Acute Idiopathic Thrombocytopenic Purpura Following Combined Vaccination Against Measles, Mumps, and Rubella

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Acute idiopathic thrombocytopenic purpura (ITP) is the most common bleeding disorder of childhood. Seventy percent of cases of acute ITP occur following viral illness.[1] Classically these infections include rubella, varicella, measles, and the Epstein-Barr virus.[2] Acute ITP has also been reported after vaccination against poliomyelitis,[3] measles,[4-6] and rubella,[7] (including combined measles-mumps-rubella [MMR] vaccination[8-12]), typhus-paratyphus,[13] smallpox,[14] and influenza and pneumococcal infections.[15] The incidence of acute ITP following MMR vaccination appears to be lower than that of acute ITP following natural rubella or measles infection.[10,16-18] Nevertheless, the occurrence of acute ITP associated with MMR vaccination is rare, and a limited amount of literature is published on the subject. This report describes a case of acute ITP developing 2 weeks after receiving the MMR vaccine.

Case Report

A 12-month-old girl of English and Persian ancestry came to the outpatient clinic on 29 October 1994 with a 24-hour history of purple spots on her extremities and body. She had no history of fever or any systemic illness and was receiving no medication. The patient had received an MMR vaccination (Merck, Sharp, & Dohme; Lot #0612A, expiration 9 May 1996) in a 0.5-mL subcutaneous injection in the left anterior thigh on 13 October 1994, 16 days earlier. On examination, purpura and ecchymotic spots were found on the lower extremities and upper extremities, and scattered lesions were found on the trunk anteriorly and posteriorly, which were not present when the child received the MMR vaccination. The lesions ranged from 0.5 to 2.5 cm. There was no hepatosplenomegaly. An initial complete blood count was obtained showing a white cell count of 9300/μL, a hemoglobin of 13.9 g/dL, and a hematocrit of 38.3 percent. A platelet count was not obtained at the time because of an insufficient blood sample. Prothrombin time, partial thromboplastin time, and electrolytes were all normal.

The patient was sent home and told to return to the outpatient clinic in 2 days for follow-up care. During that time the patient remained asymptomatic except for the purple spots. The patient remained afebrile, and on 31 October 1994 her physical examination showed no evidence of any new purpuric lesions or petechiae. A repeat complete blood count was obtained showing a white cell count of 6500/μL, a hemoglobin of 11.6 g/dL, a hematocrit of 33.0 percent, and a low platelet count of 16,000/μL. The patient was subsequently admitted as an inpatient for probable ITP.

Preinfusion blood samples were drawn to test for human immunodeficiency virus and antinuclear antibodies. The results of both tests were negative. The patient was started on 9 g of intravenous immune globulin (Sandoglobulin) per day (1 g/kg) beginning at 30 mL/h for 15 minutes. No reactions, such as high fever, flushing, or tachycardia, occurred, and subsequently the rate was increased to 60 mL/h until the infusion was complete. The patient was also given acetaminophen (Tylenol) 120 mg orally and diphenhydramine (Benadryl) 8 mg orally. The patient tolerated the infusions well and developed a transient fever on the second day of admission.

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Serial complete blood counts were as follows: On 1 November 1994 the white cell count was 4800/μL, hemoglobin 10.9 g/dL, hematocrit 29.6 percent, and platelets 28,000/μL. On 2 November 1994 the white cell count was 6000/μL, hemoglobin 10.7 g/dL, hematocrit 30.6 percent, and platelets 108,000/μL. On 3 November 1994 the white cell count was 5500/μL, hemoglobin 11.2 g/dL, hematocrit 32.3 percent, and platelets 161,000/μL.

The patient was consequently discharged on 3 November 1994. There was no new bruising; her blood pressure, pulse, and heart rate were stable; and she was active with a normal platelet count. She was seen by her primary care physician, who ordered serial complete blood counts once every week. Platelet counts were 435,000/μL 8 November 1994, 291,000/μL on 14 November 1994, 300,000/μL on 21 November 1994, and 393,000/μL on 29 November 1994.

Discussion

Although in more than 80 percent of cases of childhood acute ITP, permanent and complete recovery occurs irrespective of treatment,[19] treatment with intravenous immune globulin was initiated primarily because of the parents' preference and to avoid necessitating a diagnostic bone marrow aspirate. Though it was an expensive alternative, it was less painful and anxiety-provoking.

Because we initiated intravenous immune globulin 18 days after MMR vaccination, it was possible that the intravenous immune globulin could have affected the antigenicity of the live vaccine. Measles, mumps, and rubella immunoglobulin G (IgG) levels were measured 6 months after the MMR vaccination, and there were low-positive titers for measles IgG, positive titers for mumps IgG, and positive titers for rubella IgG. It is reasonable to conclude that either the intravenous immune globulin did not affect the antigenicity of the MMR vaccine or that the immune globulin was given sufficiently after the MMR vaccination that an immune response to the live virus vaccine was not thwarted.

Of note, the patient's initial hemoglobin of 13.9 g/dL and hematocrit of 38.3 percent on 29 October 1994 dropped to a hemoglobin of 10.9 g/dL and a hematocrit 29.6 percent during the ensuing 3 days. Because the phlebotomy technique used for the initial complete blood count was unknown, it is possible that the initial hemoglobin and hematocrit levels could have been artificially elevated if obtained by finger stick. If the initial complete blood count was drawn by venipuncture, then the next supposition would be that the patient developed a mild autoimmune hemolytic anemia secondary to the MMR vaccine. A direct antiglobulin test was not done, however, and one can only speculate on the possibility of an autoimmune hemolytic anemia. In addition, there was no gross bleeding or evidence of hematochezia or melena during hospitalization.

The occurrence of acute ITP following MMR vaccination is rare. Using MEDLINE we found a total of 47 cases of acute ITP following MMR vaccination.[8-12,20-23] In a Finnish study conducted by Nieminen et al,[10] 23 of approximately 700,000 (approximately 1 per 30,000) children immunized with the measles-mumps-rubella vaccine developed acute ITP. Similarly, in a Swedish study Bottinger et al[9] found that 16 of 589,000 (1 per 37,000) children developed severe acute ITP following vaccination. The frequency of acute ITP following a rubella infection is considerably higher, with an incidence as high as 1 per 3000 reported by Lokietz and Reynolds[16] and Bayer et al.[17] Acute ITP apparently occurs less frequently with measles and mumps infections.[18,24] These studies suggest that the incidence of acute ITP following MMR vaccination remains much lower than the incidence of acute ITP after natural infections.[10]

Acute ITP in rubella infection typically occurs a few days following the appearance of a rash, which in turn appears 18 to 24 days after contact. In the Nieminen et al study, purpura appeared within narrow time limits after inoculation, with a median of 17 days. Our patient developed acute ITP 15 days after inoculation, which was consistent with the Nieminen et al study findings. The temporal association with onset following inoculation was compatible with a causal relation.[10]

As a rule acute ITP is self-limited, particularly the postinfectious type. Most patients recover spontaneously within a few months, and approximately 90 percent recover within a year after onset. Chronic ITP (greater than 6 months' duration) occurs infrequently in childhood.[2] Acute ITP following live virus vaccination has a clinical picture similar to that seen after natural infections. The patients acquiring acute ITP in the

Nieminen et al study, despite an abrupt onset, had an overall course that was predominantly benign with complete recovery in less than 6 months.[10] The clinical course of acute ITP following MMR vaccination is practically identical to the clinical course of typical acute ITP except for a positive history of recent MMR vaccination. Our patient recovered dramatically following infusion of intravenous immune globulin. It remains to be seen whether she will have recurrences of acute ITP, but her clinical course thus far has been typical of acute ITP. Although it cannot be proved that the MMR vaccination undeniably caused her acute ITP, her negative history for a recent viral infection, negative history for a possible drug reaction, and the positive history for a MMR vaccination 15 days before onset suggest that it was a strong possibility.

Because acute ITP is believed to be an immunologic disorder, and platelet-associated IgG or IgM usually occurs, it seems logical that an attenuated live virus vaccine would have the antigenic capacity to initiate acute ITP in a susceptible patient. The higher incidence of acute ITP following natural infections suggests that its antigenic capacity is stronger than in attenuated live virus vaccines. If such is the case, it could be argued that the same individuals who develop post-vaccination acute ITP would have developed acute ITP if they had acquired the natural infection. Consequently, because of the infrequent complication of acute ITP following MMR vaccination and the benefits associated with prevention of the natural infections, the MMR vaccination should still be considered very safe and prudent to use universally. Nevertheless, because of the reports of post-MMR vaccination acute ITP, physicians should be aware of this rare complication and be prepared to take diagnostic and therapeutic steps should it occur.

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