short report
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APLASTIC ANEMIA AFTER NON-A, NON-B, NON-C HEPATITIS.

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ABSTRACT

Recent reports suggest that non-A, non-B, non-C viruses might not be uncommon etiologic agents of hepatitis-associated aplastic anemia.

A 52-year-old woman without previous contact with toxic substances or drugs developed severe aplastic anemia sixteen days after the onset of acute hepatitis. Even after exhaustive serologic testing for hepatotropic viruses and PCR study for hepatitis C virus the etiologic agent could not be demonstrated. Evolution was fatal despite treatment.

In this case the time lapse between the onset of hepatitis and the development of aplasia was shorter than in previously referred incidents. This fact supports the hypothesis that different non-A, non-B, non-C agents might be implicated in hepatitis-associated aplasia.

Key words: aplastic anemia, non-A non-B non-C hepatitis, post-hepatitis aplasia

Over the past five years second generation assays for hepatitis C virus (HCV) have led to an improvement in its detection.[1] Accordingly, descriptions of hepatitis C-associated aplastic anemia have been reported.[2] However, cases of non-A, non-B, non-C hepatitis associated aplasia have been described recently.[3] Such a fact suggests that a non-A, non-B, non-C agent might be implicated in many cases of hepatitis-associated aplasia (H-AA). Herein we report a well-documented case of H-AA in which no known hepatitis virus could be proven either by serological methods or by genomic procedures.

Case report

A 52-year-old woman was referred to our hospital because of jaundice and petechiae. She had no previous history of contact with toxic substances or drugs, nor had she received blood transfusions or blood derivatives. Prior to admission she had complained of weakness and anorexia. Choluria and acholia appeared and jaundice worsened in the following days. Acute hepatitis was diagnosed and she was followed as an outpatient. Sixteen days after the onset of hepatitis generalized purpuric lesions were noted. She was admitted to the hospital. Physical examination showed intense jaundice, generalized purpura and tender hepatic enlargement 4 cm below the right costal margin. Transaminase (AST/ALT = 842/1230 U/L) and bilirubin values (485 μmol/L) were elevated. Peripheral blood testing showed Hb 7.0 g/dL, Hct 21%, reticulocyte count 0%, WBC count 0.3×10^9/L and platelet count 11×10^9/L. Bone marrow aspirate was acellular and bone marrow biopsy revealed an absence of hematopoietic cells in an edematous and hemorrhagic stroma. HbF level was 1%. An ELISA serologic study prior to hospital admission was negative for hepatitis A IgM, HBsAg, HBcAb, HCV IgG and IgM (Ortho second generation EIA test),

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cytomegalovirus (CMV) and Epstein-Barr virus (EBV).

A diagnosis of severe aplastic anemia was established according to international criteria[4] and treatment with horse anti-lymphocyte globulin (Lymphoglobuline®, Institut Merieux, Lyon, France) was started at 2 vials for every 10 Kg bw for 6 days. Sera collected 20 and 40 days after admission were tested for the presence of HBsAg, HBsAb, HBcAg, HBeAg, HVA IgM, anti-HCV, EBV IgM and CMV IgG and IgM. Results were all negative. Specific HCV-RNA sequences were investigated by nested-PCR using primers derived from the well-conserved 5' non-coding region, once again with negative results. In addition, serological tests (immunoelectrophoresis using an enzyme-linked immunosorbent assay) for human parvovirus B19 were performed retrospectively on stored sera collected 20 and 40 days after admission. These were also all negative (IgM and IgG). Although liver enzymes and bilirubin returned to normal by the third week of admission, no hematological response to treatment followed. Ultimately, the patient died of bilateral fungal pneumonia 47 days after admission.

Discussion

Severe aplastic anemia developed in our patient shortly after acute hepatitis. Several reports on severe aplastic anemia following non-A, non-B, non-C hepatitis have recently been published. The variability of the time lapse between onset of hepatitis and the development of aplastic anemia indicates that different viruses or other infectious agents may possibly be responsible for post-hepatitic aplastic anemia. For the case referred herein this time lapse was 16 days, significantly shorter than that of previously described cases.[3] No etiologic agent could be demonstrated despite repeated serological screening for hepatotropic viruses. A possible infection due to human parvovirus B19 causing or coinciding with hepatitis was also excluded in this patient, since IgM and IgG antibodies against this virus were not present in two samples of sera collected at 20 and 40 days post admission. Although the last sera was collected 40 days after admission, and this may be too early to diagnose HCV even with second generation tests, negative HCV-PCR results exclude almost all possibility of a false negative result with the HCV serological assay. This case supports the hypothesis that hepatitis-associated aplasia after non-A, non-B, non-C hepatitis could be much more frequent than initially thought. The possibility of more than one agent being implicated is supported by the evidence of different time lapses between the onset of hepatitis and the development of aplasia.[3,5,6] The prognosis of the patient described here was poor, similar to that for the other published cases. Only anti-lymphocyte globulin could be administered; due to hepatic involvement, the possible efficacy of cyclosporin A[7,8] could not be tested.

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