

Severe Thrombocytopenia in a Young Patient with EBV Induced Infectious Mononucleosis: An Extremely Rare and Life-threatening Complication

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Abstract Epstein-Barr virus is a widely disseminated herpes virus. Humans are the main reservoir. Acute infectious mononucleosis is one of the most common presentations of acute EBV infection. Although mild thrombocytopenia is a common complication of EBV induced infectious mononucleosis, severe thrombocytopenia with counts less than $25,000/\text{mm}^3$ is extremely rare and infrequently reported. We herein, present a 22-year-old Caucasian male with no past medical history who came to our hospital with complaints of fever, sore throat, swollen lymph nodes and intermittent bleeding from his gums for the last 4 weeks. On physical examination, the patient had enlarged tonsils and cervical lymphadenopathy, however, no rashes or hepatosplenomegaly were noted. On initial Lab work the patient had a platelet count of $11,000/\text{mm}^3$, WBC count of 9,800 with 31% atypical Lymphocytes and a positive mono spot test. The patient also had a peripheral smear showing marked thrombocytopenia. EBV infection was further confirmed by serology including EBV-PCR. Other possible causes of thrombocytopenia including HIV and Hepatitis C were tested and found to be negative. The patient was treated with platelet transfusion and intravenous steroids. He was discharged three days later, after his platelet count improved to $36,000/\text{mm}^3$ on a tapering dose of steroids. Two weeks later repeat lab work revealed that his platelet count had dropped again significantly to $2000/\text{mm}^3$. He was readmitted and this time treated with Intravenous Immunoglobulin and intravenous steroids. The patient had dramatic improvement and his platelet count was $143,000/\text{mm}^3$ two days later. The patient was discharged and continued to have normal platelet counts during routine clinic follow ups few months later. Severe thrombocytopenia is a potentially life-threatening condition. Although exceptionally rare, severe thrombocytopenia can occur as a complication of EBV induced Infectious mononucleosis and should be considered by physicians as a possible differential for thrombocytopenia in the right clinical setting. Steroids and Intravenous Immunoglobulin have been used with varying success to treat this complication.

Keywords: *thrombocytopenia AND EBV infection*

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1. Introduction

Epstein Bar Virus [EBV] is a widely distributed member of the herpes virus family spread through intimate contact between asymptomatic EBV shedders and vulnerable individuals [1]. Acute infectious mononucleosis is the most well-known manifestation of EBV infection [2]. Although EBV associated infectious mononucleosis results in some reduction of platelet counts in 50% of the cases [3], severe thrombocytopenia with platelet counts less than $25,000/\text{mm}^3$ is extremely rare and infrequently reported [4,5]. We present a case of a 22-year-old male patient with severe thrombocytopenia and concomitant EBV induced infectious mononucleosis.

2. Case

An otherwise healthy 22-year-old Caucasian male presented to the Conemaugh memorial medical center Emergency Department with complaints of sore throat, fever (100°F) and cervical lymphadenopathy for the past 4 weeks. The patient also reported bleeding from his gums intermittently, and had recently completed a course of antibiotics for strep throat. On Physical examination, the patient had bilateral enlarged tonsils with exudates and bilateral cervical lymphadenopathy, no hepatosplenomegaly was noted. Initial laboratory testing revealed a Hemoglobin of 17.2 mg/dl, Hematocrit of 49%, WBC count of $9800/\text{mm}^3$ with 31% atypical lymphocytes on

manual differential as well as a platelet count of $11000/\text{mm}^3$. The results of a mono spot test and throat culture for Group A Beta strep were also positive. The patient was admitted and transfused two units of platelets, he was started on methylprednisolone 40mg every 8 hours, Azithromycin 500mg daily. During admission, further testing was obtained along with peripheral smear which showed marked thrombocytopenia with normal WBC count and relative lymphocytosis. EBV specific serology was obtained and both EBV anti IgM and IgG antibodies were positive, this was further confirmed with quantitative EBV-PCR revealing $2150 \text{ copies}/\text{mm}^3$. Serological tests for HIV and Hep C were negative. Additionally, platelet antibody screen was positive. Hepatic Function Tests showed PT/INR of 1.1 while AST and ALT were mildly elevated at 60 and 133 respectively. The patient did not show any sign of bleeding, he continued to improve clinically and 3 days later his platelet count was $36000/\text{mm}^3$. The patient was subsequently discharged on a tapering dose of prednisone and oral antibiotics. However, follow up CBC has done two weeks later the patient was once again found to be thrombocytopenic with a platelet count of $2000/\text{mm}^3$. He was again admitted and started on steroids 1mg/kg/ day and was also given Intravenous Immunoglobulin. The patient this time showed dramatic improvement in his platelet counts and two days later his counts were $143000/\text{mm}^3$. The patient was subsequently discharged home on a tapering dose of steroids. On routine follow in the outpatient clinic a few months later the patient continued to have normal platelet counts.

3. Discussion

The bulk of EBV infections worldwide is asymptomatic and EBV antibodies are seen in all population groups with 90-95% of all adults being EBV positive [6]. Although EBV is implicated in the pathogenesis of several malignancies [1], Infectious mononucleosis is the most famous clinical entity associated with EBV infection [2]. Infectious mononucleosis classically consists of a triad fever, tonsillar enlargement, and lymphadenopathy [7]. All three clinical features were present in our patient. One of the features of EBV induced infectious mononucleosis is a reduction in platelet counts. Although mild to moderate thrombocytopenia with platelet counts ranging from $[63,000/\text{mm}^3 \text{ to } 139,000/\text{mm}^3]$ have seen in most of the patients with EBV induced infectious mononucleosis [3], severe thrombocytopenia with counts below $2,000/\text{mm}^3$ are rarely seen [4]. According to Michelle L Pipp et al there were only 36 cases of severe thrombocytopenia [platelet counts less than $2,000/\text{mm}^3$] as a complication of EBV induced infectious mononucleosis reported between 1965-1997, [4]. In patients with low platelet counts irrespective of etiology severe thrombocytopenia defined as a platelet count below $50,000/\text{mm}^3$, poses the greatest risk for bleeding [8]. Life threatening hemorrhagic complications like major Intracranial Hemorrhage [ICH] and non-ICH sever bleeding is observed when platelet counts fall below 10,000-20,000 [9]. The cause of severe thrombocytopenia in patients with EBV induced infectious mononucleosis is hypothesized to be immune

mediated [3]. Our patient was also positive for anti-platelet antibodies. However, further studies need to be conducted to determine the prevalence of anti-platelet antibodies in patients with EBV induced infectious mononucleosis complicated by severe thrombocytopenia. Treatment of severe thrombocytopenia in EBV induced infectious mononucleosis can be challenging and patients may relapse even after initial response to treatment [10]. This was the case in our patient who initially responded to treatment with improvement in platelet counts, however two weeks later his platelet counts had dropped once again on repeat blood work. Although exceptionally rare, severe thrombocytopenia can occur as a complication of EBV induced infectious mononucleosis. Only a subset of patients with severe thrombocytopenia will go on to develop life threatening bleeding diathesis [4]. EBV infection should be considered as one of the differentials for patients with severe thrombocytopenia in the right clinical setting. Although there have been mixed results and varying success with Steroids and Intravenous Immunoglobulin in the treatment of severe thrombocytopenia in some cases, like in our patient there may be complete resolution and return to baseline platelet count.

4. Conclusion

Severe thrombocytopenia in individuals with EBV induced infectious mononucleosis can be potentially fatal, making its early diagnosis and treatment vital for clinicians. We recommend awareness among healthcare professionals about this extremely rare complication of a very common disease.

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