Ciprofloxacin-Induced Thrombotic Thrombocytopenic Purpura: a case report with fatal outcomes

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Abstract

Thrombotic Thrombocytopenic Purpura is a particular form of thrombotic microangiopathy, characterized by petechial lesions, anemia, renal failure and fluctuating mental status. It is usually associated with an infection, drugs, or neoplasias. Confusing and rare, it is a real diagnostic challenge.

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A written informed consent was obtained from the patient to publish this report in accordance

with the journal's patient consent policy

Abstract

Thrombotic Thrombocytopenic Purpura is a particular form of thrombotic microangiopathy, characterized by petechial lesions, anemia, renal failure and fluctuating mental status. It is usually associated with an infection, drugs, or neoplasias. Confusing and rare, it is a real diagnostic challenge.

A clinical key Message

Thrombotic Thrombocytopenic Purpura is a rare multisystem disorder characterized by generalized microvascular thrombotic lesions. This diagnosis should be promptly made due to its potentially fatal nature.

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Introduction

Thrombotic Thrombocytopenic Purpura (TTP) is a rare multisystem disorder characterized by generalized microvascular thrombotic lesions[1]. This diagnosis should be promptly made due to its potentially fatal nature.

Case Presentation

A 47 years-old patient, presented to our department of dermatology with chronic leg ulcer complicated by dermohypodermitis (figure1). He was treated with Intravenous amoxicillin-clavulanic acid and prophylaxis doses of sub cutaneous enoxaparin 40 mg per Day. A venous Doppler ultrasound was performed to explore the persistence of his leg edema, which did not show any signs of thrombophlebitis, and ciprofloxacin 800 mg IV per day was added. Two days later, a cutaneous examination was remarkable for mild petechial lesions in his lower limbs. He complained of dyspnea, sweating and tachycardia. We realized a pulmonary scintigraphy which revealed a distal pulmonary embolism. His laboratory data showed a microcytic anemia (hemoglobin level of 8.6 g/dL), thrombocytopenia (platelet count of 12000/mm3), hepatic cytolysis and renal failure. A peripheral-blood smear showed schistocytes. Coomb's test, and the rest of the immunological workup were negative. All of these symptoms led us to raise the diagnosis of TTP. The diagnosis was confirmed with ADAMTS13 activity under 5% and an elevated rate Anti-ADAMTS13 autoantibody. Three days later the patient presented with a generalized seizure with post-critical deficit state. The patient was transferred to the medical intensive care unit. Five sessions of plasmapheresis with steroids (80mg/day) were performed with a transient improvement. The patient received four doses of weekly rituximab at a dose of 375 mg/m2 per dose. The evolution was marked by a therapeutic escape and the appearance of thrombosis of multiple vessels. The Patient died of multiple organ failure, five days later.

Discussion

TTP is a particular form of thrombotic microangiopathy, characterized in its typical form by the combination of five manifestations: central nervous system damage, fever, renal failure, hemolytic anemia and a consumer thrombocytopenia [1]. A deficiency in a disintegrin and metalloprotease with thrombospondin type 1 repeat-13 (ADAMTS13) protein leads to the plasma accumulation of megamultimers of Von Willebrand Factor, and thus to platelet hyperaggregability at the origin of microthrombi. These megamultimers are released by activated endothelial cells, usually following an infection, drugs, neoplasias or pregnancy [2]. ADAMTS13 deficiency may be the result of mutations in the gene encoding the protein, resulting in the hereditary TTP observed in children. In adults, ADAMTS13 deficiency is typically acquired and due to the presence of autoantibodies which alter the activity of the protein [3], such as our patient. TTP can also be associated with different autoimmune diseases as in particular acute systemic lupus erythematosus and isolated antinuclear antibodies can be found in two thirds of cases [4]. It is common to find an episode of infectious disease which preceded PTT by few days [5]. Many viruses have been associated with an episode of PTT, as in particular the immunodeficiency human virus [6]. Many usually prescribed medications have been associated with the development of TTP. Ciprofloxacin seems to be an emerging cause of drug-induced TTP, but unlike our case, rarely leads to fatal complications [7]. However, there are no standards to incriminate the drugs as the probable cause of TTP [8].

The prognosis of TTP has considerably improved after the introduction of plasma exchange (50–75 mL/kg) once daily using fresh-frozen plasma [9]. It is the only scientifically recognized treatment modality for acquired TTP [10]. Corticosteroid therapy (methylprednisolone 1000 mg once daily) is also administered in conjunction with plasma exchange. Other reports show that the monoclonal anti-CD-20 antibody rituximab (375 mg/m2 once weekly for four doses) is effective in patients with refractory or relapsed TTP [11]. With this protocol, our patient did not respond to the treatment. Some authors explain the refractory response to treatment or relapse due to a number of factors, such as severe thrombocytopenia, age over 60 years, the presence of ADAMTS13 deficiency or inhibitor [12].

Our observation is particular due to the onset of a fatal TTP in a patient with dermohypodermitis treated with ciprofloxacin. Through this case, we would like to alert practitioners to this rare but life-threatening entity in order to establish an early diagnosis to improve the patient's prognosis and survival in TTP.

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Legend

Figure1 : Dermohypodermitis of the left leg, with peri malleolar leg ulcers and lipodermatosclerosis