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Case Report

Acute immune thrombocytopenic purpura in an adolescent with 2009 novel H1N1 influenza A virus infection

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Abstract

Although both leukopenia and thrombocytopenia are not uncommon hematological findings among patients with novel 2009 H1N1 influenza virus infection, immune thrombocytopenic purpura has rarely been shown to be associated with this novel influenza A infection. Here, we describe a previously healthy adolescent who presented with fever, influenza-like symptoms and acute onset of generalized petechiae and active oral mucosa bleeding on the third day of his illness. Severe leukopenia and thrombocytopenia were found. There was neither malignancy nor blast cells found by bone marrow aspiration. Real-time reverse transcriptase polymerase chain reaction was positive for novel 2009 H1N1 influenza infection. Novel influenza-associated atypical immune thrombocytopenic purpura was diagnosed. The patient recovered uneventfully after oseltamivir and methylprednisolone therapy.

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1. Introduction

Hematological abnormalities including leukopenia and thrombocytopenia have been well described in the 2009 pandemic of novel H1N1 influenza A virus.¹ Most of hematological abnormalities were seen in the cases of severe novel H1N1 infections. Although a few case reports have described the association of influenza virus infection with acute immune thrombocytopenic purpura (ITP), very few cases of influenza-associated ITP were reported during this novel H1N1 influenza pandemic, except for the presence of petechial rash

without hematological abnormality.^{2–5} Here, we describe a previously healthy 14-year-old boy who developed atypical features of acute ITP and was concomitantly diagnosed with novel H1N1 influenza virus infection.

2. Case report

A previously healthy 14-year-old boy presented with influenza-like illness with high fever up to 39 °C, cough, sore throat and general malaise for 3 days before admission. Ten of his classmates had similar symptoms during the same period. He was treated as if for a common cold with acetaminophen, nospapine and deschlorpheniramine at a local clinic on the first 2 days of illness. He was referred to Chang-Bing Show Chwan Memorial Hospital on November 23, 2009, the third day of illness, due to abrupt onset of extensive cutaneous petechiae, ecchymosis and painful bleeding of the mouth.

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On admission, he was alert and afebrile, without respiratory distress. His vital signs were stable, with a pulse rate of 86 beats/minute, respiratory rate of 18 breaths/minute and blood pressure of 110/90 mmHg. Physical examinations showed generalized petechiae, infected throat without ulcers, some bloody clot on the tonsils, submucosal hemorrhage over the hard palate, and some oral mucosa bleeding. There was neither lymphadenopathy nor hepatosplenomegaly. No bone pain or retrobulbar pain was noted either. A complete blood cell analysis demonstrated normal white cell count ($4.8 \times 10^9/L$) and no anemia, however, marked thrombocytopenia ($7 \times 10^9/L$) was found (Fig. 1). Blood biochemical profiles including liver transaminases, electrolytes, muscle enzymes, prothrombin time, and activated partial thromboplastin time were all within normal limits. Immunological analysis showed normal levels of C3 and C4, and was negative for antinuclear antibody. There was no identified lung lesion from the patient's chest film. Influenza virus quick antigen test was positive for influenza A virus. The nasal swab sample was obtained for virus isolation and real-time reverse transcriptase polymerase chain reaction. The novel 2009 H1N1 influenza A virus was identified and confirmed by the Taiwan Center for Disease Control on the third day of hospitalization. The patient was treated with oral oseltamivir (75 mg twice daily) on the day of admission for 5 days and a 3-day course of intravenous high-dose methylprednisolone (1000 mg once daily) from the first day of admission. He was afebrile during his hospitalization. He was still found to have transient leukopenia of $1.5 \times 10^9/L$ on the second day of admission. The nadirs of his platelet and leukocyte counts were identified on the first and second day of hospitalization, respectively (Fig. 1). He was arranged to receive bone marrow aspiration on the third day of admission. There was increased numbers of megakaryocytes without blasts, hemophagocytosis or malignant cells, which was compatible with acute ITP. His platelet count was $67 \times 10^9/L$ on the fourth day of admission. He was discharged on the sixth day, because his platelet count returned to $112 \times 10^9/L$, and he had no complaint of any discomfort or pain. We have not given the patient any other sequential oral steroids since his discharge. The platelet count was $360 \times 10^9/L$ on the 12th day

after admission. The serologic tests against cytomegalovirus, Epstein–Barr virus and adenovirus were all negative.

3. Discussion

Hematological findings of influenza virus infection are not uncommon. Leukopenia and thrombocytopenia have been widely described in the literature elsewhere, regardless of influenza A or B virus.⁶ In comparison with influenza A infection, there was a higher rate of leukopenia and thrombocytopenia seen in those with influenza B infections.⁶ For patients hospitalized because of novel 2009 H1N1 influenza infection, the incidence of leukopenia and thrombocytopenia was 20% and 14%, respectively.¹ Lymphocytopenia and thrombocytopenia are more commonly seen in those with severe pneumonia, respiratory failure and shock.^{1,7}

Childhood ITP has several unique characteristics.^{8,9} First, there is a seasonal distribution with a peak during spring and a nadir in the autumn. Second, two-thirds of children with acute ITP have a history of preceding infectious illness a few days to weeks before the onset of thrombocytopenia. Third, there is a peak incidence between the ages of 1 and 6 years. Finally, a diversity of autoimmune mechanisms has been implicated in the development of ITP. Physical examinations of childhood ITP are essentially normal, other than petechiae and bruising. Organomegaly is usually absent, and peripheral blood analysis is normal, other than demonstrating thrombocytopenia. Patients who do not meet the above-mentioned criteria are categorized as atypical ITP. For virus-associated ITP, cytomegalovirus, Epstein–Barr virus, varicella–zoster virus, hepatitis C virus and human immunodeficiency virus are the most common identified etiologies.⁴

Despite the documentation of acute ITP following influenza vaccination,^{10–12} only a few reports have described an association of acute ITP with influenza infection.^{3,5} The typical thrombocytopenia often develops 2–3 weeks after vaccination. In contrast, influenza-associated thrombocytopenia generally develops during the illness.^{3,4} The mechanism of influenza-associated ITP is not fully understood. Some evidence has suggested the shortened platelet survival time and easy clearance of platelets by the circulation.^{13,14}

In our case, acute ITP developed during viral illness. He was categorized as atypical ITP due to the age of disease onset and concomitant leukopenia, in addition to thrombocytopenia and generalized petechiae. Previous studies have shown that leukopenia and thrombocytopenia are often associated with severe novel 2009 H1N1 influenza infection. However, the present case developed leukopenia and thrombocytopenic purpura on the third day of novel H1N1 infection without pneumonia or severe illness.

The clinical outcome of this patient was good. He received oseltamivir and intravenous high-dose methylprednisolone therapy beginning after admission. He was soon afebrile and had no active mucosal bleeding from the third day of hospitalization. The hematological findings returned to normal on the fourth day. The findings of bone marrow aspiration were typical for acute childhood ITP, and no malignant or blast cells were found.

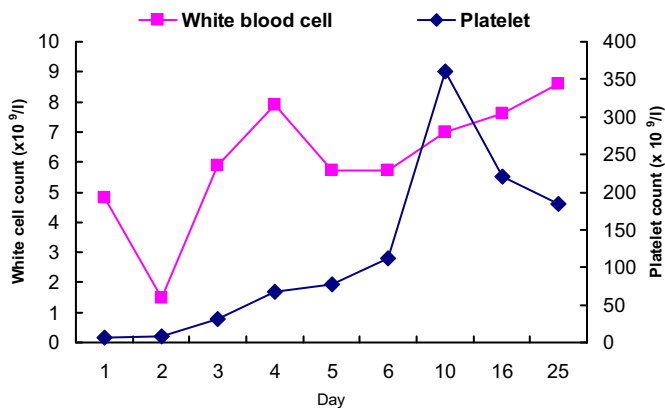


Fig. 1. Hematological findings of the patient from admission through follow-up.

In conclusion, it is important for general clinicians to keep in mind that although rare, acute ITP could be associated with acute influenza infection, regardless of the severity of illness.

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