

Erasmus MC

Universitair Medisch Centrum Rotterdam



Case studies in bleeding disorders

Dr. Marieke Kruip, MD
department of hematology

Case 1

patient, before surgery

20 years old

no medication

results:

PT	13.2 sec	(10.9-13.3)
APTT	35 sec	(28-39)
FVIII	1.23 IU/ml	(0.6-1.4)
VWF ag	1.09 E/ml	(0.6-1.4)
VWF act	0.59 E/ml	(0.6-1.4)
multimers	abnormal	

Question 1

The surgeon has seen the results and wants advise how to inform the patient.

What do you say?

1. The patient has mild von Willebrands disease type 2; it is an inherited bleeding disorder and she should be referred to a hemophilia treatment centre.
2. The patient has mild von Willebrands disease type 2; she can have surgery without precautions because of the VWF levels that are still high enough.
3. What kind of surgery are you planning?
4. None of the above

Case 1

You asked what kind of surgery was planned.

The answer is that she has aortic stenosis, due to congenital heart disease, which will be corrected.

The patient was referred to the hemophilia treatment centre.

Surgery was performed after treatment with VWF/ FVIII concentrate.

A few months after surgery blood was sent to you lab.

Case 1

FVIII	1.11 IU/ml	(0.6-1.4)
VWF ag	0.91 E/ml	(0.6-1.4)
VWF act	0.84 E/ml	(0.6-1.4)
multimers	normal	

Question 2

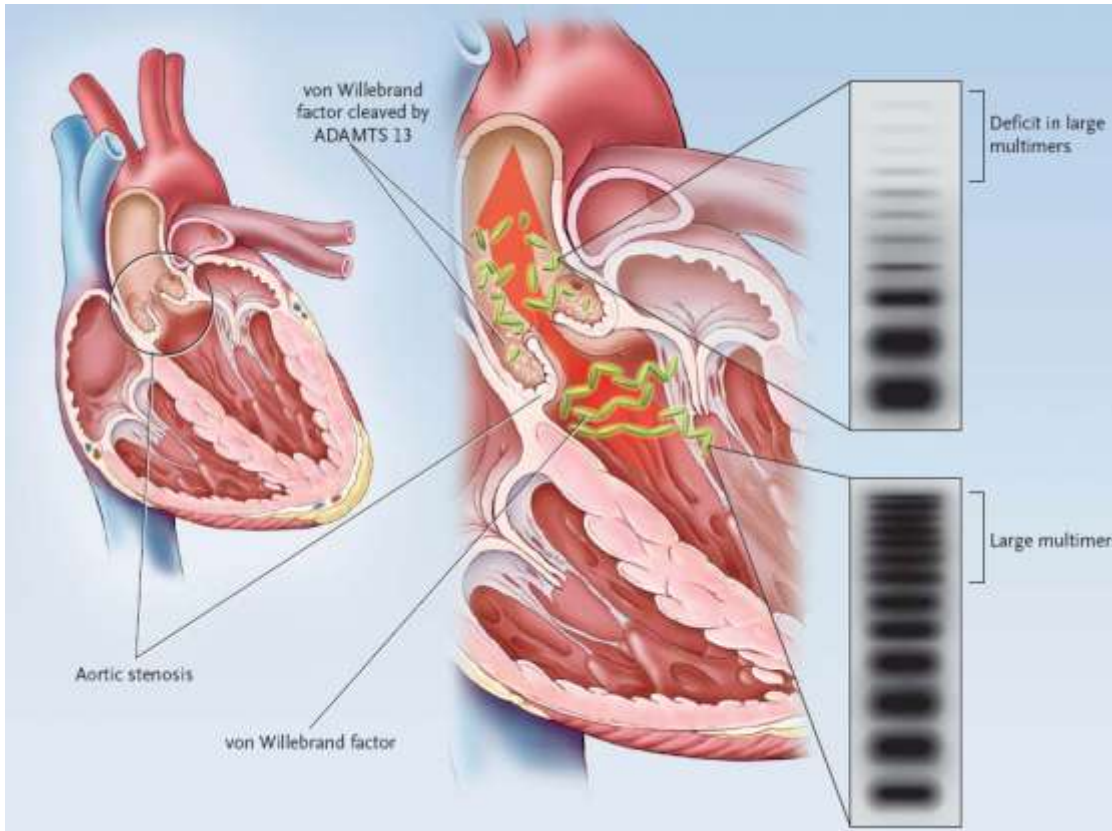
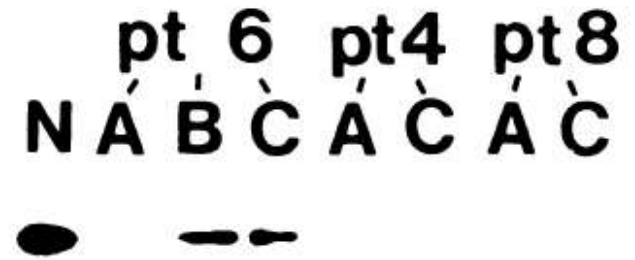
What is your conclusion?

1. The patient had acquired Willebrands disease and the von Willebrands disease is not present any more.
2. This blood samples was not from the same patient.
3. You want the testing to be repeated and you call the physician for another blood sample.
4. The patient has von Willebrands disease; you are not sure which type.

Case 1

conclusion:

acquired von Willebrand's disease, type 2a



*Gill, blood 1986,
Sadler NEJM 2003*

Case 2

2003

55 year female

bleeding disorder?

medical history:

1970 appendectomy, no bleeding

1996 nephrectomy, no bleeding

1997 hysterectomy, no bleeding

1999 vasculitis

rheumatic disease

Case 2

since 1 year easy bruising, sometimes spontaneously,
hematoma 1-5 cm

after venapunction large hematoma

no nose bleeding, no gum bleeding, no melena

pain in knees

Case 2

family history:

no bleeding disorders

medication:

no

physical examination:

healthy women

small hematoma right leg; 1.5 cm

Case 2

laboratory results:

Hb	9.7 mmol/L
MVC	99 fL
thrombo	194 x 10.9/L
leuco	12.5 x 10.9/L

normal renal and liver function tests

Case 2

bleeding time	2-3-3 minutes (< 4 min)
PT	12 sec (10.9-13.3)
APTT	87 sec (28-39)
fibrinogen	3.5 g/L (1.5-3.6)
APTT mixing study	57 sec

Question 3

The physicians calls you; she wants to know what the diagnosis is.

What do you say?

1. It is not possible to give the answer, I need more testing.
2. The diagnosis is acquired hemophilia.
3. Did she had heparin?
4. The most probable diagnosis is lupus anticoagulants.

Case 2

APTT lupus 74 sec (28-39)

APTT lupus + np 56 sec

LA dPT 1.57 (0-1.20)

LA dPT + np 1.22

ACL IgM 1 U

ACL IgG < 1 U

FVIII 0.02 IU/mL

Question 4

What is your diagnosis?

1. lupus anticoagulants
2. acquired hemophilia
3. I don't know yet, I need more testing

Case 2

Mixing with increasingly diluted plasma samples

In case of lupus anticoagulants

lupus activity will be disproportionately neutralised at higher dilutions

→ “normalisation” of coagulation factor activity

In case of specific inhibitor

irreversible binding to specific coagulation factor

→ coagulation factor activity will stay low

Case 2

FVIII 1/10	BL	E/mL	0.03 _L
FVIII 1/20	BL	E/mL	0.05 _L
FVIII 1/40	BL	E/mL	0.09 _L
FVIII 1/80	BL	E/mL	0.17 _L
FVIII 1/160	BL	E/mL	0.34 _L
FVIII 1/320	BL	E/mL	0.73
FIX 1/10	BL	E/mL	0.41 _L
FIX 1/20	BL	E/mL	0.48 _L
FIX 1/40	BL	E/mL	0.52 _L
FIX 1/80	BL	E/mL	0.69
FIX 1/160	BL	E/mL	0.90
FIX 1/320	BL	E/mL	1.41 ^H
FXI 1/10	BL	E/mL	0.33 _L
FXI 1/20	BL	E/mL	0.33 _L
FXI 1/40	BL	E/mL	0.39 _L
FXI 1/80	BL	E/mL	0.53 _L
FXI 1/160	BL	E/mL	0.76
FXI 1/320	BL	E/mL	1.37
FXII 1/10	BL	E/mL	0.54 _L
FXII 1/20	BL	E/mL	0.66
FXII 1/40	BL	E/mL	0.78
FXII 1/80	BL	E/mL	0.81
FXII 1/160	BL	E/mL	0.66
FXII 1/320	BL	E/mL	0.53 _L

Question 5

What is your diagnosis?

1. lupus anticoagulants
2. acquired hemophilia
3. I don't know yet, I need more testing

Case 2

our conclusion:

inhibitor is not specific

most likely lupus anticoagulants

Case 2

2005

a few months again bleeding tendency;

large hematoma arms and legs

joint bleeding elbow with pain, impaired mobility

bleeding in mouth

Case 2

PT	11.7 sec (10.9-13.3)
APTT	84 sec (28-39)
APTT mixing study	54 sec
LA dPT	1.57 (0-1.20)
LA dPT + np	1.22
ACL IgG	1 U
ACL IgM	1 U

Case 2

FVIII 1/10	BL	E/mL	<0.01 _L
FVIII 1/20	BL	E/mL	0.01 _L
FVIII 1/40	BL	E/mL	0.02 _L
FVIII 1/80	BL	E/mL	0.05 _L
FVIII 1/160	BL	E/mL	0.11 _L
FVIII 1/320	BL	E/mL	0.23 _L
FIX 1/10	BL	E/mL	<0.01 _L
FIX 1/20	BL	E/mL	0.01 _L
FIX 1/40	BL	E/mL	0.02 _L
FIX 1/80	BL	E/mL	0.06 _L
FIX 1/160	BL	E/mL	0.20 _L
FIX 1/320	BL	E/mL	0.51 _L
FXI 1/10	BL	E/mL	<0.01 _L
FXI 1/20	BL	E/mL	0.01 _L
FXI 1/40	BL	E/mL	0.02 _L
FXI 1/80	BL	E/mL	0.06 _L
FXI 1/160	BL	E/mL	0.25 _L
FXI 1/320	BL	E/mL	0.82
FXII 1/10	BL	E/mL	0.01 _L
FXII 1/20	BL	E/mL	0.02 _L
FXII 1/40	BL	E/mL	0.04 _L
FXII 1/80	BL	E/mL	0.09 _L
FXII 1/160	BL	E/mL	0.22 _L
FXII 1/320	BL	E/mL	0.29 _L

Factor VIII	BL	IU/ml	<0.01 _L
WVF ag.	BL	E/mL	1.24
WVF-CB	BL	E/mL	1.30
WVF-act.	BL	E/mL	1.36
Factor IX	BL	E/mL	<0.01 _L
Factor XI	BL	IU/ml	<0.01 _L
Factor XII	BL	E/mL	0.01 _L
FVIII-Inh 00	BL	E/mL	<0.01
FVIII-Inh 30	BL	E/mL	<0.01
FVIII-Inh 60	BL	E/mL	<0.01
Bethesda	BL	U	2176.0

Question 6

What is your diagnosis?

1. lupus anticoagulants
2. acquired hemophilia
3. I don't know yet, I need more testing

Case 2

lab results together with clinical information

acquired hemophilia

Case 2

no underlying disorder was found

treatment with prednisone and cyclophosphamide

no bleeding tendency

APTT 35 sec

FVIII 0.95 IU/ml

BU 0.3 U

it is not possible to stop prednisone; recurrence of inhibitor

low dose prednisone as maintenance treatment

Conclusion

for the correct diagnosis of patients with a bleeding tendency interaction between laboratory and physician is essential