




Sindrome da anticorpi antifosfolipidi

# ACQUIRED HEMOPHILIA A AND ANTIPHOSPHOLIPID SYNDROME: CONCURRENCY OR OVERLAPPING?

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**Background.** Acquired hemophilia A (AHA) is a rare bleeding disorder, with an incidence of 1.5 cases per million per year. It is caused by the development of factor VIII (FVIII) inhibitors and typically presents with recurrent muscular and soft tissues bleeding. Nearly half of AHA cases are considered idiopathic, while the remainder are secondary to autoimmune disorders, malignancies, infections, or pregnancy. Prompt recognition of the condition is essential to manage severe and potentially life-threatening bleeding episodes.

**Case report.** A 59-year-old patient, with a history of cigarette smoking and mild secondary erythrocytosis, presented to our outpatient clinic, reporting a spontaneous hematoma at right arm. The GP prescribed blood test that showed prolonged aPTTr (Table displays patient's laboratory findings). Second level diagnostic testing confirmed a prolonged aPTTr, that did not correct on mixing test after 2-hour incubation, suggesting the presence of an acquired inhibitor: F VIII was 1.2%, and the anti-FVIII inhibitor 1.7 BU/ml. The diagnosis of AHA was made, and the patient started 1 mg/kg prednisone, plus tranexamic acid. Further testing demonstrated the presence of anti B2GPI IgM and ACL IgM, while LAC was negative, and anti B2GPI IgG and ACL IgG were absent, as well as other autoimmunity tests. Chest x-rays and abdomen ultrasound excluded the presence of malignancies. After 3 weeks of steroid treatment, the patient reached F VIII level of 100%, the hematoma had regressed. Steroid was tapered. Eighty days after the diagnosis, the patient presented to the ER with left arm numbness, dysarthria, left labial fold deviation, and deficit of the VII cranial nerve. The head CT scan and the MRI demonstrated a right-sided ischemic stroke together with chronic cerebral vasculopathy. Having normal FVIII levels, the patient started anti platelet therapy. Further investigations excluded supra-aortic trunks stenosis and arrhythmias, while the presence of anti B2GPI IgM and ACA IgM was confirmed, and the diagnosis of idiopathic antiphospholipid syndrome was made. The antithrombotic therapy was switched to warfarin. A few weeks later, FVIII levels dropped to 24%: steroid therapy was restarted, but only a partial response was achieved; the patient was hence treated with Rituximab (375mg/mq every week for 4 weeks). FVIII levels increased to a full response and steroid was tapered; no effect was described on the antiphospholipid antibodies' titre. During anticoagulation, the patient never experienced hemorrhagic complications.

**Conclusions.** Cases of concurrent AHA and APS are rare and largely anecdotical , particularly when they are not secondary to malignancies or other autoimmune forms. Both AHA and APS are life-threatening and prone to recurrency if not properly treated. In our patient the two disorders manifested less than 3 months apart and are currently classified as idiopathic. The main challenge in this case lies in balancing the therapeutic approaches and ensuing close clinical monitoring.

Table: patient's laboratory follow-up

| | Day 0 | Day 30 | Day 80 | Day 120 | Day 180 | Day 240 | Day 300 |
|---|---|---|---|---|---|---|---|
| | AHA | | Stroke, APS | FVIII drop | Rituximab (1st dose) | | |
| aPTTr | 3.06 | 0.96 | 1.02 | 2.61 | 2.06 | 1.94 | 1.76 |
| aPTTr mix | 1.44 | | | | | | |
| aPTTr mix 2h | 2.02 | | | | | | |
| PTr | 1.03 | | 0.94 | | 2.29 | 2.57 | |
| Fibrinogen [g/L] | | | 3.11 | | | | |
| F VIII [%] | | 106 | 97 | 24 | 46 | 100 | 125% |
| F VIII inhibitor [BU] | 1.7 | | | | | | |
| vWF activity [%] | 134 | | | | | | |
| vWF antigen [%] | 129 | | | | | | |
| F IX [%] | 105 | | | | | | |
| F X [%] | 112 | | | | | | |
| F XI [%] | 88 | | | | | | |
| F XII [%] | 65 | | | | | | |
| LAC | Negative | | Negative | | | | |
| ACA IgM [CU] | 215 | | 164 | | 132 | | |
| ACA IgG [CU] | 5.1 | | 2.4 | | 12.1 | | |
| Anti-B2GPI IgM [CU] | 208 | | 137 | | 121.6 | | |
| Anti-B2GPI IgG [CU] | 21.3 | | 17.9 | | 19.7 | | |

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