

Severe Thrombocytopenia Refractory to Platelet Transfusions, Secondary to Abciximab Readministration, in a Patient Previously Diagnosed With Idiopathic Thrombocytopenic Purpura. A Possible Etiopathogenic Link

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Acute severe thrombocytopenia is a serious although infrequent complication following abciximab infusion that is usually managed with platelet transfusions. We present a patient who underwent multivessel percutaneous coronary intervention with concomitant abciximab administration. Soon after the procedure the patient developed severe thrombocytopenia that persisted despite multiple platelet transfusions. This patient had been previously diagnosed as having idiopathic thrombocytopenic purpura, although this diagnosis was not recorded in our medical records, and at the time of the intervention the patient had a normal platelet count. He was successfully managed with IgG administration. The clinical and therapeutic implications of this case are discussed.

Key words: *Thrombocytopenia. Glycoprotein IIb/IIIa. Platelets.*

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Trombocitopenia severa, persistente a transfusiones plaquetarias, secundaria a readministración de abciximab en paciente con antecedentes de púrpura trombocitopénica idiopática. Un posible nexo etiopatogénico

La trombocitopenia severa y aguda es una complicación infrecuente después del tratamiento con abciximab, que se soluciona habitualmente con transfusiones de plaquetas.

Presentamos el caso de un paciente sometido a intervención coronaria percutánea multivazo que, tras la administración del fármaco durante el procedimiento, desarrolló una trombocitopenia severa persistente a múltiples transfusiones de plaquetas. Este paciente había sido diagnosticado previamente de púrpura trombocitopénica idiopática, aunque no estaba referida en los registros médicos ni era evidente desde el punto de vista analítico. El cuadro se resolvió tras la administración de inmunoglobulina G. Se discuten las implicaciones clínicas y terapéuticas.

Palabras clave: *Trombocitopenia. Glucoproteína IIb/IIIa. Plaquetas.*

INTRODUCTION

Abciximab (ReoPro C7E3) is a chimeric human-murine antibody that blocks the platelet glycoprotein-IIb/IIIa (GP-IIb/IIIa) complex, thereby, inhibiting platelet aggregation. It has been shown that, when

administered with heparin and aspirin, abciximab is effective in reducing the risk of ischemic complications in patients undergoing percutaneous coronary interventions (PCI).¹ The side effects of abciximab include hemorrhagic and thrombocytopenic events.²⁻⁴

Here, we describe the case of a patient who presented with severe acute thrombocytopenia (platelet count, <20 000/ L) following abciximab treatment. The pathogenesis in this case may have involved idiopathic thrombocytopenic purpura (ITP), which had been previously diagnosed in the patient. However, there was no clinical or laboratory evidence of the

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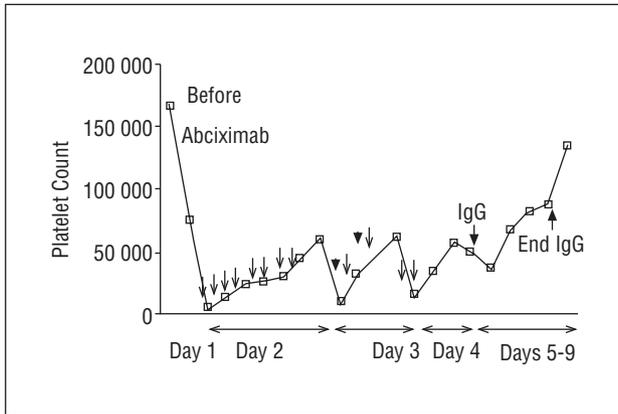


Fig. 1. The saw-tooth form of the variation in platelet count recorded during the patients' hospital stay. Each open square represents a platelet count assessment. Each open arrow indicates the transfusion of 6 units of platelets obtained by apheresis. Each solid arrowhead indicates the transfusion of 5 units of platelets from pooled blood. In total, the patient received 72 units of platelets from 22 different donors. IgG indicates immunoglobulin G.

condition at presentation.

CASE REPORT

A 70-year-old patient was referred to our hospital for coronary artery revascularization. Fifteen days previously, primary PCI had been carried out on the left anterior descending coronary artery, during which abciximab at a standard dose was used. During the procedure, severe triple-vessel disease was observed but immediate dilatation was not thought necessary.

Two weeks after the acute infarct, the patient was referred to our hospital. On admission, laboratory studies showed: hemoglobin, 12.6 g/L; leukocyte count, 4100/ L, and platelet count, 170 000/ L. After considering different revascularization options, PCI was chosen. The procedure was carried out via the radial artery, and involved treatment of the right coronary artery and of the left circumflex in 2 locations. Stents were used in both arteries. Because the angioplasty was complex, abciximab was again administered (by a bolus followed by infusion) according to standard practice. A good angiographic result was obtained.

Immediately after the percutaneous coronary intervention, persistent bleeding occurred at the access point on the radial artery, as well as in the gums. At that time, upon re-questioning, the patient reported to have been diagnosed with ITP 10 years previously, for which treatment had never been given. This earlier diagnosis of ITP was based on the observation of moderate thrombocytopenia and antiplatelet antibodies, with bone marrow findings consistent with the diagnosis. The abciximab

infusion was stopped immediately. After 4 hours, the patient's platelet count was 4000/ L. Consequently, aspirin and clopidogrel treatment was also suspended. The patient's subsequent clinical course was uneventful. There was no significant hemorrhage, and only an ecchymosis in the forearm where the artery had been punctured was noted.

The patient's laboratory findings are summarized in Figure 1. Overall, after the initial decline in platelet count to 4000/ L, the count followed a saw-tooth pattern. There were transitory increases in platelet count to as high as 60 000/ L following platelet transfusion. These increases were immediately followed, within a few hours, by significant declines. It is important to note that, within the first 36 hours after the initial poor response, 4 platelet transfusions (each consisting of 12 units obtained by apheresis) were required. During the subsequent 48 hours (i.e., on days 3 and 4), new transfusions were required on three occasions. Finally, on the fifth day after the percutaneous coronary intervention and following the observation of a further decrease in platelet count, slow immunoglobulin G (IgG) infusion at a rate of 30 g/day was established. Administration was continued until day 9, time by which platelet counts had gradually increased to a normal level without the need for further transfusions.

DISCUSSION

The incidence of severe acute thrombocytopenia in patients who are taking abciximab for the first time has been reported to vary between 0.5-1.0%.^{5,6} The incidence is greater, at 2.4%, when the drug is being administered again on a subsequent occasion.⁷⁻⁸

Although the underlying mechanism is not well understood, there are a number of explanatory hypotheses. It has been suggested that antibodies might develop against the complex formed by abciximab and the GP-IIb/IIIa receptor⁸ or that, in a paradoxical response, the drug could actually induce platelet aggregation.⁹ Aggregates may be later eliminated from the circulation.

The present patient had two predisposing factor for severe thrombocytopenia: repeated administration of abciximab and concomitant ITP. Idiopathic thrombocytopenic purpura is an autoimmune disease that, in its chronic form, can be associated with antiplatelet antibodies directed against various glycoproteins, principally GP IIb/IIIa. In cases that require treatment, glucocorticoids are usually administered. Splenectomy is reserved for the most serious and refractory cases. In treated patients, it has been reported that IgG administration improves the platelet count by blocking the reticuloendothelial system.⁶ Platelet transfusion only aggravates the

condition by stimulating autoimmune reactions.

The poor therapeutic response to repeated platelet transfusion that occurred during the first 4 days in our patient contrasts with the improvement in platelet count that is seen in the majority of reported cases and which usually takes place in 24-48 hours.⁶ This poor response was interpreted as a possible manifestation of an autoimmune reaction that had been exacerbated by abciximab readministration. The hematological response observed after 4 days of slow IgG infusion supports this hypothesis. Nevertheless, we cannot exclude the possibility that ITP did not play a causative role in the development of this complication. In any case, it is extraordinarily difficult to prove that ITP was not a causative factor or that an autoimmune reaction had not started before conformational changes were induced by GP IIb/IIIa binding with abciximab.

We believe, therefore, that a history of ITP should be regarded as a contraindication to abciximab administration, even with normal platelet counts. In patients in whom severe persistent thrombocytopenia develops during platelet transfusion, the possibility that there is an undiagnosed chronic platelet disease (i.e., chronic ITP) should be considered. Subsequently, IgG infusion should be considered as early as possible. Slow infusion is probably the best approach.

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