B|BRAUN
SHARING EXPERTISE

HAEMORRHAGE AFTER TENCKHOFF-CATHETER PLACEMENT – ACQUIRED FACTOR VIII. DEFICIENCY

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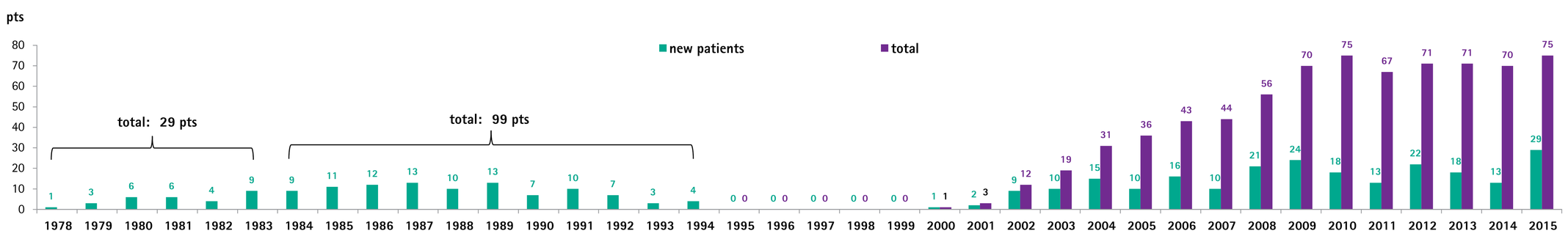
INTRODUCTION

Chronic peritoneal dialysis (PD) has been carried out in our nephrology centre since 1978, in the form of in-centre intermittent peritoneal dialysis (IPD) until 1994. Continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) hava been applied since 2000. 58 patients were treated in PD-programme (22% of prevalent dialysis patients) at the end of 2015, with a PD prevalence of 231 pmp.

Tenckhoff-catheter was inserted in 358 patients altogether: for a long period - catheters were placed via the open laparotomy technique, recently laparoscopic placement is used more frequently. In the post-operative phase (apart from a few minor surgical haemorrhages) no significant haemorrhagic adverse events were detected.

Clotting & coagulation time, prothrombin time (PT) (prothrombin activity in percentage & **I**nternational **N**ormalized **R**atio) and platelet count was included pre-operative coagulation tests for 30 years. Preliminary-routine examinations of haemorragic & coagulation time have been terminated in the last decade

3. Patients on PD 1978-2014 Szombathely, Hungary



PURPOSE OF INVESTIGATION

To present a patient case, where acquired coagulopathy - associated with generalized, massive haemorrhage - was detected in the post-operative phase.

PATIENT

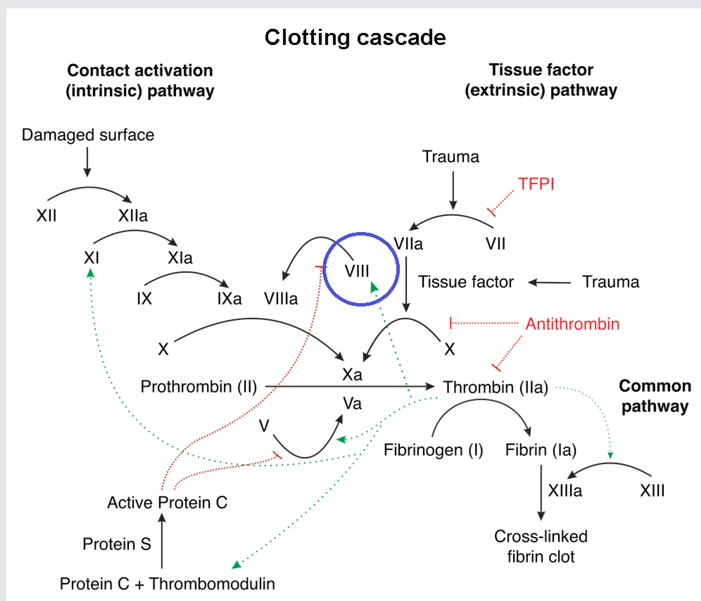
44-year-old, female, initials: Z. N.

Preceding illnesses

Tonsillectomy, sinus maxillaries polypectomy, asthma bronchial, polycystic kidney disease (confirmed in 1995), secondary hypertension, nephrology care due to chronic progressive kidney disease. She had two childbirths (the second with sectio Caesarea).

February 2015: Patient was placed on the kidney transplant waiting list.

Chosen dialysis modality: CAPD (continuous ambulatory peritoneal dialysis)



CURRENT MEDICAL HISTORY

Tenckhoff-catheter insertion and subsequent events (01.04.-09.04.2015).

Pre-operative coagulation screening (INR, platelet count) was satisfactory, haemoglobin level was 12,2 g/dL.

April 1st, 2015: laparoscopic Tenckhoff-catheter insertion: without complications.

Post-operative haemorrhage from the surgical wound, haematemesis (two bleeding gastric ulcers), haemascos and anaemia occurred on the same day afternoon. Further laparoscopy procedure: abdominal cavity drain insertion. In the following two days, three laparatomies were necessary due to haemorrhage in stomach, the abdominal cavity and abdominal wall – the patient was transferred to the intensive care unit (ICU).

The patient received continuous transfusions (red blood cell -RBC- concentrates, altogether 23U) and fresh frozen plasmas (FFP – 18U) due to major extension of the activated partial thromboplastin time (aPTI).

On the basis of haematology consultation, the possibility of **acquired factor VIII deficiency, as well as the anti-factor VIII inhibitor** had been taken into account (since aPTI could only be reduced but not normalized.), therefore the patient was relocated to the National Haemophilia Centre (1st Dept. of Internal Medicine of Medical Centre, Hungarian Defence Forces) for further treatment.

CONTINUATION OF THE PATIENT'S MEDICAL HISTORY (09.04-29.05.2015.)

Diagnosis: Acquired haemophilia due to inhibitors

At the time of patient's admission to the ward, the factor VIII activity was <0,25% (normal levels are between 70-140%), the inhibitor level was 20 U/mL Bethesda Unit (BU) – this is a serious clinical status. In such cases with high inhibitor levels (inhibitor titers) only 'bypass' procedures (Activated Prothrombin Complex Concentrates – APCC /FEIBA/ and Recombinant activated factor VII – rFVII /Novo-Seven/) are appropriate for proper haemostasis.

Due to recurrent severe bleedings (skin suffusions, metrorrhagia, stomach and colon bleeding) the patient underwent immunosuppressive treatment (steroid + cyclophosphamid) for the purpose of eradicating inhibitors along with VIII factor replacement therapy, in addition the patient received: proton pump inhibitors -PPI- (because of gastric ulcers), mesalisine (because colon ulcers) and blood derivatives (32U RBC concentrates, 8U platelet concentrates, human albumin infusions). Immunosuppression had to be terminated in two occasions due to two serious infections (sepsis due to venous cannula infection and Clostridium Difficile enteritis).

The treatment resulted in a complete remission: factor VIII activity level increased, above 200%, negative inhibition test results. **Patient recovered from acquired haemophilia.**

9. Clotting parameters I.

date 2015.	aPTI (30-40 sec) sec	PTI - 2h sec	corrected (mixed)* PTI (P+K) sec	corrected (mixed)* PTI - 2h (P+K) sec	F VIII activity (70-140%) %	FVIII inhibitor (Bethesda Unit) BU
06.03.	121.77 !	-	-	-	-	-
06.04.	122.23 !	-	-	-	-	-
09.04.	106.79	109.00	42.0 / 29.7	89.0 / 31.1	<0.25	-
10.04.	67.38	66.10	37.0 / 29.7	67.0 / 30.3	0.27	20.0
13.04.	61.22	61.20	36.0 / 29.3	61.0 / 30.3	0.26	12.0
11.05.	65.67	69.30	42.0 / 29.2	46.0 / 30.2	6.23	0.8
22.05.	46.94	47.20	36.0 / 30.1	36.0 / 30.8	220.17	negative
28.05.	42.09	-	-	-	262.98	negative
10.08.	61.00	-	46.0 / 37.0	-	189.0	negative
02.11	55.00	-	43.0 / 36.0	-	114.0	negative
02.18.2016	52.00	-	40.0 / 31.0	-	168.0	negative

** patients and normal plasma mixed in 1:1 rate*

10. Clotting parameters II.

date 2015.	INR	Thrombin time sec	Fibrinogen g/L	Lupus antikoagulant	Platelet count g/L
02.04.	0.92	15.22	3.96	negative	118
09.04.	0.85	16.23	4.36 ↑	negative	202
13.04.	0.87	17.97	3.76	negative	399
22.05.	1.02	14.13	5.13 ↑	weakly positive	311
28.05.	1.05	15.60	4.21	negative	282
08.10.	0.95	14.09	6.03 ↑	negative	311
02.18.2016	0.90	20.14	5.18 ↑	positive	265

11. Factor VIII activity and immun-inhibitor level

12. Clinical states leading to anti-factor VIII inhibitor antibody (acquired haemophilia)

Clinical state	Frequency*
▪ idiopathic	46,1-52,5%
▪ autoimmune disorders/diseases (SLE, RA, myasthenia gravis, Crohn's disease, colitis ulcerosa, dermatological diseases)	17,6-20,4%
▪ gravidity, postpartum	7,3-11,0%
▪ drugs	2,9-5,6%
▪ others (infections, allergic reactions)	6,0-8,9%

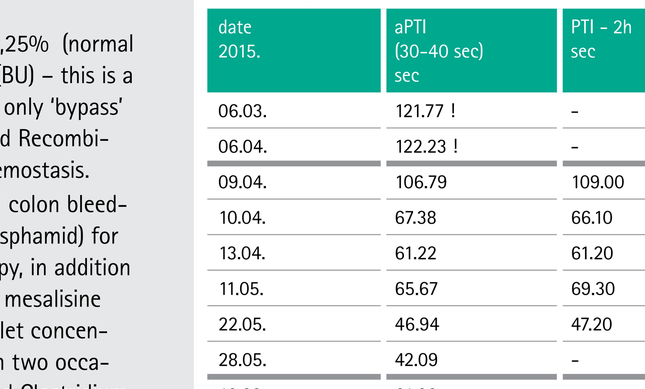
**According to various authors' data*

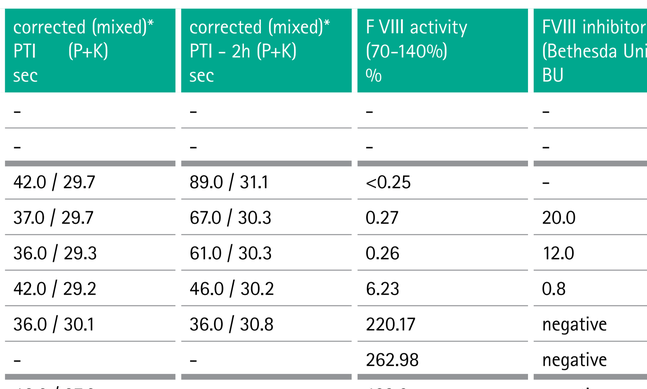
NEPHROLOGIC ASPECTS OF MEDICAL HISTORY

The Tenckhoff-catheter remained in place, but due to deterioration of renal function (and a severe malnutrition) on May 12, 2015 - the patient's education having been completed-, the patient's CAPD-treatment was initiated.

Since PET-scans qualified the characteristics of the patient's peritoneum as a "high transporter", the clinical team switched to APD-treatment (Automated Peritoneal Dialysis) in May, 2016.

The patient's weekly Kt/V marker is above the target level, current condition: satisfactory. The patient -after temporary unsuitability for transplantation is again on the waiting list.





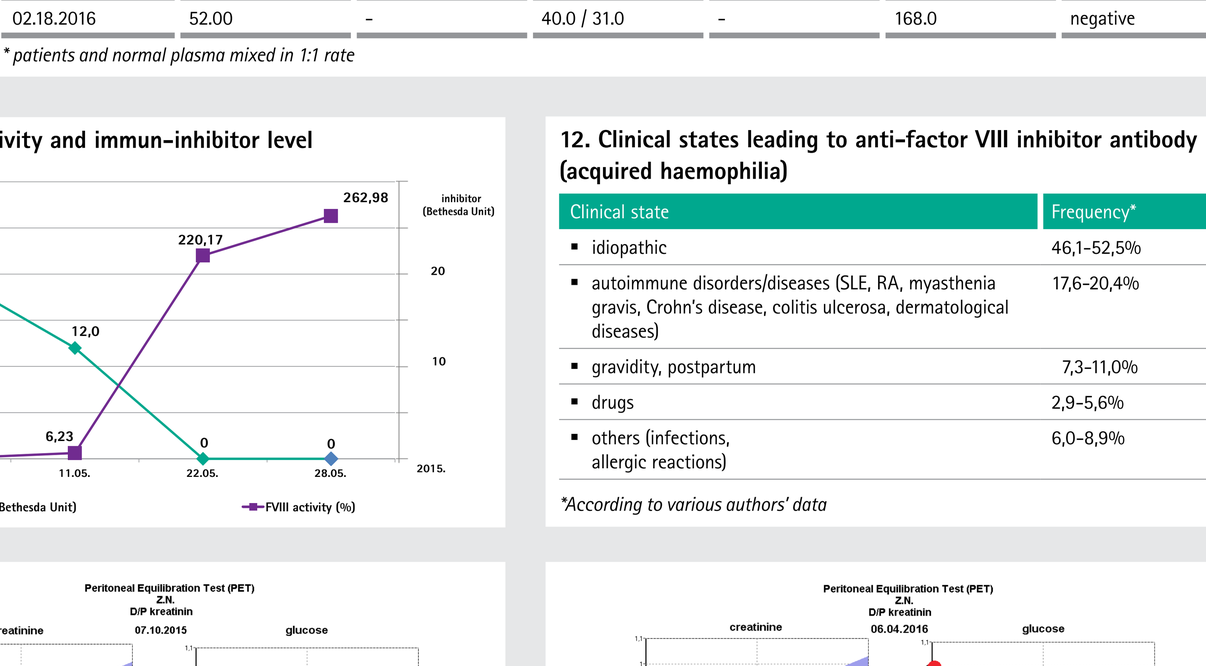
SUMMARY

- Acquired haemophilia is excessively rare but a severe haemorrhagic illness, relating to the formation of anti-factor VIII inhibitor antibodies. Adding normal plasma does not correct the aPTI-extension. In 50% of these cases the main cause remain idiophatic. Inhibitors are usually detected by Bethesda assay. Mortality associated with bleeding events is between 10-22%.
- Our patient –despite the numerous adverse reactions, severe hemorrhage, malnutrition & infections- recovered from the acquired haemophilia and her planned treatment is successfully conducted. Her condition is suitable for renal transplantation.

CONCLUSION

The previously used coagulation tests (prothrombin time – INR, thrombocytes) shall be complemented with aPTI examination in each case of patients set to renal replacement therapy.

16. Nephrological follow up



	12.05.2015	03.06.2015	03.07.2015	01.09.2015	07.10.2015	04.11.2015	03.12.2015	13.01.2016	10.02.2016	03.03.2016	06.04.2016	03.05.2016
Haemoglobin (g/dL)	9,60	9,66	11,91	13,85	13,20	12,24	13,04	10,63	12,40	12,56	12,08	12,08
Albumin (g/L)	34	33	35	38	40	40	37	40	40	45	41	
CRP (mg/L)	18,8	13,6	14,0	5,3	3,9	6,0	4,0	2,0	2,0	4,8		
Hypochrom vvt (%)	13,7	11,2	1,9	3,8	0,9	0,4	1,0	1,7	6,4	3,3	4,3	