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EDİTÖRE MEKTUP / RESEARCH

Arterial occlusion after cessation of warfarin treatment

Warfarin tedavisinin kesilmesi sonrasında görülen arteryal oklüzyon

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To the Editor,

Warfarin administration interferes with a well-balanced coagulation system including coagulation factors of prothrombin and factor VII, IX and X, as well as anti-coagulation factors protein C and protein S. With discontinuation of the treatment, the coagulation system is reactivated and thromboembolic events may occur[1]. There is a correlation between warfarin dose compliance and therapeutic interval, bleeding risk and embolism incidence. When the estimated INR (International Normalized Ratio) is out of the therapeutic range, during the aggressive warfarin treatment, the therapeutic range should be maintained, the non-pharmacological factors should be determined and the drug effect velocity should be moderate during the drug administration; however, it is not yet fully understood how to achieve all of these. Warfarin dose fluctuation is the combination of INR, and physician's experience and knowledge on patient's clinical data[2].Here in, we present a patient with acute arterial occlusion developing in the lower extremity after discontinuation of warfarin treatment.

A 45-year-old male presented to the emergency department with complaints of numbness and pain in the left lower extremity. He had diabetes mellitus, hypertension, congestive heart failure and chronic renal failure (no hemo/peritoneal-dialysis required). His physical examination revealed tachypnea and respiratory distress. He had started acetylsalicylic acid and coumadin 2 years ago due to valvular heart disease, and had discontinued these drugs 15 days ago. His general condition was moderate, GCS: 15 points, cooperative and orientated. On physical examination, his blood pressure was 155/101 mmHg, SO_2 was 93%, body temperature was 36.8 °C, and the heart rate was 131/min. Crepitations were heard in both lungs and arterial pulses were weak in the left femoral artery, whereas distal pulses were non-palpable on PE. There was no motor deficit in the lower extremities. INR was measured as[1.8].

On the Color Doppler USG examination of the left lower extremity arterial system; there was hypoechoic thrombus image in left common femoral artery lumen and Color Doppler USG examination showed lack of any color filling (occlusion). Furthermore, there was no filling observed in the left superficial femoral artery, deep femoral artery, popliteal artery and trifurcation arteries with Color Doppler Ultrasound examination (secondary to proximal occlusion).

The patient was treated with CPAP (Continous Positive Airway Pressure) due to respiratory distress. The patient was intubated and mechanically ventilated since he did not respond to treatment and PCO_2 increased up to 60 mmHg. The patient was diagnosed with pneumonia and underwent the consultation of cardiology, cardiovascular surgery and infectious diseases departments. On the transthoracic echocardiography, EF was 30%. Empiric antibiotherapy including ceftriaxone 2x1 g and clarithromycin 2x500 mg was initiated by the

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infectious diseases specialist for pneumonia. The patient was hospitalized at the intensive care unit and underwent endarterectomy + thrombectomy. Treatment with pentoxiphylline and enoxaparine was continued. The patient could not be extubated due to lack of improvement in general clinical condition. Tracheostomy was performed on the 7th day of intensive care. The patient's i.v. fluid support and antibiotic treatment continued. The patient developed cardiac arrest on the 110th day of his intensive care unit, and was accepted as ex.

Although previous studies have shown that arterial thromboembolism worsens the prognosis without warfarin treatment, some other studies have also shown that emboli can improve without warfarin treatment[1,3,4].In addition to the comorbidities in our patient, we think that this case is important in showing that there may be embolic events in young patients.

In a study that investigated embolic events as a result of discontinuation of warfarin treatment given after myocardial infarction, thromboembolic events were observed in 7 of the 25 patients who had discontinued warfarin and in 2 of 22 patients who had continued to use warfarin. Six of these patients were hospitalized and treated with warfarin and heparin for 1 week, and the patients had recovered without any sequelae. It was shown that FIX and FVII increased rapidly after cessation of treatment and FII and FX increased in 1-2 weeks[1]. In our patient, the symptoms became evident 15 days after discontinuation of drug use. This showed that the development of thromboembolic events is proportional to the increase in coagulation factors.

Moreover, it is known that diabetes mellitus is associated with the increased risk of thromboembolism. Poor glycemic control is associated with thrombin and platelet activation[1,5]. Although our patient was diabetic, he had been using oral anti-diabetic drugs irregularly. There was no change in serum glucose levels and hypoglycemia was not observed during hospitalization period. It should not be overlooked that a hypoglycemic attack may occur within the last 15 days in which warfarin was discontinued. During the follow-up, no cardiac or cerebral ischemic events were observed. Although there was no significant change in renal function tests, concomitant pneumonitis resulted in deterioration of the prognosis.

INR fluctuation may occur with many non-pharmacological factors such as vitamin K-rich food consumption, chronic alcohol consumption, decreased oral intake, malignancy, and concomitant use of acetaminophen[2,6].

The debate on the use of warfarin and the discontinuation of long-term use is ongoing, but the role of clinicians is to inform patients and their relatives in detail about the benefits of drug use and the risks of premature discontinuation. The initiation and discontinuation of the drug should be according to the physician's recommendation. Regular follow-up visits should not be skipped.

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