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Case Report

Aplastic Anemia Associated with Dengue Fever

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Abstract

Bone marrow suppression with peripheral blood cytopenias has been reported with various viral infections. Dengue fever is frequently associated with cytopenias particularly thrombocytopenia. This may be due to either bone marrow suppression or due to immunological effect. Bone marrow aplasia however may rarely be seen in patients with dengue fever and needs to be diagnosed early, as these patients have favourable outcome with immunosuppressive therapy. We present a case of a 24 years old male patient with dengue fever who manifested persistent pancytopenia. On bone marrow biopsy, he was diagnosed to have severe aplastic anemia. He was treated with immunosuppressive therapy and steroid with a favourable response.

Key words: Dengue fever; aplastic anemia

Introduction

Aplastic anemia is a syndrome of bone marrow failure characterized by peripheral pancytopenia and marrow hypoplasia. Acquired aplastic anemia can be idiopathic or different infectious agents, drugs toxins and radiations can be identified as a trigger to disease. Viral infections are frequently associated with a transient reduction of the number of circulating blood cells as a consequence of bone marrow suppression. Bone marrow failure is frequently observed with dengue and other viruses. There are number of viruses like HAV, HBV, HCV, Parvovirus B19, Epstein-Barr virus, cytomegalovirus and dengue virus which cause bone marrow suppression which may sometimes be very severe.[1] Some generalizations can be drawn from a review of virus-associated bone marrow failure. In vivo, few data analyzing virus and host mechanisms of suppressed bone marrow function are available. In vitro, various pathogenic mechanisms have been idemtified.[2] Some viruses may interfere with the proliferation and maturation of hematopoietic progenitors by infecting stromal fibroblasts (e.g., cytomegalovirus)[3] or BM macrophages (e.g., human immunodeficiency virus).[4] Moreover, there is evidence suggesting a critical role of the host's own immune response in causing BM suppression in several virus infections.[5]

Abnormal bone marrow suppression with resultant cytopenias is one of the hallmarks of dengue virus infection. Various studies have proved that infection with dengue virus leads to direct infection of bone marrow, which is likely to be a contributing factor for transient cell suppression in the peripheral blood characteristic of acute dengue virus infection.[6] Rarely there is sever bone marrow aplasia. Incidence of aplastic anemia is higher in those areas of world where arbovirus infections are endemic.[7] The pathophysiologic mechanisms involved are diverse.[8] Direct viral targeting of bone marrow has been reasoned to be a main contributing factor. Diagnosis is made by features of bone marrow failure along with absolute reticulocytopenia.
This report describes a patient of dengue fever who developed aplastic anemia during the course of disease.

Case report

A 24 year old male was admitted with one week history of fever, vomiting, cough, petechiae and bleeding gums. He had no history of drug abuse and contact with possible toxins. His general physical examination showed bilateral cervical lymphadenopathy, liver was enlarged 2 cm and tip of spleen was palpable. His complete blood counts showed pancytopenia with Hb 7.0g/dl, white cell count 2.9 $x10^9$/ul (lymphocytes 70%, neutrophil 23%, monocytes 5% and eosinophils 2%) and platelet 43 x 10^3/ul. Reticulocyte count was 0.2%. Dengue serology was positive for both IgM and IgG. Screening for other viruses were done, and result was negative. All other investigations for any malignancy and workup for B12 and folic acid deficiency were within normal range.
Red cells and platelets were transfused to him and bone marrow was advised. Bone marrow aspiration showed hypocellular bone marrow smears and fragments. Erythroid, myeloid and megakaryocytic series cells were markedly decreased with increased lymphocytes and plasma cells. No abnormal cells were seen. Findings of trephine biopsy were consistent with that of aspirate and confirmed the diagnosis of aplastic anemia. His treatment was started with intravenous immunoglobulin and methyl prednisolone. Antibiotic cover was also given to prevent infectious

complications. The patient responded well to the treatment. He was then given long-term treatment with cyclosporine and showed complete remission.

Discussion

This is one of the few cases of aplastic anemia reported in the medical literature. This patient presented with bleeding manifestations and pancytopenia. Dengue and other arboviruses are sometimes associated with bone marrow failure. Viruses can infect human hemopoietic cells and alter their proliferative capacity. Clinically the early phase of dengue is dominated by viremia associated marrow failure with poorly characterized immune response. Dengue can induce aplastic anemia through direct bone marrow invasion. Bone marrow may be a major site of virus replication during clinical infection. In addition dengue virus antigen incites an immune response, T lymphocyte activation and γ interferon production,[9] similar to abnormalities seen in idiopathic aplastic anemia.[10]

Bone marrow failure syndrome is caused by different viruses and they appear to cause hemato-suppression by a variety of mechanisms. Viral replication in the marrow cells leads to pancytopenia. This is a rare but serious complication which must be identified early. Common manifestations are neutropenia and thrombocytopenia, whereas bone marrow is markedly hypocellular with abnormal megakaryopoiesis. Infection related changes occur in lymphocytes in early phase of disease followed by reticulocytopenia, lymphocytopenia thrombocytopenia,and granulocytopenia. Bone marrow biopsy confirms the diagnosis of aplastic anemia. Severe marrow hypoplasia has been observed with Hepatitis and HIV viruses. Reports have been published about cases of aplastic anemia associated with HAV, HBV, parvovirus B 19, Epstein-Barr virus, Transfusion transmitted virus and dengue virus.[11] The pathophysiology of dengue induced aplastic anemia is not well understood, however it is believed that immune complexes and direct viral injury to marrow cells leads to cellular destruction.[12]

There have been only few case reports of severe aplastic anemia in dengue fever. Polianna et al reported a case of 15-year-old girl with anemia, bleeding from the gums, petechiae and fever and pancytopenia. Dengue serology was positive and biopsy showed severe aplastic anemia. She was treated with intravenous immunoglobulin and methyl prednisolone and had a favourable outcome.[13] Thus patients with acquired aplastic anemia treatment can be successfully treated with either immunosuppressive therapy or bone marrow transplant. Immunosuppressive therapy is first line treatment, however for those who do not respond bone marrow transplant from HLA-matched donor may be offered.[14] It has been observed that majority of patients respond to this treatment and some of them undergo complete remission.

Dengue can induce aplastic anemia through direct bone marrow invasion. This is a rare complication which must be identified early. Immunosuppressive therapy can be useful to induce complete remission.

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