CHICKEN POX ASSOCIATED THROMBOCYTOPENIA COMPLICATED WITH INTRACRANIAL HEMORRHAGE IN ADULT - REPORT OF A CASE

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Abstract

Thrombocytopenia is a common hematological complication of chickenpox. Most patients with thrombocytopenia are often asymptomatic or present with only mild cutaneous bleeding. Severe bleeding associated with intracranial hemorrhage or gastrointestinal bleeding is rare. We here report a case of a 20-year-old man with fever and pruritic vesicular rash on his face, trunk, and extremities over 2 days. This patient was admitted to an isolation room based on these symptoms. Two days later, the patient complained of a severe headache and a brain computerized tomography revealed intraventricular hemorrhage and mild subarachnoid hemorrhage. Platelet counts (2000/ul) indicated isolated extreme thrombocytopenia. The patient was managed with platelet transfusion, dexamethasone, and intravenous immune globulin – no further progression of hemorrhage occurred thereafter.

Key Words: chickenpox, thrombocytopenia, intracranial hemorrhage

Introduction

Chicken pox is a highly contagious disease caused by Varicella-zoster virus (VZV) and primarily affects children under 10 years of age. Chicken pox typically presents as a mild and self-limited disease in children, however, it can be more severe in adults or in immunocompromised patients. Following the introduction of the varicella vaccine in 1995, approximately 20 percent of those who were vaccinated developed an infection following exposure to VZV. However, vaccination was associated with a milder infection and further complications were rare. In adults, primary varicella infection has been associated with many serious complications, including diffuse encephalitis and pneumonia. Thrombocytopenia is also a common hematological complication of chickenpox, however hemorrhagic manifestations are rare and most hemorrhagic events are considered to be mild, such as petechiae, bruises, and hemorrhagic vesicles. In the current report, we present the case of a patient diagnosed with chicken pox who developed thrombocytopenia, intraventricular hemorrhage, and subarachnoid hemorrhage.

Case presentation

A 20-year-old man was admitted to Cheng-
Ching General Hospital with pruritic vesicular rash on his face, trunk, and extremities, which prompted hospital admission. The patient reported having been in good health with no history of drug use or abuse, including over-the-counter and Chinese herbal products. He had ever received varicella vaccine during childhood. Two days before admission, he reported symptoms of headache, general malaise, and fever.

Upon physical examination following admission it was revealed that multiple lesions were present in crops and in a variety of stages, including maculopapular and vesicular, as well as pustular. This was especially evident over the trunk. Central necrosis and early crusting was also visible. It was determined that the observed clinical features were consistent with chickenpox. This was further supported by high titer of immunoglobulin (Ig)M antibodies to varicella-zoster virus, but low titer of IgG antibodies in the patient's serum, confirming a diagnosis of primary varicella infection. A complete blood count revealed a hemoglobin of 11.6 g/dl, a white blood cell count of 6740/ul (67% neutrophils, 23% lymphocytes, and 9% monocytes), and a platelet count of 176000/ul. Furthermore, liver function tests, blood urea nitrogen, creatinine and electrolytes, and the parameters of coagulation were within normal range. Chest radiographs revealed diffuse bilateral infiltrates.

With a diagnosis of chickenpox, the patient was admitted to an isolation room and supportive treatment was initiated, including antihistamines for itching and acetaminophen for fever reduction. Two days following hospital admission (Day 3), petechiae and hemorrhagic vesicles developed over the patient's trunk and extremities, and severe headache and nausea was reported. Brain computerized tomography (CT) disclosed intraventricular hemorrhage and mild subarachnoid hemorrhage (Figure 1). Laboratory data showed severe isolated thrombocytopenia (2000/ul). A transfusion with 12 units of platelet concentrate was performed and the patient was transferred to the medical intensive care unit (MICU). Upon arrival to the MICU, the patient was fully conscious and alert with no decreased muscle power. A neurosurgical consultation recommended further observation since there were no significant neurological impairments. A hematological consultation revealed no abnormalities based on results from the following tests: prothrombin time, international normalized ratio, activated partial thromboplastin time, peripheral blood smear, fibrinogen level, fibrin degradation products, liver function test, Coombs test, anti-nuclear antibodies, urinalysis, and Human Immunodeficiency Virus.

A bone marrow biopsy was also performed and revealed an increased number of megakaryocytes, with normal morphology and numbers of erythroid and myeloid precursors. The next day (Day 4), a platelet transfusion resulted in a minor response of the patient’s hematologic parameters and dexamethasone and intravenous immune globulin were administered under the suspicion of chickenpox-induced thrombocytopenia. Continued therapy as described resulted in a gradual increase of platelet levels (Figure 2) and no progression of neurological signs was noted. The patient was transferred out of the MICU five days later (Day 9) and discharged two weeks after admission. No neurological sequelae nor recurrent thrombocytopenia were noted during outpatient follow up one month after discharge.
Varicella-associated thrombocytopenia usually develops early during the viremia phase or the post-infectious period weeks and months afterward. The frequency of varicella-associated thrombocytopenia has been demonstrated to be approximately 22 percent to 45 percent, with a majority of patients asymptomatic or bleeding from the skin or mucous membranes (average platelet level about 3000 to 14000/ul).6,7 More severe hemorrhage, such as intracranial hemorrhage (ICH), overt gastrointestinal bleeding, and hematuria, is uncommon. In the currently reported case, extremely low platelet levels (2000/ul) observed five days after the patient’s rash developed and severe intraventricular hemorrhage also occurred – a very rare occurrence for patients with chickenpox. Fortunately, no progression of ICH was noted and the patient didn’t have significant neurological sequellae.

Various consequences of varicella-induced thrombocytopenia have been described, including bone marrow suppression, disseminated intravascular coagulation, and virus-induced platelet aggregation followed by phagocytosis or lysis.

Discussion

Varicella-zoster virus (VZV) is responsible for primary varicella disease (chickenpox) and herpes zoster (shingles), the latter of which is believed to be an endogenous reactivation of latent VZV.1,4 Chickenpox is highly contagious – transmission is possible via indirect (aerosolized droplets) and direct contact with infected individuals. Infection can occur up to 48 hours before the onset of a skin rash, which is demonstrated by the greater than 90% secondary household attack rate.4

Chickenpox is usually mild and a self-limited disease in healthy children. However, in adults, immunocompromised individuals of any age, and pregnant women, the severity and complication rate of the disease have been demonstrated to be higher. Diffuse encephalitis is considered to be the most serious complication, and varicella pneumonia accounts for a majority of adult morbidity and mortality.1,4 Thrombocytopenia is also a common complication of chickenpox, especially in adults where it is observed at four times the frequency compared with children.5

Figure 2. Platelet count of the patient during first 7 days of admission shows rapid decline of platelet count at the early course of disease. After steroid injection and IVIG used at day 4, the patient’s platelet count increased gradually.
but the most common consequence is immune-mediated platelet destruction. Varicella viremia may induce the production of autoantibodies directed against platelet membrane glycoproteins such as GPIIb/IIIa. Autoantibodies bind to platelets and these bound platelets are subsequently phagocytosed by splenic macrophages or directly destroyed by complement. In addition, autoantibodies may also bind to megakaryocytes and decrease platelet production. In the currently reported case, a bone marrow biopsy demonstrated an increased number of megakaryocytes, which implied the increased destruction of platelets may be a critical factor in the pathogenesis of varicella-induced thrombocytopenia.

Varicella infection is one of etiology of secondary immune thrombocytopenia (ITP). The treatment strategy for varicella-induced thrombocytopenia resembles ITP. The correlation between platelet count and bleeding risk is weak possibly due to the age of circulating platelets in patients with ITP, who are younger and have greater hemostatic effectiveness than patients with thrombocytopenia due to bone marrow suppression. Therefore, the goal of treatment is not to fully normalize the platelet count, but to provide patients with a relatively safe platelet count to reduce the risk of bleeding. Bleeding risk has been demonstrated to be greatest in individuals with platelet counts less than 10,000/uL and should prompt platelet transfusion. If a patient with severe bleeding associated with ITP such as that observed with ICH or gastrointestinal bleeding, who presents with a platelet count <30,000/ul, the suggested intervention is platelet transfusion, intravenous immune globulin (IVIG; 1 g/kg, repeated the following day if the platelet count remains <50,000/ul) and glucocorticoids (methylprednisolone; 1 g intravenously, repeated daily for three doses) should be provided immediately. In the currently reported case, while ICH occurred, we immediately administered a platelet transfusion, IVIG and dexamethasone to correct platelet count. Following these interventions, no further bleeding nor progression of neurological symptoms was observed.

Conclusion

Chicken pox is considered to be a benign disease, but serious complications can occur in adult patients. Varicella-induced thrombocytopenia is a common complication of a primary varicella infection. Most patients with thrombocytopenia are asymptomatic or report minor bleeding from the skin or mucous membranes and require no treatment. However, ICH can also occur in patients with chickenpox-associated thrombocytopenia, which may be associated with a decrease in platelets to extremely low levels. For these patients, platelet transfusion, administration of steroids, and IVIG are suggested to be administered immediately.

References

水痘導致之血小板減少症併發腦內出血 - 病例報告

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摘要

血小板減少症是水痘常見的血液方面併發症，但大多數的有此併發症的病人都
是無症狀或是皮下輕微的出血，嚴重的出血如腦內出血或腸胃道出血並不常見。
在這篇病例報告中，我們提出一位二十歲的男性在住院兩天前出現發燒以及在
臉、軀幹和四肢產生許多癢且水泡狀的紅疹，所以住進我們醫院的隔離病房中。
兩天後病人突然出現嚴重頭痛而腦部電腦斷層顯示有腦室內及蜘蛛網膜下腔出
血，實驗室檢查也發現病人有嚴重的血小板減少症。因此緊急給予病人輸血小
板，類固醇及靜脈注射免疫球蛋白。之後病人的出血並未惡化。因此我們提出這
罕見的水痘導致之血小板減少症的併發症並且作文獻探討。

關鍵詞：水痘，血小板減少症，腦內出血

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