

Type 1 Diabetes Mellitus and Acquired Hemophilia

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INTRODUCTION

Type 1a Diabetes (DM1) is a challenging disease with a rising incidence (up to 40 per 100.000 in Finland and Sardinia) being less common in the African population.

It is believed to have an autoimmune basis and has been associated with other autoimmune diseases namely autoimmune thyroiditis and celiac disease.

Acquired hemophilia is a rare clinical entity characterized by bleeding diathesis induced by circulating inhibitors to coagulation factors (VIII ou IX) that compromise hemostasis.

The authors describe a case of a patient with DM1 with concomitant acquired hemophilia.

CASE REPORT

- A 23 year old African female.
- Medical history of Idiopathic oligoarthritis being investigated in Rheumatology.
- On Prednisolone 30mg daily for 1 year.
- No known allergies .
- No previous pregnancy or blood transfusions .
- Admission to the Hospital for Diabetic Ketoacidosis.
 - Hipotensive (BP 60/40mmHg), Tachycardic (120 bpm), tachypneic (35 cycles /minute).
 - Admission blood glucose 282mg/dL.
 - Arterial Blood Gases – pH 7,32 ; Bicarbonate 7,7 ; Anion Gap 24).
 - Initiated intensive iv hydration and insulin perfusion with favorable response.
- Autoantibodies:
 - Anti-insulin - positive (2,4U/mL)
 - Islet cell and Glutamate decarboxylase: negative.
- 3rd day of hospital admission: Severe hematuria.
 - Prolonged activated plasma thromboplastin time (120 seconds).
 - Mixing clotting studies : failure to correct aPTT .
 - Factor VIII activity less than 0.5% (Normal Range 50-150%).
 - Inhibitors to FVIII detected - 2.68 Bethesda Units.
 - Bleeding stopped after continuous urinary bladder lavage.
- Full autoimmune panel and Rheumatology consult were inconclusive.

Therapy:

- Insulin: 56Un of Glargine in the morning + Lispro before meals according to ingested carbohydrates and pre-prandial blood glucose levels.
- Prednisolone 1mg/kg daily .
- Cyclophosphamide 150mg daily for 5 weeks.

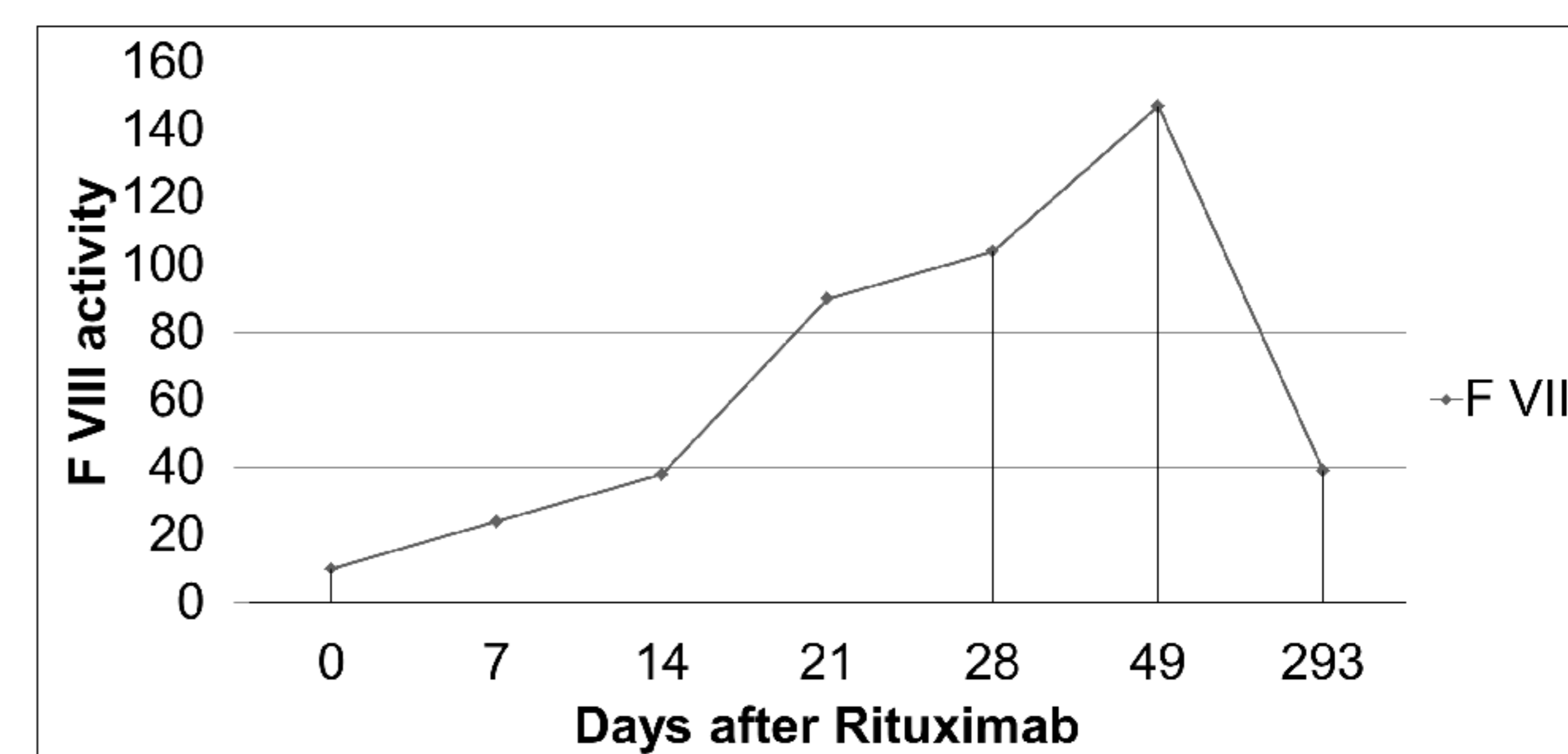
Due to persistently elevated aPTT and low factor VIII levels, Cyclophosphamide was stopped and Rituximab was started - 375mg/m² once a week for 4 weeks.

4 weeks after Rituximab therapy normalization of aPTT and Factor VIII activity was seen.

Insulin doses were also reduced after Rituximab (60 vs the initial 76Un/day).

Day of Prednisolone 1mg/kg/d + Cyclophosphamide 150mg/d	aPTT	F VIII
0	80,7	1,5
5	87,9	3,9
12	99,1	2,1
14	101	
20	>120	1
28	115	<0,5
31	103,3	

Day After Rituximab	aPTT	F VIII
0	52,5	10
7	52,6	24
14	42,9	38
21	38,5	90
28	36,4	104
35	35,1	104
42	34,2	132
49	33,4	179
100	33,3	147
132	29,7	-
293	44,2	39



CONCLUSIONS

In this case no secondary cause of the hemophilia was found, being DM1 the only autoimmune comorbidity possibly contributing to the onset of hemorrhage. Only a few cases of acquired hemophilia have so far been described to affect DM1 patients. Interestingly Rituximab improved both conditions being the patient currently hemorrhage free despite still requiring insulin.

