ABSTRACT

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system. This disease is estimated to affect 1.9 to 6.4/100,000 children/year. Classical features include a previously healthy child with sudden onset of excessive bruising, petechiae and/or mucosal bleed. In extremely rare cases, a child with acute ITP can present with spontaneous intracranial hemorrhage (ICH). The incidence of ICH in children with ITP was established as 0.1%–1.0%. We reported a baby boy of 1 month and 16 days who was admitted at Sanglah Hospital with generalized cutaneous petechiae, mucosal bleed, and seizure. His head CT scan revealed ICH in left occipitoparietal and frontal area. Laboratory investigation showed normochromic anemia with thrombocytopenia. The patient received packed red cell and thrombocyte transfusion with high-dose methylprednisolone and intravenous immunoglobulin treatment. His condition continued to improve day by day and the thrombocyte count increased above 100,000/mm³ after 10 days of hospitalization. This case showed good response to treatment with high-dose methylprednisolone and intravenous immunoglobulin.

Keywords: immune thrombocytopenic purpura, child, intracranial hemorrhage

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system.1,2 This disease is estimated to affect approximately 1.9 to 6.4/100,000 children/year. Both genders are equally affected.3,4

Perdarahan intrakranial pada anak dengan purpura trombositopenia imun

Made Ayu Cynthia Windasari, Ketut Ariawati

ABSTRAK

Purpura trombositopenia imun (PTI) merupakan suatu penyakit autoimun yang ditandai dengan penurunan jumlah platelet akibat penghancuran platelet di sistim retikuloendoitelial. Penyakit ini diperkirakan terjadi pada 1,9 to 6,4/100.000 anak/tahun. Gambaran klasik pada PTI adalah anak yang sebelumnya tampak sehat kemudian tiba-tiba mengalami memar, petekie, dan atau perdarahan mulus. Pada kasus yang sangat jarang, anak dengan PTI akut dapat mengalami perdarahan intrakranial spontan. Insiden perdarahan intrakranial pada PTI sekitar 0,1-1%. Kami melaporkan bayi berusia 1 bulan 16 hari yang datang ke Rumah Sakit Umum Pusat Sanglah karena timbul petekie di seluruh tubuh, perdarahan mulos dan kejang. Pada pemeriksaan CT scan kepala didapatkan perdarahan pada bagian oksipitoparietal kiri dan bagian frontal. Hasil laboratorium menunjukkan anemia normokromik normositer dan trombositopenia. Pasien mendapatkan terapi transfusi sel darah merah dan trombosit, metilprednisolon dosis tinggi dan imunoglobulin intravena. Setelah mendapat perawatan selama 10 hari, kondisi pasien semakin membaik dan jumlah platelet meningkat kembali di atas 100.000/mm³ setelah 10 hari perawatan. Kasus ini menunjukkan respon terapi yang baik dengan pemberian metilprednisolon dosis tinggi dan imunoglobulin intravena.

Kata kunci: Purpura trombositopenia imun, anak, perdarahan intrakranial


INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system.1,2 This disease is estimated to affect approximately 1.9 to 6.4/100,000 children/year. Both genders are equally affected.3,4
Clinical presentation of ITP varies from asymptomatic, mild bleeding to severe or life-threatening bleeding such as intracranial hemorrhage (ICH). It typically presents as sudden onset bruising, petechiae or mucosal bleed, which can be alarming to parents and doctor. In the majority of children, ITP is generally considered as an acute, self-limiting benign disorder with a 60%-80% change of spontaneous recovery occurring usually within a few months after onset. Most patients with ITP, even those with very low platelet counts, do not experience severe bleeding. Nonetheless, ICH which is its most devastating complication and is extremely rare, confers significant morbidity and mortality. In children with ITP, its incidence varies from 0.1 to 1.0.

The platelet count was less than 10,000/µL in 71.4% of the ICH cases. Patient with low platelet counts may require treatment depending on their symptoms or risk of bleeding. The goal of treatment for children with ITP is to maintain a balanced hemostasis and safe platelet count while avoiding potential side effects of therapy. For patients with a high likelihood of ICH, multi-agent combination therapy should be considered.

We report a case of baby aged 1 month and 16 days with ICH in ITP. The aim of this report is in order to know the clinical features, diagnosis, and management of ICH in ITP itself.

Case Illustration
A baby boy aged 1 month and 16 days, was referred to Pediatric Emergency Department of Sanglah Hospital from a pediatrician’s private practice in March 9, 2014 with chief complaint of generalized cutaneous petechiae which occurred since 4 days before admission. The petechiae gradually increased until it covered the entire body, and bruises of varied size started appearing two days later on his palate and limbs. There were no history of trauma, nasal bleed, gingival bleed, fever and seizures. Stool and urine color were normal. The patient had never experienced cough and rhinitis before. Patient’s mother was uncertain whether or not her son looked paler than usual.

He was born on full term through spontaneous vaginal delivery with birth weight was 3600 grams. No visible abnormality was found. He did not get any prior medication for specific disease. There was no family history for bleeding disorder. He had already got immunization (Hepatitis B and Polio) on the first day after birth, followed by BCG vaccine 1 week later. The patient was breastfed until now. His development was normal.

Physical examination revealed an alert baby, pulse, temperature, breath and heart sounds were normal. According to the Waterlow criteria, his nutritional status was overweight (113%). The head examination revealed bulging fontanel. His palpebral conjunctivae were pale, with no subconjunctival bleeding and no jaundice, while his pupils were normal in terms of size and reflexes. Inspection of the oral cavity revealed a hematoma in his palate approximately 2 cm in diameter. There were no liver and spleen enlargement. The skin examination revealed generalized cutaneous petechiae and purpuric rash with bruises on the limbs. The physiological reflexes of the patellar tendons were normal. Motor strength in the extremities was normal. Head CT-scan (Figure 1) showed ICH in left occipitoparietal and frontal area approximately 5.9 ml in volume, surrounded by perifocal edema in white matter area without any evidence of midline shift. Complete blood count investigation revealed white blood count of 9.8 10^3/µL, neutrophile count of 28.5 10^3/µL, lymphocyte count of 55 10^3/µL, monocyte count of 6.7 10^3/µL, eosinophile count 4.3 10^3/µL, basophile count of 0.4 10^3/µL, Hb 6.7 g/dl, MCV 82.8 fl, MCH 30.9 pg, MCHC 37.4 g/dl, RDW 15.3%, Hct 17.9%, and platelet 3 × 10^3/µL, reticulocyte count of 116.5 (5.4%). Blood smear examination revealed normochromic erythrocyte, no atypical lymphocyte, thrombocyte greatly decreased count but no giant thrombocyte. Coagulation test yielded the result as follows: PT 14.3 second, INR 1.2, APTT 27.4 second. Overall laboratory investigation concluded a finding of consistent thrombocytopenia and normochromic anemia.

Based on the patient’s history, clinical manifestation and laboratory findings, the patient was diagnosed as an overweight baby with ICH due to ITP. Management of these patient was administration of high-dose methylprednisolone treatment (30 mg/kg/day for 3 days) and intravenous immunoglobulin (IVlg) 0.4 g/kg/day for 5 days. Thrombocyte suspension and packed red cell transfusion was also included in the treatment regimen.

On the second day of hospitalization, patient had general seizure 15 minutes in duration, without fever, which immediately stopped after phenobarbital administration. On the third day of treatment, thrombocyte count increased to 22,000/mm³, and

Figure 1 Head CT-scan
clinically evident petechiae and hemoptysis gradually regressed. Methylprednisolone treatment was eventually tapered and IVIg treatment was continued until the fifth day of hospitalization. On day 7, there were no visible petechiae, purpuric rash, bruises and hemoptysis. On the 10th day of hospitalization, thrombocyte count reached 178,000/mm³, and the patient was discharged from the hospital with home advice of continual methylprednisolone and phenobarbital therapy. There was no definitive neurologic deficit at the time of discharge. Complete blood count (CBC) examination progress was laid out in Table 1.

**DISCUSSION**

Immune thrombocytopenic purpura is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system. Acute ITP remains a clinical diagnosis based primarily on the acquired, acute onset of the disease (thrombocytopenia duration of <12 months with or without treatment) in an otherwise healthy child, the absence of atypical features and the exclusion of alternative causes of the thrombocytopenia. Classic clinical features include a previously well child with sudden onset of excessive bruising, petechiae and or mucosal bleed. The main diagnostic tools are history taking, a physical examination, CBC test and a peripheral blood smear. Atypical findings should raise suspicion of an alternative diagnosis. The CBC demonstrates isolated (and often profound) thrombocytopenia. Some children may be anemic due to blood loss. Platelets may be normal or larger in size but consistently giant platelets (approaching the size of red blood cells) are absent. There should be normal red blood cell morphology and normal white blood count and morphology. Some children may have an increased number of normal or atypical lymphocytes on the blood smear reflecting a recent viral illness. In our case, a baby boy of 1 month and 16 days developed generalised cutaneous petechiae, purpuric rash, mucosal bleeding, seizure and ICH. Platelet and haemoglobin count was decreased, with no giant platelet and atypical lymphocytes found on the blood smear. The patient was diagnosed with acute ITP complicated by ICH.

There is a general consensus that bone marrow aspiration is not indicated in a typical case, but it should be done if there is any doubt about the diagnosis. The purpose of bone marrow investigation is to exclude the other causes of thrombocytopenia. Aert *et al.*, studied the bone marrow in 72% of cases but the diagnosis remained the same. The bone marrow examination, when done, generally reveals normal granulocytic and erythrocytic series with normal or increased number of megakaryocytes.In our case, the patient did not undergo bone marrow aspiration because he presented typical signs and symptoms of ITP.

In approximately two thirds of cases, the onset of acute ITP is preceded by an infectious illness, most often an upper respiratory tract infection. In a minority of cases, ITP follows a specific viral illness (rubella, varicella, mumps, rubeola, or infectious mononucleosis) or immunization. The risk for ITP after mumps measles rubella vaccine is estimated at approximately 1 in 25,000 doses. In children who have acute ITP, the interval between the preceding infection and the onset of purpura varies from a few days to several weeks, with the most frequent interval of approximately 2 weeks. The study reported an infection in 60.2% of cases preceding the disease in children one to 10 years of age. Both genders are equally affected. Ronchi *et al.*, reported three cases of idiopathic thrombocytopenic purpura after the first dose of recombinant hepatitis B vaccine in children below 6 months of age, in which the latency period varied from 1 to 4 weeks. Neau *et al.*, reported seven cases that developed thrombocytopenia on average 7 weeks after having received recombinant hepatitis B vaccine. The side effects after hepatitis B vaccine are estimated in one case per 100,000 administrated doses. In our case, there were no history of previous infections or use of drugs. The child developed petechiae 6 weeks after receiving the first dose of hepatitis B and polio vaccines.

Although it is a rare complication, ICH continues to be the most important cause of significant morbidity and mortality in ITP. A few studies have examined ICH in children with ITP. In a retrospective analysis, the incidence of ICH in children with ITP was found as approximately 0.1%–1.0%. Although there are no definite predictors of which child will suffer an ICH, some factors including history of recent trauma, immunization, viral infection, drug ingestion, adolescents with ITP, systemic lupus erythematosus, retinal hemorrhage, 'wet purpura' including other severe mucocutaneous bleeding, and even cerebral arterio-venous malformation may possible be high risk factors predicting ICH. In a retrospective study

**Table 1 Complete blood count progress**

<table>
<thead>
<tr>
<th></th>
<th>Diagnosis</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 10</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>9.8</td>
<td>10.3</td>
<td>6.89</td>
<td>9.9</td>
<td>10³/µL</td>
</tr>
<tr>
<td><strong>HGB</strong></td>
<td>6.7</td>
<td>8.5</td>
<td>11.8</td>
<td>11.7</td>
<td>g/dL</td>
</tr>
<tr>
<td><strong>MCV</strong></td>
<td>82.0</td>
<td>86.6</td>
<td>89.9</td>
<td>94.5</td>
<td>fL</td>
</tr>
<tr>
<td><strong>MCH</strong></td>
<td>30.4</td>
<td>31.9</td>
<td>32.3</td>
<td>32.1</td>
<td>pg</td>
</tr>
<tr>
<td><strong>MCHC</strong></td>
<td>37.9</td>
<td>36.8</td>
<td>35.9</td>
<td>35.0</td>
<td>g/dL</td>
</tr>
<tr>
<td><strong>HCT</strong></td>
<td>17.9</td>
<td>23.2</td>
<td>32.8</td>
<td>34.5</td>
<td>%</td>
</tr>
<tr>
<td><strong>PLT</strong></td>
<td>3</td>
<td>22</td>
<td>59</td>
<td>178</td>
<td>10³/µL</td>
</tr>
</tbody>
</table>
with ICH, twelve patients of seventeen cases developed ICH after the onset of ITP. In the same series, one patient ingested non-steroidal anti-inflammatory drug and four patients had a history of head trauma. In our case, we found hematoma in the patient’s palate and observed a history of immunization 6 weeks before he started developing the symptoms. The percentage of ICH occurring within 4 weeks of initial diagnosis varied from 19% to 50% in different reports. In one retrospective review, 10% (7/69) of cases of ICH occurred within 3 days of diagnosis of ITP. Trauma to the head and use of antiplatelet drugs, such as aspirin, were identified as risk factors for ICH in children who had ITP and very low platelet counts. Platelet counts of less than 20,000/mm³ was generally considered risky values for ICH. The threshold platelet count for therapy in ITP is not well known because of the lack of clinical data. A study revealed that only 1 of 56 children with complicated by an ICH had a platelet count of more than 20,000/mm³, 73% of patients had a platelet count of less than 20,000/mm³. In our patient, the platelet count was 3,000/mm³ at the onset of ICH. This low platelet account is considered the risk factor of ICH in patients with ITP. Our patient developed ICH 3 days after the onset of petechiae.

Once ICH has occurred, physicians must focus the energy on treating patients intensively. Mortality rate decreased markedly owing to these intensive treatment regimens. The therapeutic approaches taken in ITP were platelet transfusions, high-dose steroid and IVIg treatment along with various supportive care. Intravenous glucocorticoids can be interpreted as 15-30 mg/kg of methylprednisolone administered over 30-60 minute bolus injection for three days with maximum dose of 1 g/day. Platelet count recovery achieved by using high-dose parenteral glucocorticoids was faster than that obtained by oral glucocorticoids and was as rapid as that with IVIg. Duru et al. studied treatment regimen with IVIg, high-dose methylprednisolone, and no therapy at all, and showed that platelet counts at three days after starting therapy were significantly higher in both IVIg and high-dose methylprednisolone groups than in the no therapy group (P<0.01). Our patient received packed red cell and thrombocyte transfusion, high-dose methylprednisolone and IVIg treatment. His condition improved gradually and the thrombocyte count increased above 100,000/mm³ after 10 days of hospitalization.

SUMMARY

We reported a case of baby aged 1 month and 16 days, who was admitted to hospital with generalized cutaneous petechiae, mucosal bleed, and seizure. His head CT-scan revealed ICH in left occipitoparietal and frontal area. Laboratory investigation showed normochromic anemia with thrombocytopenia. The patient received packed red cell and thromboocyte transfusion with high-dose methylprednisolone and intravenous immunoglobulin treatment. His condition continued to improve day by day and the thrombocyte count increased. Intracranial hemorrhage is an extremely rare complication of ITP and this case showed good response to treatment with high-dose methylprednisolone and intravenous immunoglobulin.

REFERENCES