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Case Report

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Immune thrombocytopenia due to hepatitis a virus: case report and review of literature

Abstract

Acute hepatitis due to hepatitis A virus (HAV) is usually a self-limiting disease among children. Autoimmune complications including immune thrombocytopenia (ITP) are rare. We report an 8 year-female with massive upper gastrointestinal bleed and diagnosed to have ITP associated with acute HAV infection.

Keywords: hepatitis A virus, childhood, immune thrombocytopenia

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Suresh Kumar, Abhijit Choudhary, Arun Bansal, Deepak Bansal, Sunit Singhi
Department of Pediatrics, Graduate Institute of Medical Education and Research (PGIMER), India

Correspondence: Arun Bansal, Additional Professor, Department of Pediatrics, Advanced Pediatric Center, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Tel +919815455002, Email drarunbansal@gmail.com

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Abbreviations: HAV, hepatitis A virus; ITP, immune thrombocytopenia; GI, gastrointestinal; aCL, anticardiolipin; APLA, antiphospholipid antibodies; IVIG, intravenous immunoglobulin

Introduction

Hepatitis A virus (HAV) infection is the most common cause of infectious hepatitis among children in India.[1,2] Hematological manifestations such as aplastic anemia, leucopenia, hemophagocytic syndrome, and immune thrombocytopenia (ITP) have been rarely described with HAV infection.[3–12] We report a child with ITP due to acute HAV infection who presented with upper gastrointestinal (GI) bleed.

Case report

An 8-year old previously well female presented with history of fever and vomiting for 10 days; jaundice 7 days; and 3-4 episodes of hemetemesis and malena in last 2 days with moderate to massive blood loss. There was no history of rash, myalgia, arthralgia, or drug intake. There was no history of jaundice in close contacts. At admission, she was in hypotensive shock due to massive GI blood loss which was managed with oxygen support, intravenous normal saline bolus and urgent blood transfusion. On examination, she was a febrile, had severe pallor and icterus. There was no lymphadenopathy, edema, rash or arthritis. She had tender hepatomegaly (liver span 13cms). There was no splenomegaly or free fluid or abnormality in other systems.

Investigations at admission revealed hemoglobin 3.2 gm/dL, platelet count 14,000/mm^3, total leucocyte count 10,800/mm^3 (neutrophils 65%, lymphocytes 27%, monocytes 7%, and eosinophils 1%), and reticulocyte count of 2%. Liver function tests revealed total bilirubin 2.3 mg/dl (conjugated 0.91 mg/dl), aspartate transaminases 900U/L (normal: 15-45U/L), alanine transaminase 1125U/L (normal: 15-35U/L), alkaline phosphatase 230U/L (normal: 100-320U/L), total serum protein 6.1 gm/dl, and serum albumin 3.3gm/dl. Prothrombin time was 20 seconds, prothrombin index 70%, activated partial thromboplastin time 34 second, international normalized ratio 1.5 seconds, fibrinogen 2 gm/dl, and negative d-dimers. Serum electrolytes and renal function tests were normal. Blood culture, peripheral smears for malarial parasite, dengue IgM and IgG, widal, leptospira serology, scrub typhus IgM ELISA, and HIV ELISA were negative. IgM anti-HAV antibody was positive. IgM anti-hepatitis E antibody, hepatitis B surface antigen and IgM anti-hepatitis C antibody were negative. Abdominal sonography revealed hepatosplenomegaly, mild bilateral pleural effusion, mild ascites, and thick gall bladder wall.

She continued to have GI bleed during the hospital stay for which she received packed red cell transfusion thrice and multiple platelet transfusion. For persistent thrombocytopenia (platelet count of 5,000/cumm), she underwent bone marrow examination on day 4 which revealed normocellular marrow spaces with megakaryocytic hyperplasia consistent with ITP. She was given anti-D immune globulin on day 5 of hospital stay and after 48 hours her platelet count improved to 24,000/mm^3 along with resolution of GI bleeding. She was discharged after hospital stay of 10 days with hemoglobin of 8.1 gm/dl, platelet count of 36,000/mm^3, and decreasing liver enzymes. At 3 months after discharge, she was clinically well with platelet count of 2,47,000/mm^3.

Discussion

ITP is a self-limiting disorder presenting with a short history of muco-cutaneous bleeding in children of either sex between age group of 2-10 years. The incidence is about 4/1,00,000 children/year. It may follow a viral infection or immunization and is caused by an inappropriate immune response.[13,14] Number of viruses has been implicated in the etiopathogenesis including: HIV, hepatitis C virus, hepatitis B virus, varicella-zoster virus, rubella, influenza, Epstein-Barr virus, parvovirus B19, and dengue virus.[13–16] Few cases of ITP associated with HAV infection has been reported in children (Table 1).[3–12]

Thrombocytopenia associated with viral infections may result from bone marrow depression; increased platelet consumption due to disseminated intravascular coagulopathy, hemophagocytosis, and hypersplenism; or immune-mediated peripheral destruction of platelets in reticuloendothelial system, particularly in spleen (principal mechanism).[5,7,13–15] Thrombocytopenia occurring during the course of HAV may be due to presence of transient anticardiolipin (aCL) and antiphospholipid antibodies (APLA); anti-platelet antibodies;

or non-specific deposition of immune complexes at the platelet surface.[11,17–19] Autoantibodies against glycoproteins over platelet surface (particularly IIb/IIIa) can be detected in 60–70% of cases, but are of no prognostic and diagnostic significance.[13,14]

Index child was managed as ITP due to HAV infection and treated with anti-D immune globulin following which she had good clinical and hematological response. The treatment options include intravenous immunoglobulin (IVIG), oral steroids, and anti-D immunoglobulin. IVIG raises the platelet count rapidly (usually within 48 hours) and is therefore the treatment of choice for life threatening hemorrhage. Steroids are usually given at a dose of 1–2mg/kg/day for up to 2 weeks. Anti-D immunoglobulin is effective in Rh (D) positive children with similar efficacy to IVIG and has advantage of being given as a rapid single injection and less cost.[13,14] Treatment of ITP even in presence of very low platelet count may not be required because risk of serious bleeding is less and outcome is favorable even without treatment.[13–15] Currently, there is trend toward conservative management of children with ITP.[19,20]

Table 1 Clinico-laboratory profile, treatment and outcome of children with ITP due to HAV infection

S. No.	Author, year (reference)	n	Age, sex	Clinical presentation	Treatment	Outcome
1	Index case	1	8years, female	Fever, vomiting, jaundice and upper GI bleed. Platelet count 5000/cumm, ALT 1125 U/l, AST 900 U/L, HAV-IgM positivity, bone marrow suggestive of ITP.	Anti-D	Improved
2	Leblebısatan et al.[3]	2	8years, male	Diffuse ecchymosis on both extremities. Platelet count 10,000/cumm. ALT 350 U/L, AST 470 U/L, HAV-IgM positivity.	IVIG 1gm/kg for 3 days	Improved
			4years, male	Skin bleeds. Platelet count 1,000/cumm. ALT 1262 U/L, AST and 1143 U/L, HAV-IgM positivity, bone marrow suggestive of ITP.	IVIG 1g/kg for 3 days followed by oral methyl-prednisolone 2mg/kg	Improved
3	Samanta T et al.[4]	2		Thrombocytopenia, bone marrow suggestive of ITP.	IVIG	Improved
				Isolated thrombocytopenia.	No treatment	Improved
4	Tanir G et al.[5]	1	4years, male	Skin bleeds. Platelet count 2000/cumm, ALT 840 U/L, AST 1030 U/L, HAV-IgM positivity, bone marrow suggestive of ITP, and negative direct and indirect Coombs tests, antinuclear antibody, anti-ds-DNA, anticardiolipin and antiphospholipid antibodies.	IVIG 0.8gm/kg for 1 day	Improved
5	Venkataravanamma P et al.[6]	1	12years, female	Hematemesis, menorrhagia, purpura, and hypotensive shock. Platelet count 5000/cumm, ALT 1837 U/L, AST 2116 U/L, HAV-IgM positivity, and normal bone marrow.	No treatment	Improved
6	Shenoy R et al.[7]	1	8years, male	Generalized petechial rash and gum bleeding. Platelet count 5000/cumm, ALT 1254 U/L, AST 1116 U/l, HAV-IgM positivity, bone marrow suggestive of ITP, and negative Coombs test and antinuclear antibody.	IVIG 1gm/kg followed by prednisolone 2 mg/kg/day	Improved
7	Sakha HS et al.[8]	1	6years, male	Epistaxis, mouth bleeding, skin bleeds. Jaundice 10 days back. Platelet count <1000/cumm, ALT 171 U/L, AST 109 U/L, HAV-IgM positivity, and bone marrow suggestive of ITP, and negative antinuclear, anti-DNA and anti-smooth muscle antibodies..	IVIG 1gm/kg for 3 days	Improved
8	Scott JX et al.[9]	1	4½ years, female	Hematuria, hemetemesis and skin bleeds. Platelet count 5000/cumm, AST 2070 U/L, ALT 2150 U/L, HAV-IgM positivity, bone marrow suggestive of ITP.	Steroids	Improved

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Table Continued...

S. No.	Author, year (reference)	n	Age, sex	Clinical presentation	Treatment	Outcome
9	Avci Z et al.[10]	1	13years, female	Jaundice 6 weeks back when laboratory investigation revealed elevated bilirubin; ALT 1400 U/L, AST 1900 U/L, and HAV-IgM positivity. Presented with epistaxis and skin bleeds for 3 days. Platelet count 30000/cumm, bone marrow suggestive of ITP along with erythrophagocytosis, negative direct and indirect Coombs test, ANA, and anti-dsDNA, and IgM aCL, and slightly increased IgG aCL.	Oral methyprednisolone 2mg/kg/day.	Improved
10	Ertem D et al.[11,12]	1	5years, female	Skin bleeds. Platelet count 2000/cumm, ALT 923 U/L, AST 1053 U/L, HAV-IgM positivity, bone marrow suggestive of ITP, negative antinuclear, anti-ds-DNA, anti-smooth muscle and anti-liver-kidney microsomal antibodies, and elevated IgM anticardiolipin antibodies.	IVIG 1gm/kg	Improved

Celik et al.[21] studied the efficacy, cost, and effects of anti-D immunoglobulin, methylprednisolone, and IVIG in children with newly diagnosed ITP and found no difference between platelet counts before treatment and on day 3 of treatment. However, platelet counts at day 7 were lower in the methylprednisolone group than in the IVIG group. They also noticed that the mean cost of IVIG was 7.4 times higher than anti-D and 10.9 times higher than methylprednisolone. Alioglu et al.[22] demonstrated that IVIG (400mg/kg/day for 5 day) lead to a significant increase in platelet count at 24 hour, 48 hour, 72 hour, 7 day and 30 day when compared to anti-D (50µg/kg and 75µg/kg) among newly diagnosed ITP in children. Most of the case reports of children with ITP due to HAV have been treated with IVIG with or without steroids and have shown good clinical and hematological response (Table 1). In index patient, we preferred anti-D immunoglobulin 75µg/kg over IVIG due to financial reasons. Steroids were deferred because of active GI bleeding.

We could not find any evidence of hemophagocytic syndrome or bone marrow suppression. However, increased megakaryocytes in bone marrow aspiration and the rapid response of the platelet counts to anti-D therapy suggested immune-mediated peripheral platelet destruction, though we could not measure aCL, APLA, or anti-platelet antibodies. Index case and other case reports (Table 1) suggest that ITP does not seems to be an indicator of a fulminant course for HAV and the morbidity may be directly related to low platelet count leading to serious bleeding.

Conclusion

ITP is rarely associated with acute HAV infection. Bone marrow examination is necessary to determine the cause of thrombocytopenia. ITP due to HAV infection seems to have good outcome and treatment options include IVIG, Anti D, or steroids.

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None.

Conflicts of interest

The authors declare there is no conflict of interests.

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