Annals of Clinical and Medical Case Reports

Case Report

Subconjunctival Bleeding As Uncommon First Hemorrhagic Sign in Patient with Acquired A Haemophilia

Puccetti L[1], Ciofini S[1], Fruschelli M[2], Calzoni P[3], Fineschi D[3], Guazzi G[4], Sicuranza A[1] and Bocchia M[1]

[1]Hematology Unit/Coagulative Disorders, "Santa Maria alle Scotte" University Teaching Hospital of Siena, University of Siena, Siena, Italy

[2]Ophthalmology Unit, "Santa Maria alle Scotte" University Teaching Hospital of Siena, University of Siena, Siena, Italy

[3]Coagulative Disorders Laboratory Unit, "Santa Maria alle Scotte" University Teaching Hospital of Siena, Siena, Italy

[4]Emergency Radiodiagnostic Unit, "Santa Maria alle Scotte" University Teaching Hospital of Siena, Siena, Italy

Volume 2 Issue 4- 2019

Received Date: 06 Dec 2019

Accepted Date: 28 Dec 2019

Published Date: 02 Jan 2019

1. Case Report

Acquired A haemophilia (AHA) is a rare disease resulting from autoantibodies (inhibitors) against coagulation factor VIII that leads to bleeding. It occurs mostly in elderly but can be associated with pregnancy and autoimmune disease in youngsters (1), about 50% of cases are considered idiopathic, but AHA is also correlated with other conditions including malignancies and infections [1].

We report the case of a thirty-one years old caucasic woman at her first pregnancy, she had a spontaneous delivery at 39th weeks without complications, but eleven days later she was admitted to ophthalmologic evaluation for slight pain without visual loss in the left eye started 24 hours before. The only clinical finding was a subconjunctival bleeding (Figure 1). The ophthalmologist prescribed an evaluation of platelet count, prothrombin time (PT), partial thromboplastin time (PTT) and fibrinogen due to a small haematoma in the left arm, at the site of venous venipuncture performed after delivery. The clinical history was negative for spontaneous hemorrhages also in infantile age and at previous surgery. No bleeding tendency was observed in the main relatives.

The patient was lost at the prescribed ophthalmologic follow-up, but twelve days later she was admitted to urgent haemathologic evaluation due to large multiple cutaneous hematomas in the four extremities, an extremely painful right leg, asthenia, and moderate dyspnea. The blood pressure was 105/65 mmHg, regular heart rate 100/min, SpO2 94% without oxygen supplementation. Ultrasound evaluation of right leg showed a massive deep muscle haematoma. The circumference of the right leg was 48 cm while the left leg was 38 cm.

Laboratory evaluation showed hemoglobin level of 6.3 g/dl, platelet count of 234 x10^9/l, PT 91% (INR 1.04), PTT 66 seconds (ratio 2.33), fibrinogen 324 mg/dl, D-dimer 445 ng/dl. Twelve days before haemoglobin was 11 g/dl, platelets 241 x10^9/l, PT 93% (INR 1.03), PTT 44 seconds (ratio 1.41), fibrinogen 336 mg/dl.

An extensive study of blood coagulation was prescribed and the mixing test suggested the presence of a circulating inhibitor against factor VIII (0.4 IU/dl, inhibitor title Bethesda Unit level of 20) [2, 3]. The diagnosis of AHA was confirmed and the patient was treated with a bypassing agent (rVIIa factor) at the dosage of 90 ug/kg i.v. initially every four hours and blood transfusions. Although it has been explained as a post-pregancy case, that is considered sometimes self-limiting [4], the eradication of the inhibitor was obtained only with prednisone and cyclophospamide (both 1 mg/kg/day orally).

***Corresponding Author (s):** *Luca Puccetti, Hematology Unit/Coagulative Disorders, "Santa Maria alle Scotte" University Teaching Hospital of Siena, University of Siena, Siena, Italy, E-mail: luca.puccetti@unisi.it*

Citation: Puccetti L, Subconjunctival Bleeding As Uncommon First Hemorrhagic Sign in Patient with Acquired A Haemophilia Annals of Clinical and Medical Case Reports. 2019; 1(4): 1-9.

PTs	M/F	Age	PTT at diagnosis (ratio)	HB at diagnosis (g/dl)	FACTOR VIII (IU/dl)	Inihibitor tile (Bethesda Units)	Type of AHA	Bleeding site	Days from first haemorragic sign	Therapy	Follow-up	Relapse at 6 months
C.A.	F	59	99 (3.56)	6.6	0.9	15	Rheumatoid Arthritis	Muco-cutaneous, Muscular	13	rVIIa 90 ug/kg PDN, CY	Recovery	0
P.A.	M	78	56 (1.98)	7.2	0.7	22	Pancreas malignancy	Muco-cutaneous, Muscular, GI Cerebral	21	None	Exitus by cerebral bleeding before confirmed diagnosis	-
C.S.	M	79	102 (3.64)	9.4	0.6	10	Non small cell lung carcinoma	Muco-cutaneous, Muscular	7	aPCC 75U/kg, PDN	Followed by other unit after 3 days (?)	?
L.E.B.	F	67	100 (3.57)	10.3	0.1	12	Idiopathic/ HIV+	Muco-cutaneous, Muscular	8	Initially rVIIa 90 ug/kg, CY	Followed by other unit after 10 days.	?
C.L.	F	31	66 (2.33)	6.3	0.4	20	Post-pregnancy	Muco-cutaneous, Muscular, Ocular	21	rVIIa 90 ug/kg PDN, CY	Recovery	0
G.E.	M	74	69 (2.48)	6.2	0.6	11	Sepsis	Muco-cutaneous, Muscular, GI	12	rVIIa 90 ug/kg PDN, CY	Recovery for 10 months	1
T.A.	M	73	81 (3.11)	7.7	2.8	4	Idiopathic	Muco-cutaneous	9	PDN	Followed by other hospital	?
C.B.	F	62	103 (3.68)	7.9	0.3	39	Idiopathic	Muco-cutaneous, Muscular, Joint (left elbow)	11	aPCC 75U/kg, PDN, CY Rituximab	Recovery	0
B.R.	F		60 (2.13)	9.1	2	4	Idiopathic	Muco-cutaneous, Muscular	14	PDN CY	Recovery	0
S.A.	F	85	99 (3.54)	6.2	0.1	16	Idiopathic	Muco-cutaneous, Muscular, Joint (left shoulder)	10	aPCC 75U/kg, PDN, CY	Recovery	0
B.T.	F		101 (3.61)	6.3	0.3	24	Idiopathic	Muco-cutaneous, Muscular	11	rVIIa 90 ug/kg PDN, CY	Recovery	0

rVIIa (activated recombinant factor seven), APCC (activatd prothrombin concentrate), PTT (partial thromboplastin time), PDN (Prednisone orally 1 mg/kg/die), CY (Cyclophosphamide orally 1 mg/kg/die), Rituximab (375 mg/m^2 intravenously once weekly x 4 doses), GI (gastro-intestinal).

In our opinion, what's relevant in this case is that attention to the isolated PTT prolongation in the first examinations, although with a minimal and not common bleeding picture, could have allowed a more rapid diagnosis exposing the patient to a minor clinical picture and probably to the need of a less intensive therapeutic approach [5].

Furthermore the present is one of the eleven cases evaluated at our Centre in a period ranging from February 2017 to August 2019 (three in 2017, four in 2018, four up to august 2019) in a geographic area, taking into account the residence of patients, of about 2.8 millions of citizens (Table1).

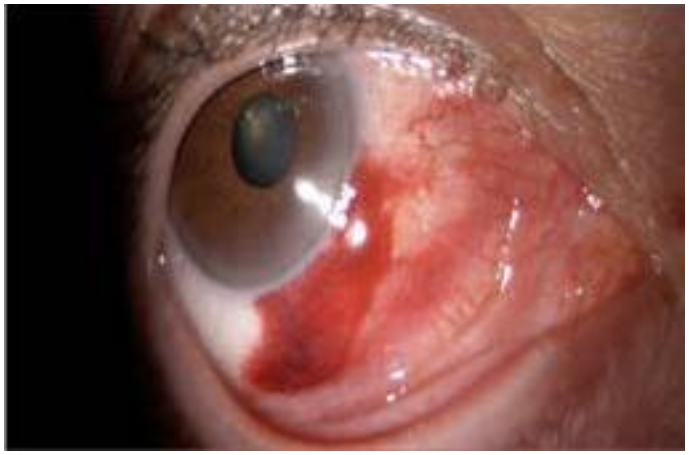

Figure 1: The only clinical finding was a subconjunctival bleeding

This suggests that AHA is really not so rare in the general population and probably most cases are lost for underdiagnosis [6]. Due to the type of relevant clinical picture encountered in our experience (eight requiring blood transfusions, ten with large muscular haematomas very near to a compartimental syndrome, two with uncommon joint bleeding, and one fatal case with massive gastrointestinal and cerebral bleeding), we encourage all putative involved clinicians and laboratorists to immediately suspect this no so really uncommon clinical picture when bleeding signs are related also to minimal laboratory alteration and not clearly influenced by specific clinical pictures and/or antithrombotic treatments. This could allow a rapid diagnosis and the start of a relative specific treatment, otherwise patients can be excessively exposed to a relevant bleeding risk that sometimes can be fatal [7].

References

1. Franchini M, Vaglio S; Marano G. Acquired hemophilia A: a review of recent data and new therapeutic options. Hematology. 2017; 22-514-520.

2. Duncan E, Collecutt M, Street A. Nijmegen-Bethesda assay to measure factor VIII inhibitors. Methods Mol Biol 2013;992:321-333.

3. Franchini M, Castaman G, Coppola A. Acquired inhibitors of clotting factors: AICE recommendations for diagnosis and management. Blood Transfus. 2015; 13: 498-513.

4. Tengborn L, Baudo F, Huth-Kühne A. EACH2 registry contributors. Pregnancy-associated acquired hemophilia A: results from the European Acquired Haemophilia Registry (EACH2). BJOG. 2012; 119: 1529-37.

5. Kruse-Jarres R, Kempton CL, Baudo F. Acquired hemophilia A: Updated review of evidence and tretatment guidance. Am J Hematol. 2017; 92: 695-705.

6. Knoebl P,Marco P,Baudo F. European Acquired Haemophilia Registry (EACH2). Demographic and clinical data in acquired hemophilia A: results from the European Acquired Haemophilia Registry (EACH2) J Thromb Haemost. 2012; 10: 622-631.

7. Charlebois J, Rivard GE, St-Louis J. management of asquired hemophilia A, review of current evidence Transfus Apher Sci 2018; 57: 717-720.