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Case Report

Differential Diagnosis for Erythema Infectiosum and Immune Thrombocytopenia after MMR Vaccination

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Abstract

Immune Thrombocytopenia (ITP) can be associated with measles vaccination. The risk of ITP has been shown to be increased in the six weeks following vaccination, with World Health Organization data estimating 1 case per 30,000 vaccinated children. It is manifested by a sharp decrease in the number of platelets in the blood and acute hemorrhagic syndrome. However, the main symptom of the disease is cutaneous bleeding like purpura, petechiae or ecchymoses. To establish a diagnosis, physicians should exclude other diseases characterized by the presence of such a rash. For example, it may be exanthema associated with infectious agent. This article presents a clinical case of immune thrombocytopenia due to MMR vaccination in triplet babies, which was diagnosed as an adverse event after immunization. Then, after receiving a laboratory test results, it was confirmed a case of parvovirus B19 infection, which coincided with the immunization.

Keywords: Adverse events following immunization; Immune thrombocytopenia; Erythema infectiosum; parvovirus B19 infection

Abbreviations

ITP: Immune Thrombocytopenia; MMR: A Vaccine against Measles, Mumps, and Rubella; IgM: Immunoglobulin class M; IgG: Immunoglobulin Class G

Case Presentation

Three 7-year-old children (triplet babies – two girls and a boy) were admitted to the emergency room of Pediatric Research and Clinical Center for Infectious Disease on the 12th of February, 2020. Immune thrombocytopenia due to measles-mumps-rubella vaccination (MMR, batch number S023779) was diagnosed on presentation. Adverse event following immunization was registered.

Anamnesis morbi: The patients had acute onset of the disease. It has been established that each child received a dose of MMR vaccine on the 5th of February. In the evening of the 7th of February (the 2nd day after vaccination), after bathing, their mother noticed a rash which was located on the legs, forearms and around knee and elbow joints and looked like ecchymoses. The children were in a low-grade fever (37.2°C). They sought for medical help the following day. The hematologist examined the children; complete blood count, coagulation test was taken–without special features; then there was made a conclusion about platelet disorders (?). It was recommended to take vitamin C andethamsylate. There were no results during the following days of the treatment: a low-grade fever and rash persisted, therefore they sought for medical help again.

Anamnesis vitae: Gravida 3, Para 2, Live birth 3; by Caesarean section; no complications at birth. The children have not all vaccines for their age due to medical exemptions. Concomitant pathology: Biliary dyskinesia, gastroesophageal reflux disease, gastroduodenitis, allergic diseases.

The children were examined in the emergency room: fever (37.5°C); the skin of normal color; some ecchymoses with a diameter of 0.5-2.0 cm on the legs, forearms and around knee and elbow joints (Figure 1); at the site of administration of the vaccine without inflammatory changes; pharynx hyperemic.

Differential diagnosis was performed with immune thrombocytopenia following immunization and exanthema, caused by infectious agents. Symptomatic therapy was recommended.

Complete blood counts, biochemical blood assay, coagulation test, determination of dynamic function of platelets were normal.

The girl, V.: erythrocytes – 3.99 x 10^{12}/L; hemoglobin – 118g/L; leucocytes – 4.4 x 10^{9}/L; platelets – 281x10^{9}/L. Activated partial thromboplastin time – 33.1 seconds; prothrombin time ratio – 13.5 seconds; international normalized ratio – 1.06.

The girl, I.: erythrocytes – 4.24 x 10^{12}/L; hemoglobin – 123g/L; leucocytes – 5.0 x 10^{9}/L; platelets – 254x10^{9}/L. Activated partial thromboplastin time – 32.7 seconds; prothrombin time ratio – 12.8 seconds; international normalized ratio – 0.99.

The boy, K.: erythrocytes – 4.42 x 10^{12}/L; hemoglobin – 125g/L; leucocytes – 3.3 x 10^{9}/L; platelets – 199x10^{9}/L. Activated partial thromboplastin time – 35.0 seconds; prothrombin time ratio – 13.9 seconds; international normalized ratio -1.10.

Immune thrombocytopenia following immunization was ruled out based on the anamnesis (the clinical manifestation on the 2nd day after the vaccination) and laboratory data (normal cell count).

Every child was carefully evaluated for evidence of infection which can cause the rash. We used a serologic method: identification of specific antibody (immunoglobulin class M and G – IgM and IgG) to parvovirus B19, Yersinia enterocolitica and Yersinia pseudotuberculosis by an enzyme immunoassay; Enterovirus

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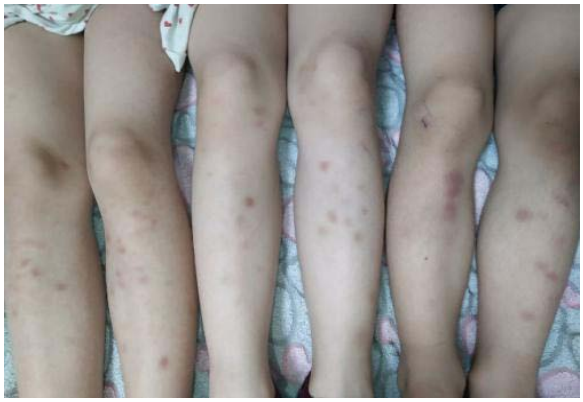

Figure 1: Erythema infectiosum, clinical manifestation (a rash).

antigens by modified complement fixation test.

The girl, V. had parvovirus B19-specific IgG antibodies and Yersinia enterocolitica, Yersinia pseudotuberculosis IgM and IgG antibodies. The girl, I., and the boy, K., had negative results for both of these infections. Antigens of Enterovirus 70 were found in fecal culture (virus shedding) in the triplets.

The diagnosis of yersiniosis was questionable despite the presence of antibodies to Yersinia spp., because clinical manifestations were not full and stopped without antibacterial therapy.

The incubation period of erythema infectiosum is variable; from 4 to 20 days to the appearance of the rash. The diagnosis is usually based on clinical and epidemiological grounds. In our case the diagnosis was confirmed by the detection of parvovirus B19 specific IgG antibodies in the girl, V. Another two children were diagnosed with erythema infectiosum based on clinical (one-time onset of the disease, identical to clinical symptoms) and epidemiological data (the patients from the same family).

There was a decline in catarrhal phenomena and the rash treatment. The patients were discharged on the 7th day of hospitalization.

Thus, severe adverse event was registered, but the connection of the disease with the vaccination was not confirmed.

Discussion

Immune thrombocytopenia is a rare autoimmune disorder, characterized by isolated shortage of platelets (<100,000/microL), with normal white blood cell count and hemoglobin.

The occurrence of ITP is between 1 and 6.4 cases per 100,000 children [1,2]. ITP can present at any age in children, but more often this disease presents at the age between two and five years and sometimes may occur in adolescence [3]. Predominance of gender with this disorder changes during the age. For example, in infants the frequency of ITP between boys and girls is 7:1 [4], but the male predominance decreases in older children [5]. Moreover, female predominance is ground up in adolescents and younger adults.

ITP typically presents with a sudden appearance of cutaneous bleeding (purpura, petechiae or ecchymoses). Bleeding signs can range from none or minimal to severe and life threatening (intracranial hemorrhage or severe gastrointestinal bleeding); serious hemorrhage is fortunately rare.

It may be present as an isolated primary condition or it may be secondary to other conditions. In most cases, the cause of ITP remains unknown, but an infection (viruses) or some immune, environmental triggers can trigger it. Almost 60 percent of children with newly diagnosed ITP have an episode of a viral disease within the past month [3,4].

However, ITP may develop after immunization, more often after Measles, Mumps, and Rubella (MMR) and MMR-Varicella (MMRV) vaccines. Usually it develops in the six weeks following MMR vaccination. In 2010 a systematic review that included 12 studies was presented, and the average performance of ITP after MMR vaccine was 2.6 cases per 100,000 doses [6]. In 93 percent of cases, thrombocytopenia was solved within six months; expression of severe bleeding was rare. However, the incidence of ITP in children, who were not vaccinated and suffered from these infections, is much higher: 1:6,000 for measles and 1:3,000 for rubella [7-9].

There have been some case reports of ITP following vaccination against poliomyelitis [10], influenza [11], varicella, hepatitis A, and tetanus-diphtheria-acellular pertussis in older children [12]. The research about the association of ITP with these vaccines needs a continuation because of the small number of reported cases.

Differential diagnosis is performed with other thrombocytopenia and thrombocytopathies (complications of acute viral infections, reactions to medications, congenital thrombocytopathies, etc., which are registered much more often than the reaction to vaccination), as well as with hemorrhagic syndromes not associated with platelet damage (vasculitis, haemophilia, etc.) [13].

According to international consensus report on the investigation and management of primary immune thrombocytopenia physicians should perform a complete history, physical examination, full blood count, and expert analysis of the peripheral blood smear at initial diagnosis. A direct anti-globulin test, baseline Ig levels are recommended to exclude coexistent autoimmune hemolytic anemia or immunodeficiency.

Children should be referred to a hematologist experienced in assessment and treatment of children with ITP. Bone marrow aspiration, biopsy, and cytogenetics should be performed if abnormal or potentially malignant cells are visualized on smear and carefully considered if there are other abnormalities of the hemoglobin and/or white cell count (with the exception of microcytic anemia) or if there is hepatosplenomegaly and/or adenopathy [14].

Corticosteroids are the standard initial treatment of ITP, with the addition of IVIG when a rapid response is needed. There are few studies dedicated to assessing the efficacy of disease-modifying antirheumatic, biologic, and nonimmunosuppressive agents as the treatment for lupus thrombocytopenia. Rituximab and thrombopoietin mimetics have been the most extensively studied therapies for primary ITP in recent years. Splenectomy is less often utilized [15].

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