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Case Report

Chronic Hepatitis B Reactivation Associated with Agranulocytosis - A Case Report

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Abstract

Hepatitis B virus is a hepatotrpic virus which can lead to progressive liver disease in form of cirrhosis and HCC. Variety of extrahepatic manifestations are to occur with acute or, more commonly, chronic heptits B. We present an unusual cause of isolated neutropenia associated with Chronic Hepatitis B reactivation. Neutropenia, is defined as an Absolute Neutrophil Count (ANC) below 1.5×10^9/L. ANC of 0.2×10^9/L or less is referred to as "agranulocytosis" carries a risk of severe, life-threatening infections with susceptibility to opportunistic organisms [1]. Neutropenia can be classified as acute or chronic; extrinsic or intrinsic. Acute neutropenia is most commonly associated with viral infection, bacterial infection and acute malaria. Viral infections presenting with neutropenia include Human Immunodeficiency Virus (HIV), infectious mononucleosis, Cyto MegaloVirus (CMV), Hepatitis A virus, and the many viral exanthematous diseases. Chronic bacterial infections and some inflammatory & autoimmune diseases (e.g., rheumatoid arthritis and sarcoidosis) are also associated with splenomegaly and neutropenia. Chemotherapeutic agents and a wide variety of other medications can cause acute isolated neutropenia [2,3].

Keywords: Reactivation; Hepatitis B; Isolated Agranulocytosis; Leucopenia; Neutropenia

Abbreviations

HIV: Human Immune Deficiency Virus; CMV: Infectious Mononucleosis Cytomegalovirus; HTN: Hypertension; DM: Diabetes Mellitus; CM: Centimetre; CBC: Complete Blood Count; Hb: Haemoglobin; G/Dl: Gram Per Decilitre; TLC: Total Leucocyte Count; ANC: Absolute Neutrophilic Count; PLT: Platelet; LFT: Liver Function Test; LFT: Total Bilirubin; Mg/Dl: Milligram Per Decilitre; D.Bil: Direct Bilirubin; SGOT: Serum Glutamic–Oxaloacetic Transaminase; U/L: Unit Per Litre; SGPT: Serum Glutamic Pyruvic Transaminase; ALP: Alkaline Phosphatase; GGTP: Gamma- Glutamyl Trans peptidase; S.Alb: Serum Albumin; S.Glob: Serum Globulin; INR: International Normalized Ratio; USG: Ultrasonography; Igm: Immunoglobulin M; HAV: Hepatitis A Virus; HEV: Hepatitis E Virus; HCV: Hepatitis C Virus; Hbsag: Hepatitis B Surface Antigen; Hbeag: Hepatitis B E Antigen; Hbeab: Hepatitis B E Antibody; Hbc: Hepatitis B Virus Hepatitis B Core; DNA: Deoxy Ribo Nucleic Acid; IU/Ml: International Unit Per Millilitre; LVEF: Left Ventricular Ejection Fraction; B/L: Bilateral; LDH: Lactate Dehydrogenase; HRCT: High Resolution computed Tomography; G6PD: Glucose 6 Phosphate Dehydrogenase; I.V: Intravenous; G-CSF: Granulocyte Colony Stimulating Factor.

Case Presentation

Mrs AB, 50 year with history of yellow discoloration of eyes and urine for last 2 months , high grade fever with chills for last 4 days, Vomiting , poor oral intake. She has no past history of HTN, DM, Hypothyroidism, blood transfusion, previous surgery, jaundice or blood transfusion. On examination, she was febrile (temp 1030F), pallor, icterus, pedal edema and hepatomegaly (2CM below costal margin). Investigation revealed CBC Hb - 11.8g/dl TLC - 1.29 $x10^9$/L, (ANC – 0.24$x10^9$L), PLT- 292 $x10^9$/L, Peripheral smear showed - leucopenia only , LFT - T. Bil - 29.2 mg/dl, D. Bil - 25.1 mg/dl, SGOT - 417 U/L, SGPT - 304 U/L, ALP - 115 U/L , GGTP - 51U/L, S. Alb -2.1 g/dl, S. Glob 2.4g/dl, INR - 1.71, USG abdomen shows enlarged liver (15.6cm), reduced echogenicity , splenomegaly (12.9 cm) shows normal echogenicity . Viral markers – IgM HAV / IgM HEV /Anti HCV / HIV I & II were all negative, HBs Ag was positive, HBe Ag -negative, HBe Ab -positive, Total IgM HBV Core antibody - positive, IgM HBc – positive , HBV DNA quantitative - 66420 IU/ml. Patient continued to have fever spikes during hospital admission. Patient was started on I.V. Fluids I.V. antibiotics, Tenofoviralafenamide 25 mg/day under barrier nursing care and isolation. Bacterial and Viral serology viz. Ricketsial, leptospira, dengue, brucella, typhidot, Malaria Antigen, Epstein Barr virus and CMV serology were all negative. LDH-221U/L, G6PD levels- normal, Vitamin B 12 and folate levels were normal. ANA, antids DNA, Coombs test were negative. S Procalcitonin - 8.73ng/ml, Urine culture and blood culture were sterile. Echocardiography shows no vegetation with LVEF 55 %, Bone marrow examination showed normal erythroid and megakaryocyte series with marked leucopenia and neutropenia. HRCT chest showed B/L lower lobe atelectasis with pleural effusion. UGI endoscopy revealed fungal esophagitis, small hiatus hernia, and no varices. Patient also given antifungals for fungal esophagitis and G-CSF for persistent neutropenia. Patient gradually improved with treatment, TLC improved, LFT improved and patient discharged after two weeks in stable condition. At discharge LFT was Total Bilirubin – 6 mg/dl, D. Bil - 5.8mg/dl, SGOT/SGPT - 142.3 U/L/ 119.8U/L, HB 9.2g/dl, TLC - 7.79 $x10^9$/L, N 59%, PLT 375 $x10^9$/L.

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Discussion and Conclusion

Our patient had reactivation of Hepatitis B as evident by deranged LFT and Hepatitis B serological markers (HBs Ag was positive, HBe Ag – neg, Hbe Ab-pos, Total HBV Core antibody– reactive, IgM Anti HBc-positive, HBV DNA – 66420 IU/ml). Reactivation of chronic hepatitis B occurs with mild or inactive hepatitis B patients on immunosuppressive agents or immunodeficient state for e.g. after cancer chemotherapy, with immunomodulator therapy, steroids for autoimmune diseases, after HIV infection, after organ transplantation and can be even spontaneous [4]. Extrahepatic manifestations of chronic hepatitis B reflect immune complex phenomena such as vasculitis, immune complex nephritis, arthritis, a serum-sickness-like illness, and polyarteritis nodosa. Immune thrombocytopenia and leucopenia are rarely associated with hepatitis B [5,6].

Neutropenia as in our case is a part of extrahepatic manifestation of chronic HBV infection. The pathophysiology of these manifestations has still not been fully elucidated, but the best accepted theories are that they are caused by circulating autoantibodies, deposition of immune complexes, local formation of immune-induced viral antigens, autoantibodies generated by the virus (which react against tissue), and/or development of a direct viral reaction at extrahepatic sites [7]. Extrahepatic manifestations are more commonly associated with hepatitis C virus (HCV) infection [8]. We had excluded all other common causes of bacterial infection such as malaria, typhoid fever, Shigella enteritis, brucellosis, and tuberculosis as well as viral infections including human immunodeficiency virus (HIV), infectious mononucleosis, cytomegalovirus, hepatitis A, Hepatitis C and the viral exanthematous diseases leading to leukopenia were also ruled out in our patient. This case report is similar to the report of Kumar et al. 2013 [9] where Hepatitis B presented as primary thrombocytopenia and leucopenia without evidence of cirrhosis but our patient had only leucopenia.. Two case reports previously published also associated agranulocytosis with viral hepatitis but not conclusively linked to hepatitis B infection [10]. Fever in the setting of profound neutropenia is a medical emergency requiring immediate treatment with broad spectrum antibiotics. Neutropenia has been reported in chronic hepatitis B due to several causes. The most common cause is hypersplenism resulting from cirrhosis and portal hypertension. Our patient had splenomegaly but no features of cirrhosis or hypersplenism. Isolated neutropenia was present and no thrombocytopenia as expected in hypersplenism. Rarely patient can have neutropenia due to other viral infections (non A-E), bacterial causes and autoimmune hepatitis which was ruled out in our patient. Patients with ANC of 0.2 x10^9/L or less invariably requires hospital admission for I.V. antibiotics and supportive treatment. Our patient was initially treated with third generation cephalosporins followed by carbapenems and fluconazole (in view of fungal esophagitis). In view of severe neutropenia she was given Injection G-CSF. In view of reactivation of chronic hepatitis B patient was started on Tenofovir alafenamide 25mg. Except for chronic hepatitis B, no other cause of neutropenia established after intensive investigations. Evidence of cirrhosis was not present in our patient which may have caused leukopenia usually with thrombocytopenia which was also not present in our patient. To the best of our knowledge, this is the first case report of agranulocytosis associated with reactivation of chronic hepatitis B in the world. To conclude, Patient presenting with isolated neutropenia should raise the index of suspicion for chronic hepatitis B reactivation.

References

1. Dale DC, Lichtman MA, Kipps TJ, Kaushansky K, Beutler B, Seligsohn U, Prchal JT and Williams. New York: Mcgraw-Hill. 2010; 939– 950.
2. Jacobson CA, Berliner N, Neutropenia, Greer JP, Arber DA, Glader B, et al, eds. Wintrobe's Clinical Hematology. 13th ed. Philadelphia, PA: Lippincott, Williams & Wilkins. 2014; 1279- 89.
3. Husain EH, Mullah-Ali A, Al-Sharidah S, Azab AF and Adekile A. Infectious etiologies of transient neutropenia in previously healthy children. Pediatr Infect Dis J. 2012;31:575–577.
4. Fattovich G, Brollo L, Alberti A, Realdi G, Pontisso P, Giustina G, et al. Spontaneous reactivation of hepatitis B virus infection in patients with chronic type B hepatitis. Liver. 1990;10:141-146.
5. Jay H Hoofnagle.Reactivation of Hepatitis B. HEPATOLOGY. 2009; 49: 156-165.
6. Pyrsopoulos NT and Reddy KR. Extrahepatic manifestations of chronic viral hepatitis. CurrGastroenterol Rep. 2001; 3:71–8.
7. Han SH. Extrahepatic manifestations of chronic hepatitis B. Clin Liver Dis. 2004; 8: 403–18.
8. ShikshaKedia, Vijaya Raj Bhatt, Sandeep Kumar Rajan, Pavan Kumar Tandra, Radwa A El Behery and MojtabaAkhtari. Benign and Malignant Hematological Manifestations of Chronic Hepatitis C Virus Infection. 2014; 5: 179–192.
9. Sanjay Kumar. Hepatitis B presenting as primary thrombocytopenia and leucopenia without evidence of cirrhosis JIACM. 2013; 14: 169-70.
10. Nagaraju M, Weitzman S and Baumann G.Viral hepatitis and agranulocytosis. Am J Dig Dis. 1973; 18:247-52.