CASE REPORT

Thrombocytopenic purpura after hepatitis B vaccine

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Abstract

Objective: to demonstrate a case of idiopathic thrombocytopenic purpura after hepatitis B vaccine and drive attention to this possible relation when other causes have been excluded.

Methods: description of a case of a patient who was 1 month and 16 days old and presented petechiae and ecchymoses one week before she entered the Emergency Room of the Hospital das Clínicas da Universidade de São Paulo. Other causes beyond Hepatitis B vaccine, received one month before the hemorrhagic state, were ruled out with the history and laboratory exams. A review of the literature about PTI revealed case reports of the disease connected with Hepatitis B vaccine administration.

Results: the vaccine was considered the probable cause. The child was treated with intravenous immunoglobulin, improving from thrombocytopenia after three days, and remaining without symptoms during one month of follow up.

Conclusion: the thrombocytopenic purpura after hepatitis B vaccine is a rare event whose causal relation is hard to prove. The diagnosis is based on the exclusion of other possible causes, but in this case, the hypothesis may be considered since new cases are being reported in the literature.

Introduction

Idiopathic thrombocytopenic purpura is a disease of probable autoimmune etiology, which affects children and adults in an estimated incidence of 10 to 125 per 1,000,000 people a year.¹ It is defined as an isolated thrombocytopenia with no other clinical associated conditions or other causes of thrombocytopenia (infection by HIV, systemic lupus erythematosus, lymphoproliferative diseases, myelodysplasias, and thrombocytopenia induced by drugs).²

It usually affects children, and the incidence in this group peaks between the 2nd and the 4th years of age, affecting boys and girls in the same proportion.²

Idiopathic thrombocytopenic purpura is manifested through mucous and dermal bleeding, and serious hemorrhages, such as intracranial hemorrhages, occur in only 0.5 to 1% of the cases.³ About 85% of the cases present benign and self-limited evolution, with spontaneous and complete recovery in up to 6 months.³

The diagnosis is based on the patient’s history, on physical examination, and on the exclusion of the causes of thrombocytopenia. It generally occurs after a viral infection episode; however, there are reports of cases of idiopathic thrombocytopenic purpura that set after measles-mumps-rubella vaccine⁴,⁵ and hepatitis B vaccine.⁶-⁹
The hepatitis B vaccine is usually well tolerated, with few side effects; but several cases of thrombocytopenia after recombinant vaccine have been described in literature.6-9

Nowadays, in São Paulo, hepatitis B vaccine is applied to all children at birth, with a booster dose 1 year and 6 months later. In July 1999, we observed another probable case of idiopathic thrombocytopenic purpura after hepatitis B vaccine in a 1 year-16 day old child.

Case report
L.A.M.S., female, born on term on June 4, 1999, by a cesarean delivery, weighing 2,920 g. Prenatal examinations showed no pathologies, with negative serologies (HIV, toxoplasmosis, rubella, and syphilis).

On the 12th day of life, she took the first dose of the hepatitis B vaccine.

The mother reported the appearance of “blotches” on the patient’s face on the 15th day of life; these blotches/rashes were treated with topical hydrocortisone.

She was vaccinated with BCG, the first dose for Haemophilus influenzae, and the second dose for hepatitis B with 1 month and 15 days of life.

She was admitted at the Emergency Room of Hospital das Clínicas in July 20, 1999, with 1 month and 16 days of life, presenting petechiae on her face, hands, and feet, and ecchymosis on her thigh for 1 week. Fever or previous infections were not reported.

<table>
<thead>
<tr>
<th>Table 1 - Laboratory examinations during hospitalization and alterations in the administration of intravenous immunoglobulin</th>
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<tr>
<td><strong>July 20</strong></td>
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<td>Hb (g/dl)</td>
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<td>Ht (%)</td>
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<tr>
<td>Leukocytes</td>
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<td>Platelets (mm³)</td>
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<td>TP</td>
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On physical examination, she presented a good general status, with petechiae on her body and palate. The liver was 1.5 cm away from the right costal margin, and the spleen was impalpable. No other alterations were found.

Laboratory examinations (see Table 1) initially indicated pancytopenia, besides normal coagulogram, and negative serologies for syphilis, toxoplasmosis, rubella, and cytomegalovirus. We required a myelogram, which revealed:

- normocellular and normomaturative granulocytic, red, and lympho-mono-plasmocytic series;
- normocellular megakaryocytic series, with decreased plateletopenia, presenting mainly acidophilic granular megakaryocytes without platelets (suggestive of idiopathic thrombocytopenic purpura). As platelets had fallen to 12,000/mm³, a treatment with intravenous immunoglobulin was initiated in the dose of 400 mg/kg/dose, and it was maintained for 5 days.

Two days after the beginning of the treatment, there was an improvement in plateletopenia: 311,000/mm³.

The child was discharged from hospital after a 5-day treatment, with platelets at 780,000/mm³. She was reevaluated one month later, maintaining platelets at 620,000/mm³.

Discussion
A causal relation between the hepatitis B vaccine and idiopathic thrombocytopenic purpura is hard to be confirmed. Post-vaccination thrombocytopenia continues to be an...
exclusion diagnosis, when other possible causes for thrombocytopenia are discarded, and the latency period between the vaccine and the appearance of the symptoms suggests this relation.

In literature, several cases of post-vaccine thrombocytopenia were reported. In 1994, Poullin & Gabriel\(^6\) described two cases of idiopathic thrombocytopenic purpura in two young women, respectively 21 and 15 years old, who developed the disease after the second and the third doses of the recombinant hepatitis B vaccine, with a latency period of 4 and 3 weeks, respectively. Both had no history of previous infection and use of drugs.

In 1995, Meyboom et al.\(^7\) reported 28 cases of thrombocytopenia after hepatitis B vaccine (recombinant and non-recombinant); eight of them presented a possible reaction to the vaccine. The latency period varied from some days up to 2 months.

Recently, in 1998, other two articles about idiopathic thrombocytopenic purpura after hepatitis B vaccine were published. Ronchi et al.\(^8\) 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.\(^9\) reported seven cases (four men and three women) that developed thrombocytopenia on average 7 weeks after having received recombinant hepatitis B vaccine.

In this case, there was no history of previous infections or use of drugs. Both the mother and the child presented negative serologies. The child developed petechiae 1 month after having received the first dose of hepatitis B vaccine. On the admission examination, pancytopenia could suggest other pathologies, such as leukosis or medulla aplasia. The myelogram performed demonstrated normal hematopoiesis and an increase in megakaryocytes, which suggests the diagnosis of idiopathic thrombocytopenic purpura. The antplatelet antibody test was not performed, since it is considered unnecessary by some authors for the diagnosis of idiopathic thrombocytopenic purpura.\(^1,2\) On the 3rd day of hospitalization, platelets had fallen to 12,000/mm\(^3\), and the treatment with intravenous immunoglobulin was indicated. In literature, there is a consensus about the treatment of children presenting platelet count below 20,000/mm\(^3\), in order to prevent serious bleedings, such as the intracranial bleeding.\(^3,10\) Both the corticosteroid and the immunoglobulin decrease plateletopenia time.\(^10-12\) Some authors, such as Davis and Raffles,\(^13\) administer intravenous immunoglobulin in platelet counts <20,000/mm\(^3\), even in children with few symptoms, because they believe that the side effects are mild in relation to the risks of serious hemorrhages due to plateletopenia. The treatment with immunoglobulin improves plateletopenia in 2 days on average, varying from 1 to 34 days.\(^10\) After 2 days of treatment, the platelets were already at the level of 311,000/mm\(^3\). This good response to the treatment with intravenous immunoglobulin also suggests the diagnosis of idiopathic thrombocytopenic purpura.\(^14\)

One month later, the child was reevaluated, and she remained asymptomatic. Only 3 to 5% of the cases become chronic; most of them are cases of children older than 7 years of age who rarely present postinfectious idiopathic thrombocytopenic purpura.\(^3\)

The case reported here is probably another case of idiopathic thrombocytopenic purpura induced by hepatitis B vaccine. The side effects after hepatitis B vaccine are estimated in one case per 100,000 administrated doses.\(^9\) The hepatitis B vaccine has a good level of efficiency, and its adverse effects, including idiopathic thrombocytopenic purpura, must not put its use in question.

References


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