Transpl Int (1995) 8: 58–60

BRIEF REPORT

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Herpes zoster-associated idiopathic thrombocytopenic purpura in a liver transplant recipient: a case report and overview

Received: 8 March 1994
Received after revision: 17 May 1994
Accepted: 19 May 1994

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Abstract Idiopathic (autoimmune) thrombocytopenic purpura has been previously reported as a rare complication in children and in a few adults following chickenpox. We report a case of varicella zoster virus-associated idiopathic thrombocytopenic purpura in an adult liver transplant recipient following dermatomal zoster. Idiopathic thrombocytopenic purpura developed 3 days after the onset of herpes zoster in our patient, with a nadir platelet count of 3000/mm^3. The patient was treated with intravenous gamma globulin with recovery of thrombocytopenia after 3 weeks. Transplant clinicians need to be aware that this serious and potentially life-threatening complication may occur with herpes zoster in transplant recipients.

Key words Liver transplantation, thrombocytopenia, herpes zoster · Herpes zoster, thrombocytopenia, liver transplantation · Thrombocytopenia purpura, liver transplantation

Introduction

Varicella zoster virus is associated with two distinct clinical syndromes, i.e., varicella or chickenpox resulting from primary infection in a susceptible individual, and herpes zoster or shingles, which is recurrence of infection resulting in a localized dermatomal infection.

Herpes zoster may occur at a rate of 5–7 cases per 1000 patients in the general population and in 7%–15% of transplant recipients. Although cutaneous dissemination outside the localizing dermatome may occasionally occur in herpes zoster, the infection for the most part follows a relatively benign self-limited course. Occasionally, systemic or visceral involvement may be observed with the onset of varicella pneumonitis, hepatitis, or meningoencephalitis. We report a serious and life-threatening complication secondary to herpes zoster, i.e., varicella zoster virus-associated idiopathic (autoimmune) thrombocytopenic purpura (ITP) in an adult liver transplant recipient. ITP is an unusual complication of chickenpox in children and rarely occurs in adults [1, 2, 5, 11–13, 16, 18]. To our knowledge, ITP associated with herpes zoster, however, has not previously been reported.

Case report

A 46-year-old male underwent orthotopic liver transplantation for end-stage liver disease due to hepatitis C virus. Sixteen days post-transplant, a low-grade fever and a vesicular eruption in the left S2 dermatomal distribution developed. Platelet count was 230000/mm^3. His medications consisted of tacrolimus (FK 506), prednisone, 20 mg orally daily, and acyclovir, 200 mg orally three times daily. Multinucleated giant cells consistent with zoster were demonstrated on Tzanck preparation from the skin lesion. Acyclovir, 10 mg/kg three times a day, was administered intravenously. Two days later the platelet count was noted to be 87000/mm^3 and then it precipitously dropped to 3000/mm^3 by the 3rd day of onset of herpes zoster. A peripheral blood smear revealed an absence of platelets with no evidence of hemolysis. Antiplatelet antibodies were positive. A diagnosis of ITP was made. Sequential platelet transfusions were given and immunoglobulin, at a dose of 1 g/kg daily, was administered intravenously for 5 days with no response

in platelet count. A bone marrow biopsy revealed a normal erythroid to myeloid ratio, increased megakaryocytes, and no evidence of an infiltrative disorder. Three additional doses of immunoglobulin (1 g/kg daily) were administered. For the next 3 weeks the platelet count ranged between 3000/mm^3 and 20000/mm^3. The patient eventually made an uneventful recovery and was discharged 36 days after transplantation. At the 2-month follow-up his platelet count was 220000/mm^3.

Discussion

Although normally a benign illness, varicella can be accompanied by a variety of purpuric syndromes with thrombocytopenia [2, 12]. ITP associated with varicella in children is rare but well-documented [1, 2, 5, 11, 12]. Only a few adults with varicella have been reported with this syndrome [1, 5, 13]. Our patient, however, developed ITP following herpes zoster and not varicella (chickenpox).

ITP occurred a median of 3 days after the onset of rash in reported cases [1, 2, 5, 11–13, 16, 18]. Ninety percent of the reported cases had platelet counts of less than 10000/mm^3. The platelet count of 3000/mm^3 in our patient is, however, one of the lowest reported and presented a potentially catastrophic situation in a surgical patient.

Possible pathogenetic mechanisms of thrombocytopenia include direct viral invasion of the megakaryocytes with subsequent inadequate thrombopoeisis [4], disseminated intravascular coagulopathy [18], and enzymatic desialylation of the platelets [16]. However, immune-mediated platelet destruction is by far the most frequent cause of thrombocytopenia [6, 17]. The viral infection leads to the formation of circulating platelet antibodies, mainly of the IgG class, that have been shown to bind to platelet glycoproteins I-IIb and IIIa [17]. ITP may occasionally follow varicella vaccination, again suggesting an immune-mediated etiology [10].

The diagnosis of ITP in our patient was established by increased megakaryocytes in the bone marrow without ineffective thrombopoeisis, evidence of peripheral destruction of platelets, and the presence of antiplatelet antibodies. The clinical, laboratory, and blood smear findings were not consistent with disseminated intravascular coagulopathy, thrombotic thrombocytopenic purpura, or another microangiopathic process.

Although distribution of the rash was characteristic of herpes zoster and the Tzanck smear from the lesion was positive, varicella zoster virus could not be isolated by viral culture. Previous studies have demonstrated that the virus is difficult to detect in culture: only 10 %–57 % of the lesions yield the virus in culture [14]. The lability and highly cell-associated nature of the virus contribute to the difficulty of virus isolation [14]. There was no evidence of another viral infection (particularly of cytomegalovirus or herpes simplex virus) systemically or locally by viral culture. A variety of drugs have been associated with thrombocytopenia. Our patient was receiving tacrolimus (FK 506) at the onset of his ITP. Although there is one reported case of thrombotic thrombocytopenic purpura associated with tacrolimus [8], hematologic adverse events have not been observed with tacrolimus. The clinical features in our patient were not consistent with thrombotic thrombocytopenic purpura and his ITP eventually resolved despite continuing tacrolimus.

Acute ITP may have a variable and prolonged course even after the resolution of the inciting viral illness. Resolution within a few days to weeks is observed in a majority of patients, although progression to chronic thrombocytopenia can occur in 10 % of the cases [16]. Immunoglobulin and corticosteroids have been successfully used in a few cases of varicella-induced childhood ITP [3, 7, 15, 16]. A response to either therapy may be seen in 70 %–90 % of the patients. A rise in platelet count, however, is more rapid with immunoglobulin, with most responders demonstrating a rise within 1–5 days. The usual dosage of immunoglobulin is 400 mg/kg per day for 2–5 days. Alternatively, 1 g/kg per day can be used for 1–2 consecutive days as induction. The need for additional dosages should be determined by clinical response and platelet count. We were reluctant to use corticosteroids in our patient for fear of further augmenting his immunosuppression. Furthermore, in a trial of childhood acute ITP, the immunoglobulin treatment group seemed to progress to a chronic form less often than the steroid-treated group [9].

In summary, we have described an unusual but potentially life-threatening complication of a common infection (herpes zoster) in a transplant recipient. Clinicians need to be aware that herpes zoster, a relatively benign illness, can be accompanied by serious hemorrhagic complications and that the rare case of ITP associated with herpes zoster must be recognized.

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