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Case Report

Fatal case of aplastic anemia associated with parvovirus B19 infection: a case report

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ABSTRACT

Parvovirus B19 is a recognized cause of transient aplastic crisis in individuals with haemolytic disorder. However, reports are scarce that this virus is causative of acquired aplastic anemia even in healthy individuals. Hence, we report a case Parvovirus B19 induced aplastic anemia in a previously healthy individual.

Keywords: Aplastic anemia, Parvovirus B19, Primate erythrovirus 1, IgM ELISA, PCR, Northeast India.

INTRODUCTION

Human parvovirus B19 (B19), also known as Primate erythrovirus 1, is the only known human pathogenic member of the family *Parvoviridae*, with disease manifestation varying with the immunological and hematological status of the host. In normal, immunocompetent individuals, B19 causes erythema infectious in childhood and acute symmetrical polyarthritis in adults. Although B19 has a marked tropism for P antigen present in erythroid progenitor cells [1], it has been shown to affect myeloid and platelet production in normal volunteers as well [2]. Studies have implicated B19 as a causative agent in a wide range of hematological disorders such as chronic anemia, transient erythroblastopenia, neutropenia and thrombocytopenia. B19 infection in immunocompromised hosts results in pure red cell aplasia (PRCA) and transient aplastic crisis in individuals with underlying hemolytic disorders [3]. Few reports have also suggested an association of B19 with aplastic anemia in previously healthy immunocompetent host [4-7]. Here, we report a previously healthy adult female developing severe aplastic anemia due to Parvovirus B19 infection. To the best of our knowledge, this is the first report of B19 induced aplastic anemia from North-east India.

CASE REPORT

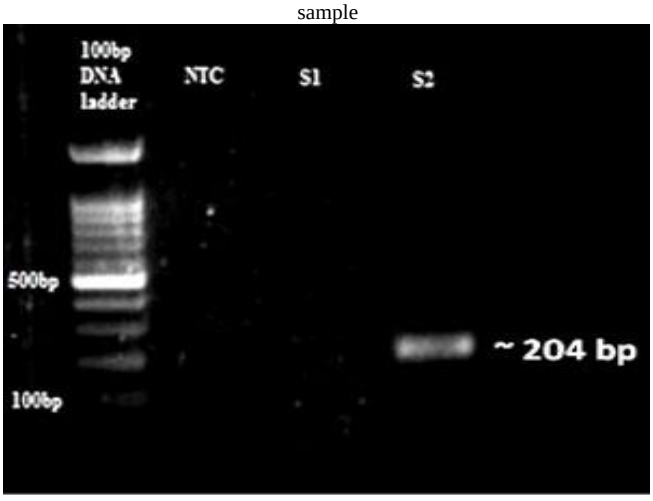
The patient, 49 years married female, was admitted in Assam Medical College and Hospital, Dibrugarh, Assam with complaints of bleeding per vagina, fever and pain in the lower abdomen for the last fifteen days. The patient was apparently healthy 15 days back. There was no history of rash or polyarthritis. There was no history of any drug intake or exposure to radiation. There was no previous or family history of any bleeding diathesis. The patient had attained menopause 9 months back. Physical examination revealed severe pallor, pulse rate 100/min, blood pressure 120/80mm Hg and tenderness in the hypo gastric region. There was no icterus, lymphadenopathy or hepatosplenomegaly. Initial laboratory investigation revealed the following: Hemoglobin 3.9 gm/dl, total WBC count 800 cells/mm^3, RBC count 1.42 million/mm^3, platelet count 6000/mm^3, packed cell volume 11.4%, mean corpuscular volume 80.1 fl, mean corpuscular hemoglobin 27.3 pg, mean corpuscular hemoglobin concentration 34.1 g/dl, prothrombin time 12.15 seconds and international normalized ratio 1.05. Differential count revealed neutrophil 27%, lymphocyte 64%, eosinophil 1% and monocyte 8%. Reticulocyte count was 0.4%. Peripheral blood smear showed predominantly normocytic picture with hypochromic with mild anisopoikilocytosis. Severe leucopenia with neutropenia and markedly reduced platelets were also found in

the peripheral blood smear. Ultrasonography revealed mildly bulky uterus with anterior wall myoma and left ovarian complex cyst. Chest X-ray was normal. Biochemical investigations revealed the following: Total bilirubin 0.4 mg/dl, direct bilirubin 0.19 mg/dl, aspartate transaminase 14 IU/L, alanine transaminase 16 IU/L, alkaline phosphatase 65 IU/L, gamma glut amyl trans peptidase 39 IU/L, lactate dehydrogenase 160 IU/L, urea 42mg/dl and creatinine 0.63 mg/dl. Hemoglobin electrophoresis revealed normal adult hemoglobin. Sucrose lysis test and osmotic fragility tests were normal. Thyroid function tests were within normal range. Routine urine examination was normal. Tests for HIV, Malaria, Leptospirosis and S. Typhi were all found to be negative. Bone marrow examination revealed grossly hypo cellular marrow showing marked depression of the erythroid, megakaryocytes and myeloid series. No giant pronormo blasts were seen. A diagnosis of acquired aplastic anemia was established [8].

Further to detect a possible etiological agent behind the condition, we performed Enzyme linked Immuno sorbent assay (ELISA) to detect IgM antibodies for the following viruses: Hepatitis A, B and C virus, Epstein Barr virus, Cytomegalovirus, Rubella and Parvovirus B19. Parvovirus B19 IgM antibodies was positive whereas the other viruses were found to be negative. ELISA was done using commercially available kit (DRG International, USA).

The sample was further subjected to Polymerase chain reaction (PCR) for presence of B19 DNA. For this, DNA was extracted from whole blood DNA using QIAamp® DNA blood mini kit (QIAGEN, Hilden, Germany) according to the manufacturer's instructions. The extracted DNA was subjected to PCR assay which was carried out using primer set: B_{19} VP1uF (5'-CATGCCTTATCATCCAGTA-3') and B_{19}VP1uR(5'–TTGGCTATACCTAAAGTCAT-3')with a desired amp icon size of 204 bp as described previously.[8] Amplification products were analysed by electrophoresis on 2% acarbose gel and visualized under ultraviolet gel documentation system. The sample was found to be positive for presence of B19 DNA (Figure 1).

Figure 1: Detection of Parvovirus B19 DNA (204 bp) in 2% acarbose gel. NTC- negative template control, S1- normal healthy control, S2- patient's sample



Due to financial constraints, the patient could not afford immunosuppressive therapy or HLA-matched bone marrow transplantation. The patient was managed empirically on broad spectrum antibiotics and filgastrim for febrile neutropenia. Whole blood transfusion and platelet transfusion were given to correct anemia and thrombocytopenia. Her condition improved marginally after treatment and she was discharged against medical advice. However, the patient could not thrive and died 3 days later at home.

DISCUSSION

Aplastic anemia is a syndrome of bone marrow hematopoietic failure characterized by pancytopenia and marrow hypo cellularity [9]. In most cases of acquired aplastic anemia, the etiology remains unclear while in others, the disease has been recognized to be associated with certain drugs, chemicals, irradiation and viral infections [10]. Viruses such as Epstein Barr virus, Hepatitis A, B and C virus, Cytomegalovirus and Rubella virus precede aplastic anemia in some patients. Parvovirus B19 has been implicated in the development of aplastic anemia in some reports [11, 12]. However, the causal relationship between the virus and the disease remains unclear. In this report, we described a healthy menopausal adult female presenting with bleeding per vagina. Although, the classical rash and arthritis was absent in this patient, serological analysis confirmed acute infection with Parvovirus B19. Detection of viral DNA by polymerase chain reaction further confirms the infection.

Parvovirus B19 is a common infection worldwide. Approximately 50% of children have detectable IgG by the age of 15 and seropositivity increases to 90% in adults. Human erythroid progenitor cells is the only known host to Parvovirus B19 [13]. This tropism arises due to presence of P- antigen in human erythrocytes to which the virus has high affinity [14]. However, some reports suggest that B19 DNA are detected in leucocytes of infected patients [15]. And the virus inhibits colony proliferation in megakaryocyte precursors [16]. B19 has been recognized as a cause of transient aplastic crisis in individuals with hemolytic disorders. However there are very few reports which suggest that the virus may be associated with acquired aplastic anemia in normal immunocompetent individuals. The present report further suggests an association between acquired aplastic anemia and Parvovirus B19 infection.

The role of Parvovirus B19 in the pathogenesis of aplastic anemia still remains to be elucidated. Experiments on healthy volunteers have shown that infection with B19 results in drop in hemoglobin concentration, lymphopenia, neutropenia and a drop in platelet count.[2]One hypothesis may be the direct cytotoxic effect of on-structural(NS1) protein of the virus on the marrow cells. NS1 protein of B19 has been demonstrated to play a critical role in G1 arrest and apoptosis induction in human erythroid progenitor cells [17]. A very recent report has demonstrated that the NS1 protein is also involved in G2 arrest in erythroid progenitor cells through

activation of the ATR (ataxia-telangiectasia mutated and Rad3 related) pathway [18]. This, however, fails to explain how a vast majority of individuals infected with the virus fail to show any aplastic crisis. Another plausible explanation into the crisis would be some form of autoimmune mechanism that leads to destruction of the marrow cells expressing viral proteins. Increased levels of cytokines following an infection may result in pancytopenia and reduced hematopoiesis [19]. This hypothesis is supported by the fact that remission of pancytopenia and marrow aplasia occurs with immunosuppressive therapy [20].

In conclusion, our report suggests that Parvovirus B19 may be considered as a cause of acquired aplastic anemia even in individuals without underlying disease. However, further studies are required to establish a causal relationship between the virus and the disease.

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Conflict of interest: None

Ethics Statement

Written informed consent was taken from the patient.

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