FACTOR VIII DEFICIENCY: INHIBITION OR ABNORMAL CONTACT?

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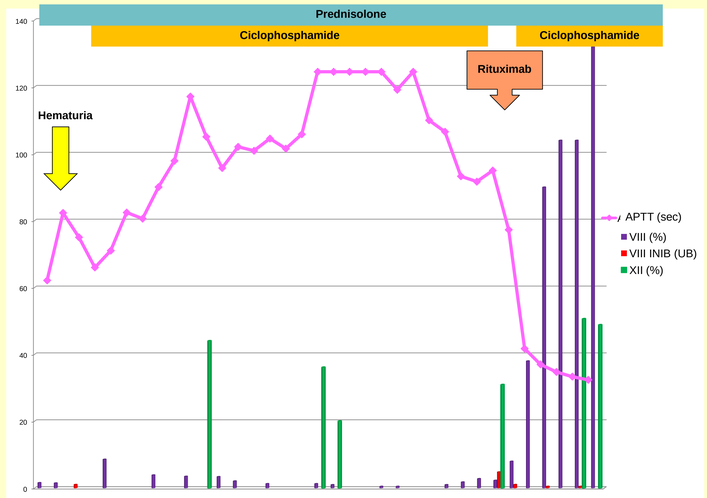
OBJECTIVES

Initiation of the intrinsic pathway occurs when prekallikrein, high-molecular-weight kininogen, Factor XII (FXII) and FXI are exposed to a negatively charged surface, interacting with the phospholipids of circulating lipoprotein particles (contact phase). The working mechanism of FVIII inhibitors (autoantibodies) is time and temperature-dependent. Both situations influence aPTT and their clarification can be difficult.

The authors intend to present the case of a patient with increased aPTT and FVIII low levels, with hematuria, whose diagnostic clarification has been very challenging.

Patient results evolution and therapeutic



METHODS

Female, 22 years old, hospitalized for inaugural diabetes, secondary to corticoid therapy (prednisolone) prescribed six months before for migratory oligoarthritis. Sudden hematuria and aPTT elevation (60-120 sec), previous results border-line. Microcytic hypochromic anemia since three years ago, due to menometrorrhagia and *H. pylori* positive gastritis, Dress syndrome due to salazopirine and acute hepatitis after ciprofloxacin treatment. Without previous transfusions or hemorrhagic discrasia. Family history of rheumatoid arthritis, absence of hemorrhagia. Preformed laboratorial investigation of aPTT elevation (HemosIL® Reagents).

RESULTS

- F VIII activity levels average 2.3% (RV: 50-150%)
- F VIII inhibitor titer :1.05 to 4.5 BU
- F XII between 20% to 50.6% (RV: 50-150%; the lowest levels meet the highest values for aPTT)
- All the other factors were in reference values, except for FvW R:Co (RV: 50-180%) and FvW: Ag (RV: 50-180%) that were very high, probably due to the inflammatory process
- Lupus anticoagulant were negative.

Medicated with ciclophosphamide, rituximab and prednisolone, with hematuria and coagulation abnormalities resolution.

CONCLUSIONS

Acquired hemophilia A in association with Factor XII inhibition

As referred in the literature, in this patient FVIII inhibitor did not correlated with FVIII levels.
Presence of FVIII inhibitors probably type 2 (second-order kinetics), as the FVIII was not complete inactivated. There was always a residual concentration of Factor VIII, except in one occasion. Although the sudden hematuria was soon quelled, these autoantibodies presented a strong resistance to immunosuppressant therapy, even with low titers of antibody.
The exuberance of APTT (>120") measurements coincided with the lowest FVIII (<1%) and FXII (20%) levels. All the other coagulation factors were between the reference values.
With the eradication of the antibodies and normalization of Factor VIII levels, FXII also increased (to borderline levels of 50%) and aPTT normalized.
Did FVIII inhibitor also inhibited FXII?

REFERENCES

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