Case Report

Relapse of Immune Thrombocytopenia Associated with Varicella 20 Years after Splenectomy

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Abstract

A 45-year-old man who had undergone splenectomy 20 years earlier for immune thrombocytopenia (ITP) presented with a fever, arthralgia and vesicular skin rash. The skin rash was typical for varicella, as confirmed on serological studies. He exhibited isolated thrombocytopenia and was diagnosed with ITP. In addition, an accessory spleen was detected. The platelet count responded to treatment with prednisolone (PSL), and the varicella subsided uneventfully following therapy with acyclovir. Furthermore, the platelet count was maintained after PSL was discontinued. This case suggests an etiological link between varicella and very late relapse of ITP after initial splenectomy.

Key words: immune thrombocytopenia, varicella, splenectomy

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Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disorder characterized by isolated thrombocytopenia and a common cause of thrombocytopenia in both adults and children (1, 2). The first-line therapy for patients with ITP is steroids, while splenectomy is the second-line therapy of choice in those refractory or intolerant to steroids or for whom steroids are contraindicated (1, 2). Splenectomy is effective in increasing the platelet count in approximately 80% of patients, and the response is expected to be sustained in more than 60% of responders treated without additional therapy for more than five years (1), although a considerable number of patients subsequently relapse (2-6). Most cases of relapse occur within the first two years after splenectomy; relapse seldom occurs thereafter (4).

Varicella (chickenpox) is a viral infection commonly seen in children and is known to be associated with ITP (7). The incidence of ITP among children with varicella is estimated to be 1:25,000, and ITP associated with varicella accounts for 1.9% of pediatric ITP cases (8). In contrast, varicella is a very rare disease in adults; thus, ITP associated with varicella is accordingly extremely rare in adults.

We herein report a case of ITP in a patient who relapsed 20 years after splenectomy associated with varicella.

Case Report

A 45-year-old man visited our emergency room with complaints of fever and arthralgia. He had a history of contact with a child with varicella two weeks earlier and reported that his symptoms had developed one day prior to his visit. He had been diagnosed with ITP at 25 years of age and was initially treated with steroids; however, he became refractory to steroid therapy and subsequently underwent splenectomy, which resulted in sustained normalization of the platelet count, and was no longer under medical surveillance.

The patient was febrile and had generalized small vesicles with a halo predominantly on the trunk. This finding was judged to indicate the characteristic vesicular skin rash seen in patients with varicella (Fig. 1). The white blood cell count was 7.0×10⁹/L with a normal differential, a red blood cell count of 4.53×10¹²/L, a hemoglobin level of 14.1 g/dL, a hematocrit level of 40.5% and a platelet count of 14×10⁹/L. The results of coagulation studies were normal except for mild elevation of the fibrinogen level. Blood chemistry tests...
The patient was diagnosed with varicella and subsequently admitted, at which time treatment with intravenous acyclovir was started. The following day, the platelet count further decreased to 8×10^9/L. Bone marrow aspiration showed increased morphologically normal megakaryocytes; however, the production of the platelets was reduced. The cells of the erythroid and myeloid series were normal. These findings were consistent with a diagnosis of ITP. A computed tomography scan of the abdomen and ⁹⁹mTc-Sn colloid liver-spleen scintigraphy both demonstrated an accessory spleen (Fig. 2). Treatment with prednisolone (PSL) was started at a dose of 1 mg/kg, and the patient’s platelet count promptly responded, attaining a level of 300×10^9/L within one week. Both IgM and IgG against varicella zoster virus (VZV) were negative on admission, then turned positive one week later, thus confirming the diagnosis of varicella. PSL did not aggravate the course of varicella, and the patient was discharged when crust formation of the skin rash was completed. The dose of PSL was subsequently tapered over the next five months and then stopped. The anti-VZV IgM became negative. Currently, the platelet count remains within the normal range 17 months after the discontinuation of PSL.

Discussion

ITP is categorized as primary or secondary based on the presence or absence of an obvious initiating and/or underlying cause (9). More than 80% of cases of ITP in children are acute and usually preceded by viral infection (7). A variety of viral infections, including unidentified infections, precede acute ITP in children, with varicella being one such disease. Serum immunoglobulins obtained from children with varicella-associated ITP have been shown to react with
platelet surface glycoproteins GPIb, GPIIIb, GPIIIa (10) and GPV (11), suggesting that cross-reactivity between antibodies against VZV and platelets is involved in the development of ITP. On the other hand, most cases of adult ITP are chronic and not preceded by viral infection. As varicella in adults is a rare disease itself, with less than 100 cases being reported annually in recent years from 284 hospitals in Tokyo designated to report all varicella cases (12), ITP associated with varicella is very rare in adults. In addition, we found only three such cases in the literature (13-15).

Splenectomy is a widely accepted second-line treatment for ITP. While splenectomy is effective in increasing the platelet count in approximately 80% of patients (1), no preoperative factors can be used to identify patients likely to respond to splenectomy (4, 5, 16, 17). In addition, approximately 20% of responders to splenectomy subsequently relapse (3-5, 16-19). Most episodes of relapse occur within two years after splenectomy (5), with a plateau in the remission curve after 12 years reported in one study (19), although some patients relapse after a prolonged period (5, 6, 17, 19). The longer the follow-up period after splenectomy, the greater the frequency of late relapse, with the longest latent period being 30 years after splenectomy in a patient treated with splenectomy at 7 years of age (6). Nonetheless, the latent period of 20 years after splenectomy noted in the present case appears to be one of the most distant cases of relapse reported to date. In addition, the role of the residual accessory spleen detected in the present patient should be considered. However, as a considerable portion of splenectomized patients relapse without evidence of an accessory spleen and the removal of an accessory spleen, even when detected, is not always effective (3, 6, 20), the contribution of the accessory spleen appears to be small.

We are unable to determine whether the present case involved relapse of chronic ITP associated with varicella infection or the new development of acute ITP preceded by varicella. Although the prompt response to PSL implies an acute nature, the extreme rarity of varicella-induced acute ITP in adults and the observation that concurrent varicella infection leads to relatively frequent episodes of relapse among patients with chronic ITP (8) make the former assumption more likely.

With the extension of the post-splenectomy period and the increase in the adult population not immune to VZV, it is assumed that cases of late relapse in splenectomized adult ITP patients with varicella will be encountered more frequently in the near future and that recognition of and attention to this condition are therefore warranted.

The authors state that they have no Conflict of Interest (COI).

References