Agranulocytosis: A Rare Complication of Infectious Mononucleosis and Recovery After IVIG Therapy

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ABSTRACT

A six-year-old boy was admitted with acute agranulocytosis four weeks after the onset of infectious mononucleosis. His bone marrow aspiration revealed maturation arrest of myeloid series. He was hospitalized for agranulocytosis and he was put on intravenous immunoglobulin (IVIG) (400 mg/kg/day) on the third day of hospitalization for two days. His white blood cell count increased to 4200/mm^3 (1176 PMNL absolutely) on the fifth day. This may suggest that IVIG therapy may be effective for early recovery from agranulocytosis which is a very rare complication of infectious mononucleosis.

Key Words: Agranulocytosis, Infectious mononucleosis, intravenous immunoglobuline therapy.

ÖZET

İnfeksiyöz Mononükleozun Nadir Görülen Bir Komplikasyonu Olarak Agranülositoz ve IVIG Tedavisi ile Düzelme

Altı yaşında bir erkek çocuk, infeksiyöz mononükleozun başlangıcından dört hafta sonra akut agranülositoz ile hastaneye getirildi. Kemik iliği aspirasyonu miyeloid seride maturasyon duraklaması gösterdi. Hastaneye yatırılan hastaya, yatışının üçüncü günü, iki gün süre ile intravenöz immünglobulin (400 mg/kg/gün) başlandı. Beyaz küre sayısı beşinci gün 4200/mm^3 (PMNL: 1176/mm^3)'e yükseldi. Bu da intravenöz immünglobulinin infeksiyöz mononükleozun nadir komplikayonlarından biri olan agranülositozda etkili olabileceğini göstermektedir.

Anahtar Kelimeler: Agranülositoz, İnfeksiyöz mononükleoz, intravenöz immünglobulin.

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INTRODUCTION

Infectious mononucleosis (IM) is known as a benign and usually self-limiting clinical presentation of Epstein-Barr virus (EBV) infection. Mild neutropenia is one of the well known hematological complications occurring in as much as 40% of cases[1]. However agranulocytosis (less than 200/mm^3) is very rare[1-4].

A CASE REPORT

In this case report, we describe a patient with acute agranulocytosis associated with IM and recovery from agranulocytosis after IVIG therapy.

A six-year-old boy was admitted to Hacettepe University İhsan Doğramacı Children's Hospital because of a cervical mass behind his left ear, abdominal pain, fever, and jaundice lasting for a week. He was treated with amoxicillin-clavulonic acid for five days before admission. On his physical examination, his heart and respiratory rates and body temperature were 82/min, 20/min and 36.8°C respectively. Tonsillar enlargement with membranous exudation, pharyngeal erythema and cervical lymphadenopathy were noted. Spleen was palpated 3 cm below the left costal margin. Liver was nonpalpable. In laboratory examination, total white blood cell (WBC) count was 6900/mm^3 with 66% lymphocytes, 8% monocytes, 26% PMNL; hemoglobin was 12.1 g/dL, platelet count was 325.000/mm^3. Serum transaminases were; ALT: 97, AST: 134 IU/L, bilirubin and other liver enzymes were normal. Titers of viral capsid antigen (EBV VCA) IgM was high, EBV nuclear antigen (EBNA) IgM, IgG were negative. His throat culture was negative for bacterial causes. He was diagnosed as IM and he was called for a follow up visit two weeks after discharge. Three days after he returned to his home, he had ear pain and was again recommended amoxicillin-clavulonic acid treatment by a pediatrician. He used amoxicillin-clavulonic acid for one week but he had rash all over his body on the seventh day and his medicine was changed to clarithromycin by the same doctor. Then, twenty-three days after the first admission, he was again admitted to our hospital with fever, difficulty in swallowing because of sore throat and a mass on his left side of neck. On his physical examination, he had a fever of 38.2°C, multiple cervical, submandibular, inguinal lymphadenopathy, tonsillitis with membranous exudates and gingivitis. His WBC count was 3400/mm^3 with 90% lymphocytes and 10% Downey cells, without any PMNL on blood smear, hemoglobin was 11.7 g/dL, platelets were 212.000/mm^3. His bone marrow aspiration revealed maturation arrest of myeloid series at band stage with increased number of histiocytes and plasma cells. His liver enzymes were normal. He was hospitalised because of agranulocytosis. On the second day he had still fever and antibiotic treatment was started. On the third day WBC count was 2500/mm^3 with no PMNL on blood smear, and the patient was put on IVIG therapy 400 mg/kg/day. After two days of IVIG therapy his WBC increased to 4200/mm^3 with 28% PMNL on peripheral blood smear. His body temperature were within the normal limits after the fourth day of hospitalisation. Blood cultures and throat culture did not reveal any microorganism. His WBC count was 6100/mm^3 with 4% bands, 38% PMNL, 1% eosinophil, 1% basophil, 7% monocytes, 49% lymphocytes on the eight day, antibiotic treatment was stopped and he was discharged.

DISCUSSION

Infectious mononucleosis is known as a benign and usually self-limiting disease. Complications of EBV infection is believed to be immune mediated rather than cytotoxic and many events can occur because of the host's response to the EBV infection of the B-cell[5]. In addition to EBV specific antibody response, production of nonspecific antibodies and auto antibodies can be seen[5]. A mild neutropenia can be observed in the second week of acute illness as much as in 40% of patients but agranulocytosis (less than 200/mm^3) is a very rare complication[1-4].

After four weeks from the first symptoms, our patient was admitted with agranulocytosis which is a rare complication. The exact mechanism of agranulocytosis is not well established. It has been speculated that it involves either hypoproduction or a maturation arrest of myeloid cells in the marrow due to direct effect of EBV or antibody mediated peripheral destruction of myeloid cells; autoantibodies to myeloid cells can result in neutropenia or agranulocytosis[1,4,5]. Our patient showed maturation arrest at band series on bone marrow aspirates. We started IVIG therapy and after two days of treatment his total WBC count reached to 4200/mm^3 with 28% PMNL on peripheral blood smear. In studies of patients with ITP, IVIG have been shown to produce a temporary blockade of Fc receptors in the reticuloendothelial system[6,7]. Peripheral monocyte Fc receptors are reduced in number follo-

wing treatment with IVIG[6]. In most of the studies, it was shown that, mechanism of action of immunoglobuline is through the Fc portion of the administered immunoglobuline or through the suppressive effect on endogenous antibody production because of anti-idiotype antibodies. Also, IVIG has been shown to modulate the synthesis and release of cytokines and cytokine antagonists[8]. Since we don't know the exact mechanism of agranulocytosis, we can not say the exact mechanism of this improvement by IVIG. Agranulocytosis may occur due to immune mediated mechanisms. There is need for further studies to demonstrate the mechanism of agranulocytosis in EBV infections whether it is due to production abnormality or an immune-mediated mechanism.

This report is suggested to be a reminder of late and rare complication of IM. Patients with classical symptoms of IM should be followed up for late complications like agranulocytosis and they may be treated with IVIG as a choice of treatment for early recovery from agranulocytosis.

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