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A massive gross haematuria in an 85-year-old patient with acquired haemophilia A

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ABSTRACT:

The authors herein present a case report of an 85-year-old female patient with massive gross haematuria in the course of acquired haemophilia A. Acquired haemophilia in the geriatric population is a rare but severe bleeding disorder. It is caused by suddenly appearing autoantibodies that interfere with coagulation factor VIII activity. The diagnosis of acquired haemophilia should be considered in any patient who presents with bleeding and a prolonged activated partial thromboplastin time (APTT).

Key words: haematuria, haemophilia, acquired haemophilia

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Introduction:

Haemophilia is the oldest known hereditary bleeding disorder, recognised even in ancient times. There are three types of the disease: haemophilia A, haemophilia B, and haemophilia C. Haemophilia A is caused by a decrease in plasma coagulation factor VIII activity, haemophilia B by a decrease in plasma coagulation factor IX, and haemophilia C by a decrease in plasma coagulation factor XI. Depending on the degree of deficiency of the coagulation factor, the following are distinguished: severe (< 1% of norm), moderate (1–5% of norm), and mild (5–50% of norm). Almost half of the recognised forms of haemophilia are classified as severe. The most typical symptom of haemophilia is spontaneous haemarthrosis, which leads to joint destruction (haemophilic arthropathy) and secondary muscle atrophies. In addition, intra-muscular bleeding, haematuria, gastrointestinal bleeding, intracranial bleeding (a frequent cause of death), and bleeding from surgical and dental extraction wounds may occur primarily in the severe form of the disease. At present, there is no causative treatment of the disease available and no full recovery is possible. Supplementation with concentrates of deficient coagulation factors is used. The implementation of such treatment results in a significant extension and improvement in the quality of the patients' lives [1–2].

Although haemophilia is usually associated with a genetically conditioned disorder, it also occurs throughout life as an acquired haemophilia. The disease in this form especially affects elderly patients.

Case report:

An eighty-five-year-old female patient was admitted to the Geriatric Clinic due to massive gross haematuria observed by the patient and the patient's relatives five days before she appeared in the Hospital Emergency Department. The symptoms were accompanied by diffuse lower abdominal pain and increased body temperature (the highest observed fever was 39°C).

In the patient's history, persistent atrial fibrillation, moderate mitral regurgitation, and chronic obstructive pulmonary disease and nicotine use were reported. The patient had taken chronically (for three years) dabigatran at a reduced dose due to old age (2x110 mg), metoprolol in extended-release form (1x25 mg), spironolactone (1x25 mg), sustained-release form of indapamide (1x1.5 mg), simvastatin (1x20 mg), and inhalants: formoterol 12 µg (2x1) and budesonide 400 µg (2x1).

At admission, the patient was conscious, her general condition was described as mean, blood pressure (RR)

Table 1. Patient's laboratory findings.

Test name	Patient's test results	Normal limits
WBC	10.48 10^3 /ul	3.98-10.04 10^3 /ul
RBC	4.65 10^6 /ul	3.93-5.22 10^6 /ul
HGB	13.4 g/dl	11.2-15.7 g/dl
MCV	88.4 fl	79.4-94.8 fl
PLT	191 10^3 /ul	132-370 10^3 /ul
CRP	19.58 mg/l	<5.00 mg/l
Creatinine	0.85 mg/dl	0.6-1.10 mg/dl
Potassium	3.7 mmol/l	3.5-5.0 mmol/l
Sodium	138.2 mmol/l	136-145 mmol/l
ALT	10 U/l	<36 U/l
AST	17 U/l	<34 U/l
Amylase in body fluids	124 U/l	5-410 U/l
Total bilirubin	0.78 mg/dl	0.2-1.2 mg/dl
APTT	157.2 s	26.4-37.5 s
INR	1.24	0.9-1.2
PT	15.6	9.4-13.8

100/60, atrial fibrillation with mean ventricular function about 80/min, 16 breaths/min, physiological vesicular murmur, she walked by herself, but with difficulty, and she was without visible peripheral oedema and cutaneous lesions. In the physical examination, she emphasised tenderness of the abdomen, without features of muscle defence and peritoneal symptoms. Additional tests were carried out (see Table 1)

An issue requiring special attention was a considerably prolonged activated partial thromboplastin time (APTT). In the general urine test there were fields densely covered with erythrocytes, quite numerous bacteria, 10-20 leukocytes per high-power field, and a significant protein content of 267 mg/dl.

No abnormalities in the gall bladder and liver were found in the ultrasound performed in the abdominal cavity. In the body of the pancreas a hypoechoic area of $13 \times 6 \times 9$ mm was described for further diagnosis. On both sides, pelvicalyceal systems were marked, on the right side the calyx up to 8 mm wide and the renal pelvis 6 mm wide, whereas on the left side the calyx up to 10 mm wide and the renal pelvis 9 mm wide. Due to the urgency of the ultrasound examination, bladder filling was not achieved, and consequently no full assessment was possible. There was no evidence of free fluid in the abdominal cavity.

Based on the entire clinical presentation, suspicion of pyelonephritis was put forward, empiric antibiotic therapy with ceftriaxone (1×2 g) was administrated until the urinal culture examination results were ob-

tained. Due to the observed haematuria, dabigatran was discontinued (CHA2-DS2-Vasc 4 pkt HAS-BLED 3 pkt).

The patient was consulted urologically, and cystoscopy was performed in accordance with the recommendations, which showed no pathological changes in the bladder, while the right ureter showed rhythmic projections of bloody urine. After the cystoscopic examination, the patient's diagnosis was extended with a computed tomography of the abdominal cavity and pelvis revealing in the right renal pelvis a lack of contrast in the form of numerous thrombi. On the borderline of the head and body of the pancreas, the change previously described in the ultrasound examination, measuring 15×8 mm, hypodense, subject to slight contrast enhancement, was visualised.

During the hospitalisation, the patient was observed with a persistent gross haematuria, without significant improvement after the implemented conservative treatment, and gradual anaemia of the patient (decrease in Hgb value to 8.8 g/dl), as well as massive ecchymosis at the injection sites. A decision was made to extend the diagnosis of coagulation disorders - a correction test and determination of coagulation factors were made (for results see Table 2).

The patient was consulted haematologically: on the basis of the recommendations issued, a total of 20,000 units of FEIBA (coagulation factor VIII inhibitor) was ordered from the Regional Blood Donation Centre and transfused, and prednisone 80 mg was added to the medication. After stabilisation of the patient's con-

Table 2. Correction test and determination of coagulation factor results.

Test name	Patient's test results	Normal limits
Correction test	No correction - after addition of normal serum, the APTT time was not normalised	correction (+)
Factor VIII	0.5%	70-150%
Factor IX	88.90%	70-120%
Factor XI	53.60%	70-120%

dition, the patient was transferred to the Department of Haemostasis and Internal Disorders at the Institute of Haematology and Transfusion Medicine in Warsaw for further treatment.

Discussion:

The present case of an elderly patient with massive gross haematuria describes a rare geriatric point of view. The primary cause of haematuria may be the use of the DOAC (direct oral anticoagulant) dabigatran. According to the Summary of Product Characteristics, patients aged 80 years and over should take a dose of 220 mg in the form of one 110-mg capsule twice a day due to the increased risk of bleeding in this population [3]. The patient was treated according to the above recommendations. Dabigatran induces a dose-dependent and short-term (1-4 h after administration) prolongation of activated partial thromboplastin time (APTT) and prothrombin time (PT), while its effect on international normalised ratio (INR) is less reliable [4]. Prolongation of APTT four times and persistence of these values, despite the withdrawal from treatment with DOAC, excludes dabigatran as the cause of the observed disorders. The degree of haematuria is also not justified by the suspicion of urinary tract infection that has been raised during the diagnosis.

Isolated haematuria as a symptom of acquired haemophilia is a rarely observed phenomenon. Acquired haemophilia is usually associated with multiple haemorrhagic complications, such as ecchymosis and haematomas within the skin and subcutaneous tissue (94%) or intra-articular bleeding (9%). There is also prolonged bleeding in places of intravenous injection and other iatrogenic interventions with disruption of tissues, bleeding into the gastrointestinal tract and central nervous system [5]. Mortality connected directly or indirectly with haemorrhagic complications reaches 10–22% in the population of ill persons [7].

Acquired haemophilia A is a disease caused by the presence of autoantibodies that inhibit coagulation factor VIII activity. The occurrence of autoantibodies is a rare disorder detected in one person per 1-4 million of the

general population. Acquired autoantibodies against coagulation factor VIII are polyclonal in nature and belong to the immunoglobulin IgG class [6]. The disease most often appears in older people aged 60-80 years. About 50% of patients are diagnosed with the idiopathic form of the disease; in the remaining 50% at the time of diagnosis, a coexisting condition is detected, most often cancer (12.5%), rheumatoid arthritis (14.6%), systemic lupus (10.4%), or other autoimmune disorders (8.3%) [7].

Conclusions:

The patient's case indicates the need to search for the causes of isolated haematuria in the elderly population, also among rare in clinical practice conditions, including acquired coagulation disorders. Proper diagnosis and start of causative therapy is associated with a better prognosis and helps avoid factors increasing the risk of massive multi-organ bleeding.

Conflict of interest: None declared.

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