

CASE REPORT

**THROMBOCYTOPENIC PURPURA AFTER
INFLUENZA A H1N1 VACCINE**

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ABSTRACT

Idiopathic thrombocytopenic purpura (ITP) is probably a disease with autoimmune etiology, defined as an isolated thrombocytopenia not associated with any clinical condition. Other causes related to thrombocytopenia are: HIV infection, systemic lupus erythematosus and drug-induced thrombocytopenia. In this report we describe a case of ITP developed after vaccination against influenza A H1N1 in a 64-year-old female patient, hypertensive, offset and in use of antihypertensives, with no history of ITP, after review of clinical history and laboratory tests. The patient's physical examination revealed pallor, ecchymosis in the trunk, limbs and oral mucosa, with bleeding gums. Absence of adenomegaly and palpable splenomegaly, fever or other signs and symptoms of relevance. The blood count and bone marrow examination showed severe thrombocytopenia with platelet count of 7,000/ μ L and hypercellularity of the megakaryocytic series (other series were normal), respectively. A transfusion of concentrate platelet was performed and after treatment with specific poly immunoglobulin (IVIG) and corticoids, the patient showed clinical improvement and laboratory indexes were normalized. ITP after vaccine against influenza A H1N1 is a rare event whose causal relationship is difficult to prove, and the diagnosis is based on exclusion of other possible etiologies.

KEY WORDS: Thrombocytopenic purpura; vaccines; Influenza A; H1N1.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP), currently known as immune thrombocytopenia, is an autoimmune disorder characterized by low platelet count in the peripheral blood, which affects children and adults at an estimated incidence of 10-125 per 1,000,000 people per year (James et al., 1998).

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The pathophysiology of the disease is not completely understood, but auto antibodies are identified, usually from the IgG class, targeted against platelet membrane glycoproteins (GP IIb / GP IIIa and GP Ib) (Novaretti et al., 2015). After the platelet has an antibody bound to its membrane, it is identified by macrophages located in the spleen, where they are destroyed, producing thrombocytopenia. In most patients with ITP, the bone marrow shows an increase in the production of megakaryocytes to try to compensate for the excessive destruction of platelets, although there are cases where this phenomenon does not occur. The reason for this last situation is that autoantibodies are also targeted against antigens present in megakaryocytes (Novaretti et al., 2015).

The clinical picture of ITP is characterized by low platelet count and different degrees of mucocutaneous hemorrhage, being the most common petechiae, ecchymosis, epistaxis and gingival (Salama, 2011; Novaretti et al., 2015). Severe bleeding, such as intracranial bleeding, occurs in only 0.5% to 1% of cases (Imbach & Kuhne, 1998). In approximately 85% of cases, the evolution is benign and self-limiting, with spontaneous and complete recovery in up to 6 months (Imbach & Kuhne, 1998).

First-line treatment of ITP includes the use of corticosteroids, where 70% of patients respond satisfactorily. In the remaining 30%, it is necessary to use supplementary treatment regimens, such as the intravenous use of immunoglobulins, anti-D vaccination, immunosuppressive drugs such as azathioprine, cyclophosphamide, danazol and interferon alpha. Recently, the use of rituximab and thrombopoietin analogues, such as tmbopag and romiplostin, has been incorporated (Roque-García et al., 2012).

HIV infection, systemic lupus erythematosus, lymphoproliferative diseases, myelodysplasias and drug-induced thrombocytopenia constitute risk groups for the development of severe forms of the disease, and it is important to consider the hypothesis of visceral leishmaniasis / HIV coinfection in the differential diagnosis (James, 1996). ITP may start after administration of several vaccines, including measles-mumps-rubella (MMR), hepatitis A and B, diphtheria-tetanus-pertussis (acellular) and varicela (Perricone et al., 2014). The ITP associated with the vaccine is supposedly caused by a molecular mimicry, which results in the activation of autoreactive B or T cells, by peptides of the vaccine that exhibit structural similarity with antigens found in platelets (Nagasaki et al., 2016). In addition, there are other mechanisms capable of inducing post-vaccine ITP, such as, activation of the viewer, polyclonal activation and the presence of superantigens (Perricone et al., 2014). Cases of ITP associated with vaccination for influenza A H1N1 are rare and for this reason often the etiology is not adequately elucidated. Therefore, the present report aims to describe a case of ITP after vaccination against influenza A H1N1.

CASE REPORT

A 64-year-old woman, from Quixadá, CE, hypertensive, compensated, using antihypertensives (amlodipine 5mg, Nebivolol 5mg, and levanlodipino Arcoxia 90 mg), was admitted to the Unimed Regional Hospital in Fortaleza after an episode of drop attack preceded by a feeling of faintness and weakness. On admission, she presented pallor, ecchymosis in the trunk, in the upper and lower limbs and in the oral mucosa, with gingival bleeding, symptoms of 10 days of development, according to the patient's report a few hours after vaccination against influenza A H1N1. No palpable nodes or spleen, absence of fever or other signs of infection were evident.

Laboratory tests conducted at the time showed the following results: blood count - erythrocytes 4,470,000/ μ L; hemoglobin 14.6 g/dL; hematocrit 43.2%; leukocytes 5,500/ μ L and platelets 7,000/ μ L. The myelogram showed granulocytic, red and lympho-monocytoplasmic series normocellular and normomaturative and hypercellularity of the megakaryocytic series. Negative serology for HIV 1/2, toxoplasmosis, rubella and syphilis.

Without a defined diagnosis and as an urgency, it was decided to treat thrombocytopenia with blood transfusion, but the patient did not show any significant improvement. In view of the clinical findings and laboratory results, the diagnosis of ITP was established, possibly induced by administration of the influenza A H1N1 vaccine.

Treatment was initiated with 1 g/kg polypspecific immunoglobulin (IVIg) for 3 days together with intravenous methylprednisolone 30 mg/kg in 500 mL of serum glycoside at 5% in infusion of hours for 3 days. On subsequent days, the dose was halved until an equivalent dose of 1 to 2 mg/kg oral prednisone was achieved. Prednisone was maintained for 3 to 4 weeks, followed by gradual reduction from 10 mg per week to the dose of 0.5 mg / kg and then discontinuation with slow removal of 5 mg per week. Clinical and laboratory controls were performed and after normalization of the number of platelets, the control became biweekly for six months with a final platelet count of 325,000/ μ L.

DISCUSSION

The causal relationship between the H1N1 influenza A vaccine and the ITP is difficult to prove. The diagnosis of post-vaccinal ITP continues to be performed by exclusion, when other possible causes of thrombocytopenia are ruled out. The latency time between the vaccine and the onset of symptoms suggests this relationship.

In the literature there are few reports of thrombocytopenic purpura after vaccination against influenza A H1N1. In 2011, a case of post-vaccinal Henoch-Schönlein purpura in a 39-year-old patient from the city of Rio de Janeiro with a history of lower limb purple, arthralgia and diffuse abdominal pain, who appeared a few hours after influenza A H1N1 vaccine was described. She had hemorrhagic blisters on the legs and feet (Pimentel et al., 2011). Recently, three cases of ITP associated with influenza A vaccine in female patients over 70 years of age were described (Nagasaki et al., 2016).

Cases of ITP of post-vaccine etiology have been described associated with hepatitis A and B vaccine. In 1995, Meyboom et al reported 28 cases of thrombocytopenia possibly associated with hepatitis B vaccine and 5 with hepatitis A vaccine. Latency time ranged from a few days to 2 months in cases associated with hepatitis B vaccine (Meyboom et al., 1995).

In the present report, the determination of the vaccine's etiology (influenza A H1N1) of the ITP was performed by exclusion, since the patient had no prior history of drug use or recent infections, presenting clinical signs of purpura and laboratory tests of thrombocytopenia, which were confirmed by the negative result of the serological tests performed. The occurrence of ITP with vaccine etiology is a relatively infrequent event, but most of the cases reported in the literature affect female patients (Pimentel et al., 2011; Perricone et al., 2014). Corroborating with these studies, this case was also identified in a female patient.

Platelet transfusion was performed with the objective of reducing the risk of complications caused by major hemorrhages, since the patient had a platelet count below 10,000/ μ L and signs of localized microhemorrhages. After transfusion of a platelet concentrate unit and initiation of treatment with polyspecific immunoglobulin and corticosteroids, a gradual increase in the number of platelets was observed, with normal values being identified after approximately 2 months of treatment initiation.

Taking into account the case described here and the annual influenza vaccination campaigns carried out in Brazil, the present report draws the attention of the medical team to possible adverse effects produced by the influenza A H1N1 vaccine, in particular ITP.

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