Leucopenia: A Rare Extrahepatic Manifestation of Acute Hepatitis A

Dear Sir, Hepatitis A infection is a common cause of viral hepatitis in developing world. It is acquired by feco-oral transmission. Patients usually have self-limited disease with uneventful recovery. Extrahepatic manifestations of acute hepatitis A are uncommon and include rash, arthralgias and other rare ones. Hematologic effects include thrombocytopenia and rarely red cell aplasia and aplastic anemia. We recently came across a case of a young female who presented with prodromal symptoms with isolated leucopenia.

A 29-year-female presented with low-grade fever, vomiting and right upper quadrant abdominal pain for 3 days. She denied history of jaundice in past, surgical intervention, exposure to potentially hepatotoxic drugs, alcohol intake or blood transfusion; there was no suggestion of chronic liver disease. Examination revealed mild icterus, tender hepatomegaly, there was no evidence of splenomegaly, lymphadenopathy, ascites, pedal edema or flapping tremors.

Liver function tests and blood counts and their trend are summarized in Table 1. Evaluation showed leucopenia with adequate platelet count and hemoglobin, IgM anti-HAV was positive. Acute hepatitis E, B and C were ruled out. Peripheral smear showed reduced leucocytes with differential count percentage within normal range (predominantly neutrophils), no atypical lymphocytes or other abnormal cells were found and platelet counts were normal. Ultrasound of the abdomen showed mild hepatomegaly, normal portal vein diameter and ruled out splenomegaly and ascites. Absence of fever, normal serum procalcitonin levels and blood culture ruled out infective etiology of leucopenia. She was treated symptomatically with intravenous fluids and anti-emetics and showed gradual improvement in symptoms, and was discharged on day four in a stable condition. Leucopenia and liver function tests improved on follow up. She continues to be asymptomatic on follow up of three months from the onset of symptoms.

Our patient had prodromal symptoms due to acute hepatitis A. She had leucopenia, which improved on the follow up. There were no atypical lymphocytes, which have been described in association with hepatitis A and several other viral fevers. Although hematologic complications including leucopenia occur more frequently in pediatric patients with acute hepatitis A, they have been rarely described in

adults.^{1,2} Hematologic manifestations rarely dominate the clinical picture as it was seen in our patient.

In 1961, Kivel described two patients with acute hepatitis in whom hematologic features dominated the clinical course; these manifestations were thought to represent systemic effects and likely bone marrow suppression which are common to several viral illnesses.³ However, the hepatotropic viruses were not known at that time. Of the viruses causing hepatitis, herpes simplex virus is most often associated with leucopenia.⁴ The likely mechanism appears to be bone marrow suppression due to direct cytotoxicity of the virus or immune mediated destruction of cell lines.⁵ Theoretically, severe neutropenia may predispose to infections, however, to best of our knowledge, such an instance has not been reported with hepatitis related leucopenia. Our patient had adequate absolute neutrophil count and it was confirmed on the peripheral smear.

To conclude, isolated leucopenia is uncommon hematologic complication of acute hepatitis A, it has spontaneous recovery in majority of patients and should be recognized to avoid unnecessary investigations, as a follow up usually suffices.

CONFLICTS OF INTEREST

The authors have none to declare.

REFERENCES

1. Çetinkaya B, Tezer H, Özkaya Parlakay A, Revide Sayli T. Evaluation of pediatric patients with hepatitis A. *J Infect Dev Ctries*. 2014;8(March):326–330.
2. Cunha BA, Teper RS, Raza M. Fever in a traveler returning from the Amazon. Do not forget hepatitis A. *IDCases*. 2016;4:18–19.
3. Kivel RM. Hematologic aspects of acute viral hepatitis. *Am J Dig Dis*. 1961;6:1017–1031.
4. Kaufman B, Gandhi SA, Louie E, Rizzi R, Illei P. Herpes simplex virus hepatitis: case report and review. *Clin Infect Dis*. 1997;24:334–338.
5. Rosenfeld SJ, Young NS. Viruses and bone marrow failure. *Blood Rev*. 1991;5(June (2)):71–77.

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Table 1 Summary of Investigations and Their Trend.

Day from onset of illness	Total leukocyte count ($10^9/L$)	Nutrophils (%)	Lymphocyte (%)	Platelet count ($10^9/L$)	Hemoglobin (gm/dL)	Total bilirubin (mg/dl)	Direct bilirubin (mg/dl)	SGOT (units per liter)	SGPT (units per liter)	Protein/albumin (g/dL)	INR
4	2.2	57	37	160	12.3	2.49	1.74	2340	2400	7.4/3.8	1.1
5	3.9	–	–	–	–	–	–	–	–	–	–
6	1.9	–	–	–	–	3.33	2.18	1500	1940	5.8/3	1.06
8	2.7	–	–	–	–	–	–	–	–	–/3.2	1.04
21	–	–	–	–	–	0.97	0.8	577	653	7.8/4	–
36	4.26	–	–	–	–	1.47	1	229	422	8.6/4.3	–

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