

Hepatitis A Virus Infection Associated with Cryoglobulinemic Vasculitis

Atypical symptoms, especially immune complex disorders, are uncommonly reported with hepatitis A virus (HAV) infection. We report an 8-year-old child who contracted HAV infection complicated by cryoglobulinemic vasculitis, and responded well to oral steroids. HAV infection may be considered in the etiology of cryoglobulinemia in children.

Keywords: *Acute hepatitis, Cryoglobulinemia, Vasculitis.*

Hepatitis A virus (HAV) infection in children is described as a mild condition, mostly asymptomatic. It is still a major public health problem in developing countries [1]. Atypical manifestations are very rare. We report a case of an 8-years-old girl who presented with acute hepatitis due to HAV infection complicated by cryoglobulinemic vasculitis.

An eight-years-old girl, with no significant medical history, presented to emergency department for an acute fever (up to 39 Celsius) (degree) and jaundice evolving for 5 days. She had white stools and very dark urine. The child was asthenic and anorexic. Serological screening was positive IgM anti-HAV antibodies. Management consisted of symptomatic measures, and the child was discharged home.

She persisted to have jaundice and pruritus. By eight weeks, she had an acute onset of epistaxis, arthritis of large joints (knees), and vasculitic rash (of legs, forearms, and the back), evolving for 2 days. The child was conscious with no neurological symptoms. She had normal body temperature and blood sugar. We found no other clinical abnormalities. Dipstick test was positive to proteins (2+) and blood (3+). Laboratory analysis showed cholestasis and hepatic cytolysis with no liver failure (prothrombin time = 84.4%, SGPT = 178 IU/l, SGOT=141 IU/L, total bilirubin = 66.1 mg/l, GGT = 101 IU/l, ALP=110 IU/l). Ultrasonography showed hepatosplenomegaly with acalculous gallbladder and thickened wall. The first hour, CRP=38.25 mg/L, she had normochromic normocytic anemia (hemoglobin, 10.1 g/dL), lymphocytosis ($7220/\text{mm}^3$), mild proteinuria (180 mg/24h), and features of inflammation (ESR=80 mm). HAV

serological test identified negative IgM antibodies and positive IgG antibodies. Due to the atypical manifestations, we biopsied the vasculitic rash and found a leukocytoclastic vasculitis. Negative serodiagnosis of Epstein Base virus, hepatitis B, C and E virus, Cytomegalovirus HIV eliminated another viral cause of this condition. While, repeated blood cultures to look for a bacterial or fungal infection remained sterile. There were no additional clinical or biological abnormalities suggesting an autoimmune cause for the vasculitis (e.g. systemic lupus erythematosus, systemic juvenile arthritis, or systemic vasculitis as Wegener granulomatosis and polyarthritis nodosa). In this context, anti-nuclear antibodies, anti-DNA antibodies, rheumatoid factor, and anti-nuclear anti-cytoplasmic antibodies were negative. Biological tests to look for Wilson disease and autoimmune hepatitis were normal. Cryoglobulin assay was positive to IgM, IgA, and IgG (mixed cryoglobulinemia type II). Management consisted of starting oral steroids (prednisone) at 1 mg/kg/day. Ten days later, we noted total regression of cutaneous, and osteoarticular symptoms. The regression of clinical and biological cholestasis was achieved by three months, and prednisone tapering started. Steroids were withdrawn by the sixth month. The child remains asymptomatic, with a normal liver function.

Cryoglobulinemia have been mainly described in Hepatitis B and C virus infections, there are rare case reports with HAV, mostly in adults [3]. The intrinsic mechanism by which viral hepatitis promotes cryoglobulin production is unclear. Virus persistence, may represent a continuous stimulus for host immune system unable to produce neutralizing antibodies; and cryoglobulins may represent the product of virus-host interactions in this context [4]. Treatment with oral steroids has shown benefit in adults [5]. Some authors suggest genetic predisposition to immune complex disorders after viral infections as the likely pathogenesis [6].

Treatment with steroids is effective in reducing the atypical manifestations of acute HAV infection in the form of cryoglobulinemia-related symptoms. Further studies are necessary to establish physio-pathogenesis and standardized protocols for the management of this rare condition.

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REFERENCES

1. Ghosh A, Kundu P. Hepatitis A with superadded salmonella paratyphi a infection presenting with exudative pleural effusion and acalculous cholecystitis. *Indian Pediatr.* 2017;54:514-5.
2. Rook M, Rosenthal P. Hepatitis A in Children. *In: Maureen*

MJ, editor. *Viral hepatitis in children: unique features and opportunities.* 1st ed. New York: Springer; 2010.p.14-5.

3. Lauletta G, Russi S, Pavone F, Vacca A, Dammacco F. Direct-acting antiviral agents in the therapy of hepatitis C virus-related mixed cryoglobulinaemia: A single-centre experience. *Arthritis Res Ther.* 2017;19:74.
4. Jay A, William F. Acute and Chronic Viral Hepatitis. *In: Frederick J, Ronald J, William F, editors. Liver disease in children.* 3rd ed. New York: Cambridge University Press; 2007.p.369-82.
5. Munoz-Martines SG, Diaz-Hernandez HA, Suarez-Flores D, Sanchez-Avila JF, Gamboa-Dominguez A, Gracia-Juarez I, *et al.* Atypical manifestations of hepatitis A virus infection. *Rev Gastroenterol Mex.* 2018;83:134-43.

Cephalic Tetanus Presenting as Ptosis

A 7-year-old unimmunized boy developed cephalic tetanus following chronic suppurative otitis media. We wish to emphasize that possibility of cephalic tetanus should be considered in an unimmunized child presenting with ptosis.

Keywords: *Immunization, Management, Otitis media.*

Tetanus can be generalized or localized. Cephalic tetanus is a rare variant of localized tetanus, involving 1 to 3% of total reported cases [1]. The objective of this report is to describe a case of tetanus secondary to chronic suppurative otitis media in an unimmunized child, presenting with isolated ptosis, an unusual presentation of cephalic tetanus.

A 7-year-old boy belonging to a low socioeconomic status family, presented in the pediatric casualty. Five days prior to hospital admission, parents noticed child having oral ulcers secondary to tongue biting. Since 3 days, he was having multiple episodes of intermittent tightening of all 4 limbs lasting for few seconds and clenching of teeth during which he sustained multiple tongue bites. During these events, child was conscious, no facial deviation/asymmetry and no bladder bowel incontinence. There was no history of fever, trauma, animal bite or recent vaccination history. There was no history of difficulty in feeding, breathing or arching of body/opisthotonus. Child was having left ear discharge on-and-off since two years of age, for which he was taking treatment from local practitioner.

On examination at admission, child was conscious, following commands, and hemodynamically stable. On oral examination showed multiple cuts on tongue with oral ulcers. There was reflex spasm of masseters on

touching the posterior pharyngeal wall (spatula test - positive). Left eye ptosis was present. Rest of the cranial nerves examination including pupillary reactions were normal. During examination child had tightening of all four limbs with teeth clenching lasting for less than a minute. He was conscious during the event which was self-aborted. CNS examination done after this event was normal. Baseline hematological work-up, liver and renal function tests and serum calcium and electrolytes were normal. Lumbar puncture and cranial computed tomography (CECT Head) were normal.

By the history, examination and his unimmunized status, tetanus was strongly suspected and was started on treatment for tetanus in the form of intravenous. Ceftriaxone and metronidazole, along with supportive management. Intramuscular and intrathecal tetanus immunoglobulin (TIG) along with one dose of tetanus toxoid was given. Intravenous diazepam was started to control spasms. He was monitored for neurological and respiratory deterioration. Child started improving clinically, tetanic spasms reduced and diazepam was tapered slowly and was discharged on oral diazepam on the 14th day of admission. The parents were counselled and planned for catch up immunization. He was followed-up one week after discharge, with full recovery of ptosis, no spasms. The otorrhoea had ceased.

Tetanus is strictly a clinical diagnosis, there is no laboratory test to confirm it. In our case the diagnosis was strongly suspected by the history, examination and unimmunized status of child.

Cephalic tetanus is defined as a combination of trismus and paralysis of one or more cranial nerves. The facial nerve is most frequently implicated but cranial nerves III, IV, VI, VII, and XII may also be affected [2,3]. Facial nerve palsy without trismus at presentation could be the first sign of