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CASE OF ACQUIRED COAGULOPATHY

Abstract

In recent years, the number of patients receiving anticoagulant therapy is growing rapidly worldwide. This is due to the rapidly expanding scope of their application: an increasing number of patients with non-valvular heart disease, including atrial fibrillation, the risk of thromboembolic events, an increase in the number of surgical interventions, especially in cardiac surgery (in the treatment of valvular heart disease, cardiac anomalies, infective endocarditis, inserting of cardiac pacemakers, and conducting electrical cardioversion), the use of anticoagulants in the treatment of other organs and systems (in neurology, vascular surgery, obstetrics and gynecology). Despite the wide range of anticoagulants for a modern physician, one of the most studied and often prescribed one is warfarin. Warfarin is a coumarin anticoagulant of the indirect action, a competitive antagonist of vitamin K. However, along with high availability and efficiency of its use, it has a large number of possible contraindications and use patterns, such as: a lot of drug-drug and other interactions, the need for careful control of the dosage and the regimen of the drug use, strict control of the international normalized ratio throughout therapy. This drug should be used in patients who use alcohol and have cognitive impairment with caution. In this group of patients, in addition to personal awareness of patients, it is necessary to conduct explanatory conversations with relatives/caregivers about all possible side effects and measures for their prevention. Non-observance of precautionary measures at therapy by warfarin can lead to severe consequences, and in rare instances even death. Among such consequences is warfarin-induced coagulopathy. We present a clinical case of the development of severe acquired (warfarin-induced) coagulopathy in a patient with cognitive dysfunction.

Key words: *warfarin, acquired coagulopathy, cognitive impairment*

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ICU — intensive care unit; INR — international normalized ratio; AF — atrial fibrillation

Acquired coagulopathies are one of the most common syndromes of critical conditions. According to the literature, clinical signs of coagulopathy (bleeding) are observed in 16%, and laboratory signs — in 66% of patients in the intensive care units (ICU) [5]. One of the reasons for the development of acquired coagulopathy is an overdose of anticoagulant agents, in particular warfarin.

Warfarin is an indirect anticoagulant, one of the substances that inhibit coagulant element of hemostasis. Their administration prevents the formation of blood clots and stops the growth of blood clots

already formed. This property of indirect anticoagulant agents is actively used in cardiology, neurology and surgery [2].

The mechanism of warfarin action is an impairment of the metabolism of vitamin K, which is a cofactor for synthesis of II, VII, IX and X coagulation factors [4]. When taking warfarin it is mandatory to perform regular laboratory monitoring of INR (International Normalized Ratio) throughout the course of therapy. INR is a laboratory test recommended by WHO, which reflects the state of the blood coagulation system. The optimal INR

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value in patients receiving warfarin is determined individually for a particular clinical situation and is usually in the range of 2–3 [4].

Warfarin poisoning is rarely intentional; usually it is the result of an accidental overdose. It should be remembered that the effect of warfarin is influenced by many factors: food, drinks, taking related drugs. Therefore, during its administration, the diet should not be changed dramatically, and when changing concomitant drug therapy, its effect on the warfarin effectiveness should be carefully studied. Clinical signs of warfarin overdose (the appearance of hematomas, hematuria, blood in the stool, menorrhagia) are not specific. The most severe complications are intracranial hemorrhages, which develop in 2% of patients.

The bleeding risk index for patients using warfarin takes into account four independent factors: age of 65 years and over; previous stroke; a history of gastrointestinal bleeding; recent myocardial infarction, and hematocrit below 30% [6]. Elderly patients taking this anticoagulant agent should be carefully monitored because they have a high risk of adverse effects. This is evidenced by our observation.

The female patient M., 77 years old, was delivered by an ambulance crew to the sanitary inspection room of the hospital on 15.03.2018 with complaints of dyspnea, weakness, palpitations, coughing and hemoptysis for two weeks.

In her youth, she often had tonsillitis and underwent tonsillectomy. During two pregnancies and childbirth, a cardiac malformation was suspected, but the patient was not examined. In 2009, she had ischemic stroke, at the same time atrial fibrillation (AF) and concomitant mitral defect was detected. In 2010, she underwent mitral valve replacement (bicuspid mechanical prosthesis) with the subsequent prescription of warfarin. INR was maintained at 2–3 and was monitored regularly.

In 2017, her memory deteriorated sharply after a “transient ischemic attack”. The patient monitored INR rarely, adjusting the dose of warfarin by herself from 2.5 to 5 mg/day. (INR dated 13.03.2018: 15.58).

Physical examination data: the condition of the patient was severe, the patient was inhibited, answered questions with difficulty, she confused events and dates. The skin was pale, multiple hemorrhagic rashes (petechiae, ecchymoses) on the skin of the body, upper and lower extremities were observed. The largest (Figure 1) ones were on the left side of the abdomen spreading to the lower back (up to 20 cm in diameter), the inner surface of the left thigh (up to 15 cm) and the left forearm (up to 8 cm). There was a purple color hematoma on the tongue up to 1.5 cm in diameter, towering above the surface.

The breath sounds were vesicular, diminished, with respiration rate 30 per minute, there were fine crackles in the lower lung fields on both sides and dry rales in the interscapular region. The heart sounds were arrhythmic, mechanical valve clicking was detected, the heart rate was 120 beats per minute, pulse deficiency was up to 40 per minute, and the blood pressure was 140/80 mm Hg. The abdomen was soft, tender in the right subcostal space. The inferior margin of the liver (at percussion) was at the site of umbilicus. Feet and shins were swollen. The patient was admitted to the ICU.

Laboratory tests data: complete blood count: anemia (RBC — 2.08 T/l, Hb — 76 g/l, Ht — 21%), leukocytosis (15.9 g/l), thrombocytosis (748 g/l), INR — 12.4.

Warfarin-induced coagulopathy was diagnosed. The treatment included warfarin discontinuation, transfusion of fresh frozen plasma, packed RBCs, administration of Vicasol, Ferrum Lek, treatment of



Figure 1. Extensive hematoma in the left subcostal space with spreading to the lower back

respiratory (oxygen) and heart (furosemide, bisoprolol, lisinopril, digoxin) failure. INR was monitored daily.

On treatment, the patient's condition improved, hemoptysis and hematuria disappeared, congestion in the systemic and pulmonary circulation decreased, and normal sinus rhythm was achieved. The complete blood count of 20.03.2018 showed: RBC — 3.0 T/l, Hb — 96 g/l, Ht - 30%, INR - 1.92. The patient was transferred to the rehabilitation department, where warfarin administration was resumed under the control of the INR (within 2–3), first at a dose of 2.5 mg/day and then 5 mg/day.

The patient was examined by a neurologist in the department, the following diagnosis was made: "Multifocal brain damage due to repeated cardiogenic embolism with silent lacunar infarctions, mild cognitive impairment". The patient was discharged on the 12th day of hospital stay for outpatient treatment. The INR value was 2.6.

Before discharge, the conversation was held with the patient's relatives about the importance of adhering to a selected dose of warfarin, regular monitoring of INR, taking related drugs (bisoprolol, digoxin, lisinopril, Ferrum Lek) and regular monitoring by community-based medical staff.

Thus, we observed an elderly patient who developed a severe hypocoagulation syndrome associated with an overdose of warfarin. A prerequisite for warfarin therapy is strict patient compliance with the prescribed dose of the drug under regular monitoring of INR [7]. In the case of an incorrect dose regimen or if the patient does not adhere to the regimen, an overdose may develop with potential serious and even life-threatening complications, as happened in our patient.

In addition, the treatment of elderly patients should be carried out with special precautions, since the synthesis of coagulation factors and hepatic metabolism are reduced, which can result in an excessive anticoagulant effect of warfarin [3]. Furthermore, the risk of cognitive impairment increases, as a person ages, especially in people with AF. This arrhythmia can lead to a decline in cognitive abilities or even

dementia through various mechanisms, most often as a result of a stroke. In addition to clinical strokes, "silent" strokes, which are often seen in AF, can also lead to the development of cognitive impairment [8]. This is confirmed by this case: based on the results of the examination of our patient, "Multi-focal brain damage due to repeated cardiogenic embolism with silent lacunar infarctions, mild cognitive disorders" was diagnosed by a neurologist.

Considering all of the above factors, warfarin therapy should be strictly controlled by the patient personally, or if it is impossible (alcoholism, cognitive disorders, dementia), by the relatives or relevant medical staff.

Conflict of Interests

The authors declare no conflict of interests.

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