**CASE REPORT**

**Immune Thrombocytopenia Due to Mycoplasma pneumoniae Infection**

**ABSTRACT** Mycoplasma pneumoniae is one of the major causes of lower and upper respiratory tract infections in children. The most common type of the infection is a lower respiratory tract infection. But also Mycoplasma pneumoniae can be associated with extrapulmonary manifestations even in 25% of patients. Hemolytic anemia, thrombocytopenia, disseminate intravascular coagulation and hemophagocytic syndrome are the most common hematologic complications. In this article, a patient with Mycoplasma pneumoniae pneumonia and immune thrombocytopenia is described because of its rare occurrence and different clinical features.

**Keywords:** Immune thrombocytic purpura; Mycoplasma pneumoniae; thrombocytopenia

Mycoplasma pneumoniae is one of the main agents of lower and upper respiratory tract infections in children. It is more frequently found in school age children and young adults, but is rarely seen under 5 years of age.¹ The incubation period is usually 2-3 weeks. Symptoms are variable and most commonly presented with cough, weakness, fever and headache. Mycoplasma pneumoniae infections are seen only in humans, and it spreads through aerosols. Outbreaks can be seen in public areas such as barracks, schools.²

The most common type of the infection is respiratory tract infection. But also Mycoplasma pneumoniae can be presented with extrapulmonary manifestations even in 25% of patients. Mycoplasma pneumoniae cause these complications with different immune mechanisms.³ Extrapulmonary complications are encephalitis, transverse myelitis, meningitis, Guillain-Barré syndrome, nausea, diarrhea, vomiting, pancreatitis and hepatitis. Other complications can manifest as erythema nodosum, urticaria, myocarditis, pericarditis, arthritis and hematological complications. Hemolytic anemia, thrombocytopenia, diffuse intravascular coagulation and hemophagocytic syndrome are the most common hematologic complications.⁴ In this article, a patient with Mycoplasma pneumoniae pneumonia and immune thrombocytopenia (ITP) was presented because of its rare occurrence and different clinical features.
CASE REPORT

A 2-year-old girl presented to the hospital with a persistent fever for 3 days. She had cough and fever. Her mother reported that she had developed cough for a few days before the onset of her fever. Her immunizations were up to date, according to the schedule. She was febrile at 39°C, tachycardic and her respiratory rate was 30 per minute. There was no lymphadenopathy. A skin examination revealed mild petechiae. Her abdomen was mildly tender, and distended with no organomegaly. She was oriented, neurological examination was normal. She had no bone or joint pain or swelling. Complete blood count revealed a white blood cell count of 7.07 x10⁹/L, hemoglobin of 9.7 g/dl, and a platelet count of 19 x10⁹/L. No blasts were identified in the blood smear, and platelet morphology was within the normal range, with 1-2 large platelets per field. Further laboratory evaluation was prothrombin time (PT): 12.1 s, INR: 1.1, partial thromboplastin time (PTT): 28 s, aspartate transaminase (AST): 44 IU/L, alanine transaminase (ALT): 33 IU/L, lactate dehydrogenase (LDH): 264 U/L, and erythrocyte sedimentation rate: 74 mm/h, urea: 22 mg/dL, creatinine: 0.3 mg/dL, B12, and folic acid levels were normal. No evidence of viral infections—including the Hepatitis virus A, Hepatitis virus B, Hepatitis virus C, Epstein-Barr, Rubella, and Cytomegalovirus—was found. Frontal chest radiograph showed a diffuse pattern of increased interstitial markings (Figure 1). Empiric treatment of piperacillin-tazobactam and clarithromycin was started with diagnosis of pneumonia according to age group by doctors of intensive care unit.

The patient continued to have fever spikes to 39-40 °C every 5-6 hours after admission until the third day. Since platelet count was 19 x10⁹/L and it was in the period of acute infection, first platelet transfusion was given considering infectious thrombocytopenia. Intravenous immunoglobulin (IVIG) was given at 0.6 mg/kg/day for 3 days when there was decrease to 10 x10⁹/L. She was monitored closely for complications associated with thrombocytopenia: she had minimal petechial lesions but also did not develop bruising, or severe bleeding during admission. The control platelet count after IVIG was 35 x10⁹/L. After she completed a 7-day course of piperacillin-tazobactam and clarithromycin in hospital, she was afebrile with a normal examination. Her platelet count revealed 124 x10⁹/L. Mycoplasma pneumoniae IgM positivity was detected in serological tests ELISA (Enzyme-Linked ImmunoSorbent Assay). Clinical, laboratory and radiological studies were also found to be compatible with Mycoplasma pneumoniae infection. She completed a total 14-day course of clarithromycin.

IVIG was repeated because of the decrease in platelet count at 3 weeks after first dose. Treatment with a dose of 1 g/kg/day resulted in a suspected allergic reaction and fever. Therefore treatment was continued with methylprednisolone at 4 mg/kg/day for 5 days after bone marrow examination on day 22 of treatment. Bone marrow aspiration smear showed increased mature and immature megakaryocytes was consistent with ITP (Figure 2). The platelet count of the patient on follow-up was shown (Table 1). Second day of methylprednisolone platelet count revealed 62 x10⁹/L and, platelet count was 445 x10⁹/L on fifth day of treatment. Informed consent was obtained from patient relatives.

DISCUSSION

Immune thrombocytopenic purpura is an autoimmune disease characterized by autoantibody-
coated thrombocytes being destroyed in the reticuloendothelial system and decreasing the platelet count. ITP is one of the most common hematologic disorders in childhood. Incidence of ITP is 4-8 per 100,000 children each year. 50-80% of newly diagnosed ITP patients have a history of infection in the last 1-3 weeks. Non-specific respiratory tract infections are the most common cause of ITP. Specific infections such as rubella, mumps, measles, pertussis, varicella, Ebstein-Barr virus, parvovirus, cytomegalovirus, hepatitis A, B, C or bacterial infection can be detected in 20% of patients. In our case, *Mycoplasma pneumoniae* IgM positivity was detected in serological tests. Definite diagnosis of *Mycoplasma pneumoniae* infection requires either PCR (Polymerase chain reaction), special culture isolation or serologic tests using immunofluorescence and enzyme immunoassays that detect immunoglobulin IgM and IgG. *Mycoplasma pneumoniae* IgM antibodies indicate recent infection, but also false-positive test results may occur. Nevertheless clinical, laboratory and radiological studies were found to be compatible with *Mycoplasma pneumoniae* infection. In differential diagnosis, thrombocytopenia secondary to infection, malignancy and macrothrombocytopenia syndromes were considered. The PT-PTT values were in the normal range and there was no evidence of diffuse intravascular coagulation. When compared to thrombocytopenia secondary to infection, platelet counts were very low, and the number of megakaryocytes increased more than expected in bone marrow smear. For this reason thrombocytopenia secondary to infection wasn’t considered. No blasts were identified in the blood smear, and platelet morphology was within the normal range, with 1-2 large platelets per field. There were no abnormally giant platelets and Döhle bodies that would suggest a macrothrombocytopenia syndrome. In our patient, platelets at different sizes (normal and large) were seen in peripheral blood smear compatible with ITP in contrast to macrothrombocytopenia syndromes. Also malignancy was not considered in the clinical and laboratory findings.

In a study of 2031 patients with diagnoses ITP, mean age of diagnosis was 5.7. Demircioğlu et al. reported that male/female ratio is 1.5 in their study. The most common complaints were petechial-ecchymosis (83%), epistaxis (25%), hematuria (4%). Severe gastrointestinal and intracranial hemorrhage can be seen in some of the patients.

Our case is a 2 year old girl who has a common age distribution in terms of ITP. She had minimal petechial lesions but also did not develop bruising, or severe bleeding during admission.

IVIG and corticosteroids are usually used in the treatment of ITP. The initial dose for IVIG is 0.8-1 g/kg, and the duration of treatment is determined by the platelets count follow-ups. Steroids are used in the literature at different doses, with 1-2 mg/kg/day being the most frequently used for several weeks in divided doses. Scoring systems have been developed to detect the severity of thrombocytopenia and reduce the risk of bleeding.

| Table 1: Platelet- WBC counts, Fever peaks, antibiotics according to treatment days. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Day             | 1               | 2               | 3               | 4               | 7               | 22              | 23              | 26              | 52              |
| Treatment       | Platelet transfusion | IVG 0.6 g/kg/d | IVG 0.6 g/kg/d | IVG 0.6 g/kg/d | IVG 1 g/kg/d | Methylprednisolone | Methylprednisolone |
| Platelet x10⁹/L| 19              | 10              | 35              | 124             | 329             | 22              | 62              | 446             | 326             |
| 4 mg/kg/d 2 day | Methylprednisolone | 4 mg/kg/d 5 day |

FIGURE 2: Bone marrow smear reveals increased immature-mature megakaryocytes (May-Grünwald & Giemsa x100).
in patients with thrombocytopenia. Risk of bleeding is very high in sudden onset, acute phase of infection, and children under 10 years. In our case, platelet count was 19x10^9/L, she had minimal petechial lesions and it was in the period of acute infection. For these reasons treatment was started according to my clinical experience and scoring systems. However, there are also different opinions applied to various centers in the literature. First of all platelet transfusion was given considering thrombocytopenia secondary to infection. Because thrombocytopenia occurred concomitantly with the infection in contrast to ITP. IVIG was given for 3 days when there was not enough increase. After the infection in contrast to ITP. IVIG was given for 3 days when there was not enough increase. After 3 weeks, treatment with methylprednisolone was started with a suspected allergic reaction and fever with IVIG treatment. Both therapies achieved safe levels of platelet count. Although bone marrow aspiration is not routinely recommended in the diagnosis of ITP, it was performed in order to assess the atypical course of the disease and evaluate pre-steroid bone marrow.

ITP can develop rarely due to *Mycoplasma pneumoniae* infections. Cases in the literature described distinguish them from classic ITP. First of all, thrombocytopenia occurred concomitantly with the infection in contrast to classic ITP that have an interval of days to weeks between infection and thrombocytopenia onset. Secondly, cases experienced severe course with severe bleeding episodes like fatal intracranial hemorrhage in contrast to classic ITP that 3% severe bleeding and less than 0.6% fatality can be developed. Several mechanisms are thought to explain differences with the classic ITP. The infecting agent can play a role in the pathogenesis of Mycoplasma induced ITP. It can destroy the platelet with through direct connection to it. The etiology of the thrombocytopenia due to *Mycoplasma pneumoniae* infection seems to be autoimmune, similar to ITP. Thrombocytopenia was observed during the active infection period in our patient, and the early IVIG and clarithromycin treatment resulted in a significant increase in platelet count.

In conclusion, unlike normal, concurrent immune thrombocytopenia can be seen during *Mycoplasma pneumoniae* infections. High suspicion and early diagnosis is important in preventing complications related to unnecessary transfusion and thrombocytopenia.

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**Conflict of Interest**

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**Authorship Contributions**

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