

## Recurrent Gallbladder Hydrops and Sclerosing Cholangitis in 11-Year-Old Male with Hyper IgM Syndrome

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Hyper Immunoglobulin M (hyper IgM) is a rare immunodeficiency disorder first reported in 1961<sup>[1]</sup>, characterized by recurrent infections with low levels of serum IgA, IgG and IgE and normal to high levels of serum IgM<sup>[1]</sup>. Onset of manifestation of X-linked HIGM occurs in the 1<sup>st</sup> or 2<sup>nd</sup> year of life with recurrent pyogenic infections especially of upper and lower respiratory tract and diarrhea in 40% of the patients<sup>[1]</sup>. *Cryptosporidium* infections are a common cause of diarrhea in these patients complicated with hepatobiliary disease, which is severe and often fatal<sup>[1]</sup>. Gallbladder hydrops occurs in acutely severe ill children with inflammatory or non-inflammatory conditions<sup>[2]</sup>. Treatment is based on correction of immunity by immunoglobulin replacement and aggressive antimicrobial therapy. Infections, liver disease and malignancy are common causes of mortality, therefore, stem cell transplantation is necessary to increase the survival rate up to 68%<sup>[3]</sup>.

Our case is an 11-year-old boy born from non-consanguineous parents whose three siblings expired due to infections during infancy. Our patient also had recurrent severe infections during that period. The work-up depicted the diagnosis of hyper IgM syndrome due to very low levels of IgA, IgG and IgE with high levels of IgM. He was repeatedly (four times) hospitalized because of abdominal pain and palpable mass at the RUQ. At physical examination, the abdomen

showed tenderness at RUQ and a palpable mass, there was no organomegaly. Abdominal ultrasound revealed a distended gallbladder with slight wall thickening, compatible with hydrops. Magnetic resonance cholangio-pancreatography (MRCP) showed variable narrowing and dilation of bile ducts, suggestive of sclerosing cholangitis. Laboratory investigations showed increased Liver Function Tests (LFTs). Only during the first hospitalization, *Cryptosporidium parvum* oocysts were present in stool, therefore therapy with Paramomycin (50 mg/kg/day) and Azitromycin (10 mg/kg/day) was initiated. After treatment, clinical symptoms and paraclinical findings were normal. In the next admissions, in spite of the presence of the same clinical symptoms, parasites were not seen in stool examination. Nevertheless, all symptoms improved with anti *cryptosporidium* treatment.

This is, to our knowledge, the first report of recurrent gallbladder hydrops and sclerosing cholangitis in a child with hyper IgM syndrome associated with *Cryptosporidium* infection. In children with X-HIGM, *Cryptosporidium* has high prevalence (up to 24%)<sup>[4]</sup>. These patients have involvement of small bowel with chronic diarrhea and biliary tract disorders. This disease presents with chronic diarrhea and RUQ pain. Further evaluations with ERCP or MRCP showed distortion of the biliary structure<sup>[5]</sup>. In immunocompromised patients, *Cryptosporidium* infections cannot be eradicated<sup>[6]</sup>. Approximately 1/6 patients with immunodeficiency disorders have hepatic disease<sup>[7]</sup>, more than 50% of which is caused by Cryptosporidiosis<sup>[8]</sup>. Early diagnosis is very important because, with adequate treatment, serious complications can be prevented. Curative therapy for *Cryptosporidium* infections include stem cell transplantation<sup>[7]</sup>. In our patient diarrhea was not present, but in stool *Cryptosporidium parvum* was found. This situation is rare, especially in immunodeficient patients, as these children usually have chronic diarrhea with malabsorption and malnutrition, and diarrhea is a typical clinical manifestation of *Cryptosporidium* infection. With anti-*Cryptosporidium* therapy, the organism cannot be eradicated, and drugs only

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inhibit its proliferation. Further evaluation with electron microscopy showing parasitophorus vacuoles in the intestinal microvillus or PCR is necessary to confirm the state of infestation.

**Key words:** Cryptosporidium; Hyper IgM Syndrome; Sclerosing Cholangitis; Gallbladder Hydrops

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## Unrevealing of Primary Vesicoureteral Reflux which is Not Harmful for Kidneys in Children Should Be Considered as Success

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Uncovering of harmless primary vesicoureteral reflux (VUR) results in follow up of just a VUR image causing unnecessary stress for the parents, patients and physicians. Furthermore, voiding cystourethrography, gold standard for VUR

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diagnosis, is an invasive method having radiation hazard.

Following questions will remain unanswered until non-invasive diagnostic methods for VUR are discovered: Is VUR a physiological phenomenon that disappears during growth in children? Which VUR is benign or harmful for the kidney<sup>[1]</sup>? Is the degree of VUR a sufficient parameter to state that it is harmless?

It is necessary to look over the results of some studies for making comments on the questions above. The prevalence of VUR in healthy children was reported as 0.4-1.8% based on statistical calculations. However, this ratio increased up to 17.2% based on the assessments in healthy renal units<sup>[2]</sup>. Spontaneous resolution rate of VUR is decreased as its grade increases. Today, we need a non-invasive gold standard method for diagnosis of VUR in both healthy and ill children<sup>[3,4]</sup>.

The last recommendations of American Academy of Pediatrics was based on a formal meta-analysis of recent studies that did not detect a statistically significant benefit of prophylaxis in preventing recurrence of febrile UTI in infants without reflux or those with grades I to IV VUR<sup>[5]</sup>. A previous study showed that antimicrobial prophylaxis did not reduce the risk of recurrent UTI, but rather led to infections with resistant microorganisms<sup>[6]</sup>. In conclusion, unrevealing of harmless primary VUR in children should also be considered as success.

**Key words:** Vesicoureteral Reflux; Kidney; Children

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