Hepatitis-associated aplastic anemia: successful outcome following immunosuppressive therapy

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Hepatitis-associated aplastic anemia is an uncommon variant seen in young, previously healthy individuals. The pancytopenia follows hepatitis by a few weeks and is usually severe and prolonged. Bone marrow transplantation remains the cornerstone of therapy. However, immunosuppressive therapy has been found to be effective. We report an 8-year-old girl who had non-A, B, C and E hepatitis-associated severe aplastic anemia. She became transfusion-independent and had consistent, albeit incomplete recovery after immunosuppressive therapy with antithymocyte globulin and cyclosporine. [Indian J Gastroenterol 2005;24:175-176]

A plastic anemia (AA) is a bone marrow failure syndrome, presumed to be of immune origin. In most cases, aberrant immune response is triggered by exposure to environmental agents such as drugs, toxins or chemicals. Aplasia is estimated to develop in less than 0.07% of all pediatric hepatitis cases. In most such cases, serological tests for hepatitis A, B and C viruses are negative. We describe our experience in one such patient.

An eight-year-old girl presented to us with history of spontaneous skin bleeds for one month. There was no history of pallor or fever. She had never received blood transfusion. She had history of jaundice three months back, which lasted for one month. Investigations done then revealed total serum bilirubin 24 mg/dL, (conjugated fraction 60%), Serum ALT and AST levels were 944 and 1056 U/L (normal <15), respectively. Serum alkaline phosphatase level was 22 KAU/L (normal 5-12), Serum total protein was 5.3 g/dL with albumin 2.5 g/dL. Platelet count was 0.5%. Total leukocyte and absolute neutrophil counts were 10,000/mm3. Serum bilirubin was within normal limits; ALT and AST levels were 42 and 40 U/L, respectively, and alkaline phosphatase level was 18 KAU/L. Bone marrow aspiration was dry and trephine biopsy showed hypocellular marrow with depression of all three cell lines. Anti-nuclear, anti-mitochondrial and anti-liver-kidney-microsomal antibodies were negative.

References


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a 15.6 cm x 13 cm x 6 cm multi-loculated chest wall abscess on the right side and right-sided pleural effusion; in addition there were osteomyelitic changes in the manubrium, axillary lymphadenopathy, and a small apical lung lesion. Considering the possibility of tubercular osteomyelitis and cold abscess he was started on non-hepatotoxic anti-tubercular drugs. However he developed progressive desaturation and hypotension needing mechanical ventilation and inotropic supports, and eventually expired.

Bacteremia in liver cirrhosis is well known, the risk appearing to increase with more advanced Child class. _Escherichia coli_ is the most frequently isolated organism. Susceptibility to infection in cirrhosis is related to impaired defense mechanisms due to impaired reticuloendothelial function, portosystemic shunting, increased intestinal permeability. Recurrent bacteremia may also be due to bacterial factors that confer a survival advantage (e.g., adhesins that facilitate mucosal colonization).

Infections in atypical sites, often secondary to previous episodes of bacteremia, can often pose a diagnostic dilemma. Bacterial arthritis complicating cirrhosis has been described. Dental infections may also be a source of recurrent sepsis. However there are very few reports of skeletal infections in liver cirrhosis described in literature. They are often detected after repeated failed searches for source of infection. Co-morbidities like diabetes, alcohol abuse, and immunosuppression are factors likely to be correlated with mortality with such infections in cirrhotics.

A high index of suspicion can help in early recognition of skeletal infections as possible source of infection in cirrhotics that need appropriate and prolonged courses of antibiotics and other therapeutic interventions.
With a diagnosis of severe aplastic anemia, she was administered antithymocyte globulin (ATG) (*Atgam*; Pharmacia & Upjohn, 15 mg/Kg/day for 5 days), methylprednisolone (2 mg/Kg/day IV for 5 days, replaced by oral prednisolone on day 6, which was tapered and stopped by day 30) and cyclosporine (7.5 mg/Kg/day). Hematological parameters showed partial recovery. Her hemoglobin is maintained around 8 g/dL, with total leukocyte and absolute neutrophil counts of 3,700 and 1,800/mm³, respectively. Platelet counts have consistently been above 20,000/mm³. She has been transfusion-independent for eight months.

Hepatitis-associated aplastic anemia typically occurs in young, previously healthy individuals. A male preponderance is recognized. Hepatitis is usually severe, though self-limiting. It has been suggested that while itself unlikely to be the etiology for hepatitis-associated aplastic anemia, hepatitis A may be a surrogate marker for another microbial agent that is transmitted under related conditions. Profound pancytopenia follows the hepatic phase after 2-12 weeks. Pancytopenia is sustained, and usually culminates in death, if untreated. The extremely poor prognosis and fear of aggravating liver injury with immunosuppression had prompted earlier workers to recommend stem-cell transplantation as the mainstay of therapy. It still remains a therapeutic option in young patients for whom an HLA-identical donor is readily available.

Brown *et al* treated 10 patients of hepatitis-associated aplastic anemia with immunosuppressive therapy; 7 responded. Several reports of similar successful outcome have been published. Whereas liver enzymes typically return to normal within a month of starting therapy, hematological improvement is usually slower and incomplete. The platelet count is known to be the last to recover. Incomplete recovery of blood counts in aplastic anemia following immunosuppressive therapy or androgens is well known, and has been our experience in the past as well. Demonstration of increased activated CD8 cells and improvement with immunosuppressive therapy probably point to an immune basis for this entity.

**References**


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