
Alpha 1 Antitrypsin levels	Normal	Normal
MR cholangiogram	–	Normal

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