

Rivaroxaban as long term therapy of recurrent venous thromboembolism complicated with repeated skin necrosis

Riwaroksaban w leczeniu przewlekłym nawrotowej żyłnej choroby zakrzepowo-zatorowej powikłanej nawracającą martwicą skóry

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A 41-year-old woman with significant protein C deficiency (60%), antiphospholipid syndrome and recurrent venous thromboembolism (VTE), had experienced the first episode of lower limb deep vein thrombosis ten years previously. Subsequently, she suffered four VTE recurrences, including acute pulmonary embolism during pregnancy. She was successfully treated with a body weight-adjusted full dose of enoxaparin sc. In view of the potential lifelong anticoagulation, and significant subcutaneous haematomas at the injection sites after several years of anticoagulation with low molecular weight heparin sc, the patient was successfully switched to warfarin with more than a one month overlap period. She was advised to continue vitamin K antagonist (AVK) with a target international normalised ratio (INR) of 2.0–3.0. Approximately one year later, she was readmitted due to painful necrotic skin lesions of the buttock and left breast. They resolved completely after an unfractionated heparin injection followed by an intravenous infusion. Anticoagulation with warfarin was ceased and the patient was treated with nadroparin. However, she refused long term anticoagulation with subcutaneous drugs and was treated with warfarin instead, with a target INR of 3.0–3.5. Last year, she was admitted to our department once again because of recurrent episodes of necrotic skin lesions in the area over the right ilium (Fig. 1). On admission, INR was 1.8 because, by mistake, she had stopped taking warfarin two days earlier. We immediately ceased warfarin and administered unfractionated heparin in a bolus injection of 10,000 IU, continuing with an aPTT-adjusted infusion. Pending the complete regression of changes, low molecular weight heparin in a therapeutic dosage was recommended. After full regression of the skin lesions, we initiated treatment with rivaroxaban at 20 mg once a day. However, on the second day before scheduled dose of rivaroxaban we observed slight skin changes (Fig. 2), which disappeared spontaneously in a few hours after rivaroxaban administration. Therefore we established treatment with rivaroxaban at 15 mg twice a day. She was followed up for six months without any further complications, then we recommended 20 mg once a day. Skin necrosis during AVK treatment is a very rare complication and is usually associated with protein C deficiency, protein S deficiency or antiphospholipid syndrome. Initially, the skin becomes painful, erythematous and indurated, then skin necrosis develops due to thrombosis of subcutaneous venules. The lesions usually occur in the fatty areas of middle-aged women who have accidentally omitted the drug. They require an urgent bolus of unfractionated heparin followed by UFH infusion with an aPTT-adjusted dose or low molecular weight heparin in a therapeutic dosage. The reinstatement of AVK should be started with very low doses with simultaneous heparin anticoagulation. Rivaroxaban is a selective, direct factor Xa inhibitor. It seems to be useful in the chronic anticoagulant treatment of patients with protein C deficiency and recurrent venous thromboembolism, because it does not decrease this protein level. To the best of our knowledge, this is the first case of an effective treatment of a patient with protein C deficiency and antiphospholipid syndrome with rivaroxaban.



Figure 1. Necrotic skin lesions in the area over the right ilium in patient with significant protein C deficiency and antiphospholipid syndrome



Figure 2. Slight skin changes in the same patient during treatment

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