FACTOR XIII DEFICIENCY AS UNDERLYING CAUSE OF UNEXPLAINED BLEEDING

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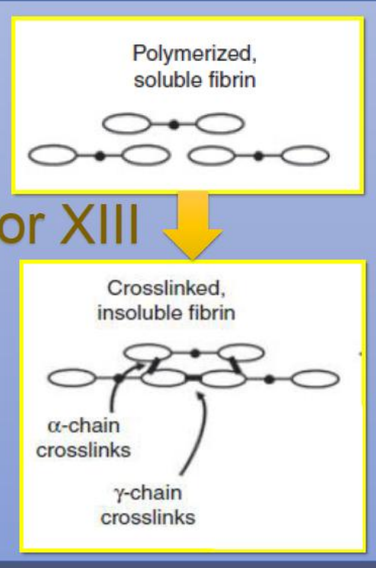
Introduction

FACTOR XIII DEFICIENCY

Factor XIII deficiency is an uncommon coagulation disorder that cannot be detected by conventional clotting tests.

Congenital form, generally due to mutations in F13A1 gene, presents with early life-threating haemorrhages in homozygotes.

Acquired deficiency, a more rare state, has been associated with certain drugs and inhibitors against FXIII.



Materials and Methods

01/01/2010 — *A retrospective single- center study* — 10/31/2013

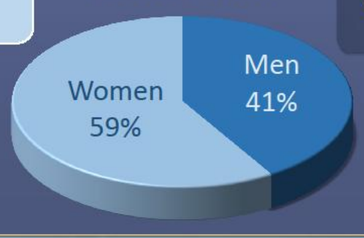
63 patients

With Unexplained hemorrhage

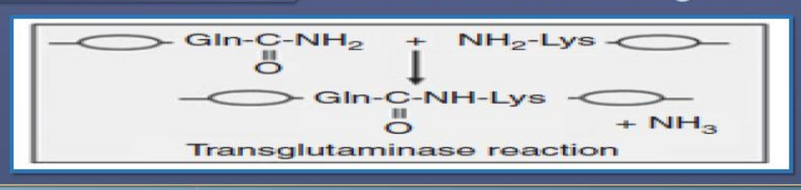
- Mainly after surgery
- or
- Spontaneous intracraneal bleeding at perinatal period

→ No relevant findings in conventional haemostasis assays

Sex distribution

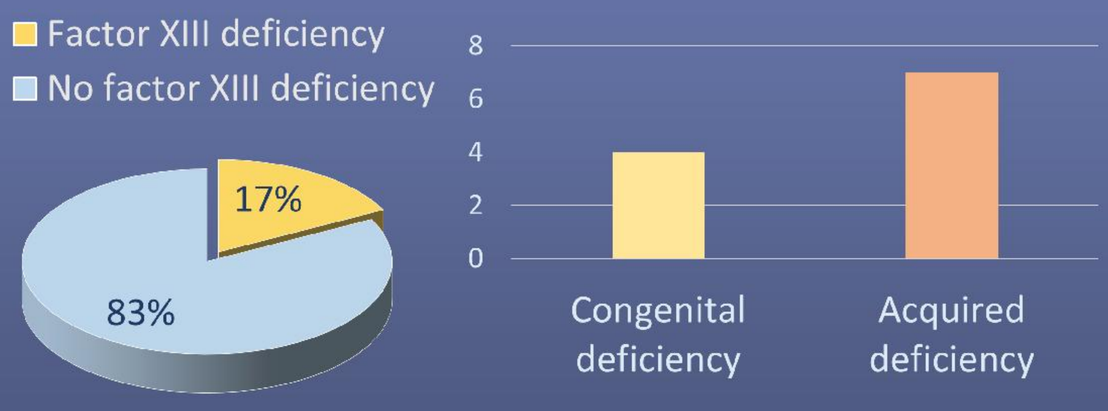


- A panel of haemostasis tests
  - -Routine tests of blood coagulation
  - -Platelet function assays
- Factor XIII → was measured by a functional chromogenic method



Results

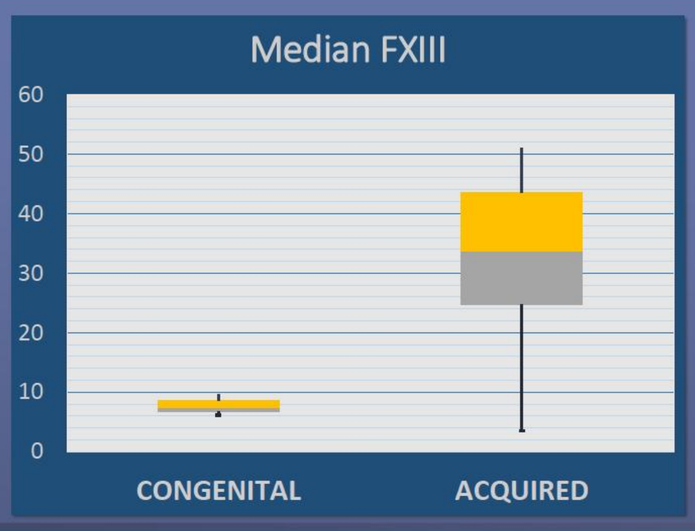
- In 11 out of 63 patients (17,46%) FXIII deficiency was identified: 4 congenital and 7 acquired



- In all acquired deficiencies, the presence of an inhibitor was discarded; 4/7 patients had platelet dysfunction too

Type of haemorrhage	CONGENITAL DEFICIENCY	ACQUIRED DEFICIENCY
Mucocutaneous bleeding	75%	28,6%
Hemorrhage after surgery or intracraneal bleeding	50% (0% ICH)	100%

- In 9/11 patients FXIII concentrate was administered, achieving bleeding control in 7
- In 3 congenital deficiency, prophylactic substitutive therapy was started avoiding new bleeding episodes (except for a posttraumatic muscle haematoma) with a median FXIII through levels of 10.25 U/dL



Median FXIII at first diagnosis work up:

- Congenital : 6,8 U/dL
- Acquired 33,7 U/dl.

- Two patients with acquired deficiency died of non haemorrhagic complications, 3 patients developed spontaneous remission of the deficiency in a median time of 2 months and 2 are still receiving substitutive therapy.

Conclusions

In congenital deficiency, maintenance of FXIII through levels in the range of 5-10% is enough to avoid bleeding manifestations. The acquired deficiencies are at least as frequent as congenital ones, develop haemorrhage episodes at higher levels of factor and respond to therapy in a thrifty way. For these reasons, we conclude that quantitative tests for FXIII are essential for diagnostic approach in high index clinical suspicious cases, such as those with unexplained bleeding.