

THROMBOTIC THROMBOCYTOPENIC PURPURA ASSOCIATED WITH HIV INFECTION: REPORT OF TWO CASES

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ABSTRACT

We report two cases of thrombotic thrombocytopenic purpura (TTP) in advanced stage HIV-positive patients ($CD4^+ < 0.05 \times 10^9/L$). Clinical symptoms were relevant, but their course was not fulminant; the two patients responded to different therapies (plasma or plasma plus plasmapheresis, and steroids), showing rapid improvement in symptoms. One patient remained asymptomatic with zidovudine only, while the other relapsed (probably due to an intercurrent infection). This second person is now asymptomatic on zidovudine plus low doses of steroids.

Key words: HIV, thrombotic thrombocytopenic purpura

Thrombotic thrombocytopenic purpura (TTP) is an unusual syndrome characterized by microangiopathic hemolytic anemia, thrombocytopenia, neurologic symptoms, renal involvement and fever.¹

A few cases of TTP have recently been reported in HIV-infected patients.²⁻⁹

We too observed two cases of TTP among 64 patients with severe HIV-related thrombocytopenia (3.1%).

We report these cases and discuss clinical findings and therapy.

Case report #1

A 27-year-old man was referred to our Department for fever, malaise, weakness, somnolence and epistaxis. The patient had a past history of heroin abuse. On the day of admission laboratory tests showed hemoglobin 6.4 g/dL, platelet count $17 \times 10^9/L$, reticulocyte count $210 \times 10^9/L$ (11%), leukocyte count $5.6 \times 10^9/L$. A peripheral smear showed numerous schistocytes and an occasional nucleated erythrocyte. The creatinine level was 173 mmol/L, lactic dehydrogenase level 354 IU/L,

haptoglobin 9 mg/dL, bilirubin 60 mmol/L, urinalysis 2.1 g/L protein. Coagulation studies were normal and the results of direct and indirect Coombs' tests were negative. A bone marrow biopsy showed erythroid hyperplasia without any other relevant alterations.

The patient was found to be HIV-positive, but antigenemia was negative; the $CD4^+$ level was $0.048 \times 10^9/L$. No signs of opportunistic infection were present.

The patient was treated with prednisone (1 mg/Kg/day) and plasmapheresis with exchange of 2000 mL fresh frozen plasma daily (ten courses).

Response to treatment was immediate: peripheral blood smears showed a decrease in schistocytes and in reticulocyte count; the platelet count rose to $45 \times 10^9/L$ and clinical symptoms improved. Plasmapheresis was stopped and prednisone reduced. The patient remained asymptomatic and was discharged. Prednisone was then tapered and zidovudine (500 mg/day) was started. After three weeks the platelet count rose to $100 \times 10^9/L$ and hemoglobin reached 11 g/dL. The patient remains in remission after 28 months of follow-up.

Case report #2

A 32-year-old man was admitted to our Department for fever, weakness, somnolence and confusion. He had been a heroin abuser in the past and was diagnosed as HIV positive 5 years earlier; AIDS was diagnosed 2 years ago. He was treated with zidovudine (500 mg/day) and trimethoprim-sulfamethoxazole. On admission laboratory tests showed hemoglobin 6.2 g/dL, reticulocyte count $152 \times 10^9/L$ (8%), platelets $38 \times 10^9/L$, leukocyte count $1.1 \times 10^9/L$. Schistocytes were very numerous in the peripheral smear. Creatinine was 110 mmol/L, lactic dehydrogenase 244 IU/L, haptoglobin 14 mg/dL, bilirubin 94 mmol/L, and urinalysis showed 4.6 g/L protein.

Coagulation tests were normal and the results of direct and indirect Coombs' tests were negative. A bone marrow biopsy showed myelodysplastic features only (micromegakaryocytes, dysmegakaryopoiesis). The patient was treated with methylprednisolone (40 mg/day) and fresh frozen plasma (3 units daily \times 14 days). He showed a rapid improvement in hematologic parameters: hemoglobin rose to 10.5 g/dL, leukocyte count reached $2.2 \times 10^9/L$, platelets $96 \times 10^9/L$. Reticulocytes and schistocytes decreased and the patient showed clinical improvement. Upon discharge plasma was stopped and steroid therapy was decreased.

Three months later he was again referred to our Department because of persistent diarrhea. A stool culture was positive for *Clostridium difficile* and hematologic parameters showed a recurrence of TTP. Treatment was begun with fresh frozen plasma and methylprednisolone (1 mg/Kg/day) and produced a rapid improvement in laboratory values and clinical symptoms. Pneumonia was also discovered but it responded to antibiotic therapy. Plasma was stopped and steroid therapy was reduced. The patient is asymptomatic after 6 months of follow-up.

Discussion

Since the work by Boccia et al.² was published, 32 cases of HIV-related TTP have been reported in the literature.³⁻⁹ The association

between HIV/AIDS and TTP was not due to ascertainment bias, according to Karpatkin.⁴

Most cases were characterized by a fulminant clinical syndrome. Nevertheless, a recent report⁹ emphasized the possibility of low-grade forms of TTP. According to many authors they occur late in the natural history of HIV-related disorders.

We observed two cases of TTP among 64 severe HIV-related thrombocytopenias (3.1%). This rate is not significantly different from that observed in our experience for all cases of TTP with respect to other types of thrombocytopenias (2.8%).

These two cases occurred in advanced HIV infection ($CD4^+ < 0.05 \times 10^9/L$). Clinical symptoms were relevant, but their course was not fulminant; the two patients responded to different therapies (plasma or plasma plus plasmapheresis, and steroids), showing a rapid improvement in symptoms. One patient remained asymptomatic with zidovudine only, while the other relapsed (probably due to an intercurrent infection). He is currently asymptomatic receiving zidovudine plus low doses of steroids.

In conclusion: 1) the association between TTP and HIV infection is well known, but has yet to be proven statistically significant; 2) it can be manifest in different clinical forms (low-grade to fulminant); 3) low-grade forms can be underestimated and require a high degree of clinical suspicion; 4) these different forms respond to different types of treatment.¹⁰

References

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