BREACH
BELGIAN RESEARCH AIDS&HIV CONSORTIUM

ACQUIRED HEMOPHILIA A:
An uncommon cause of bleeding in a HIV-infected patient

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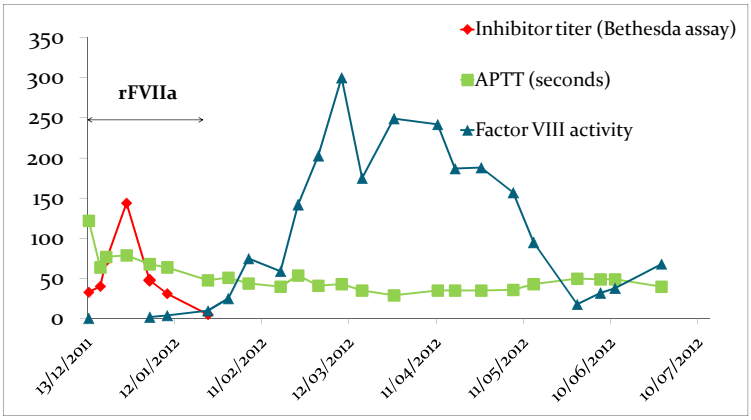
CASE REPORT

A 59-year old man presented at the emergency room for increasing macroscopic hematuria evolving for one week. Recent cystoscopy showed bleeding of undetermined origin and urinary tract ultrasonography was normal. He developed painful swelling of his left leg above the knee and complained of left back pain. Medical history included HIV infection diagnosed 26 years ago, well controlled by efavirenz, emtricitabine and tenofovir (CD4 cell count 695/mm³, undetectable viral load) and insulin requiring type 2 diabetes for which glargin was recently introduced. The hemogram was normal (Hb: 15.8 g/dl, Platelet count: 221000/mm³). Coagulation tests revealed normal PTT but prolongation of APTT (122 seconds, normal :<40 sec). The patient was admitted for further investigation. Hematuria persisted and hemoglobin level progressively decreased , requiring red cell transfusion. After one week, new signs appeared: right arm edema, bruisings and hematomas in declive parts.
Complete hemostasis investigation then revealed undetectable factor VIII levels and a specific factor VIII inhibitor (Bethesda assay).
The final diagnosis was acquired hemophilia A.
Control of acute bleeding was achieved using therapeutic doses of bypassing agent rFVIIa. A prophylactic regimen has been used for six weeks, until factor VIII became detectable again (figure). The main complication was a voluminous hematoma of the right upper leg at the puncture point of an angiography realized to identify the origin of hematuria. This last episode required ICU management.
Since any medication can potentially trigger this autoimmune disorder, anti retroviral therapy and insulin scheme were modified. Causal treatment was initiated immediately with 1 mg/kg/day of methylprednisone and high-dose IVIg. After three weeks of this treatment, factor VIII inhibitor activity started to decrease and after six weeks, it was followed by progressive elevation of factor VIII levels (figure). Corticotherapy was adapted according to factor VIII values and six months later the patient still required between 16 and 32 mg of methylprednisone.



Evolution of APTT, inhibitor activity and factor VIII activity after steroid treatment was started.

Acquired hemophilia is rarely reported in HIV-seropositive patients.

To our knowledge this is the fourth case report associating the two conditions (2, 3). In two cases, the acquired factor VIII inhibitor developed after immunomodulation with pegylated interferon-α for hepatitis C coinfection (2). Migliore et al report spontaneous appearance of factor VIII antibodies in a HIV-infected patient without any coinfection (3).

Acquired hemophilia A is a rare bleeding disorder caused by autoantibodies directed against clotting factor VIII. The incidence is approximately 1 per million/year with a high mortality rate of more than 20%. AHA may be associated with pregnancy, autoimmune diseases, malignancy, infections or medication and occurs most commonly in the elderly. Approximately 50% of the patients remain idiopathic with no known underlying pathological condition (1). In our case, the occurrence of the disease could be attributed to HIV-related dysregulation of immunity. Potential triggers could have been an intercurrent viral infection or the glargin insulinotherapy.

The diagnosis is based on the **isolated acquired prolongation of APTT** along with reduced FVIII levels and identification of a specific factor inhibitor. The treatment involves two aspects. First, haemostatic strategy that includes control of acute bleeding and prophylactic regimen until factor VIII becomes detectable. Second, eradication of antibodies (1). The choice of steroids as a first line to eradicate the inhibitor is conform to the recommendations. Other lines of treatment include IVIg, cyclophosphamide and rituximab (4, 5).

CONCLUSIONS

- Acquired hemophilia A is rare but not exceptional, even in HIV-seropositive patients where auto-immune disorders are well known. Diagnosis and management of these patients remain challenging.
- The clinician must keep a high level of suspicion in front of bleeding associated with prolonged APTT. Automatically generated alerts can help prompt diagnosis.
- Next to the treatment, one should focus on limiting invasive diagnostic and therapeutic procedures to avoid iatrogenic complications.

REFERENCES

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