

Rebleeding In Central Nervous System after Use of Rivaroxaban for Treatment of Deep Venous Thrombosis in a Patient with Cerebral Vasculitis

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Abstract

Introduction: Rivaroxaban is a direct, specific inhibitor of Factor Xa, which targets Factor Xa and Factor Xa free and coagulated in the prothrombinase complex.

Objective: To report a case of CNS rebleeding after using Rivaroxaban for treatment of DVT.

Methodology: Information was obtained in medical records, interview with the patient and literature review based on the diagnosis confirmed by imaging and laboratory tests.

Case Report: Patient, female, 45 years, admitted to a neurological ICU, transferred from another hospital under mechanical ventilation due to lowering of consciousness level, headache and hemiparesis. Brain MRI and angiography MRI showed acute ischemia and hemorrhages in different territories, with vascular stenosis, compatible with cerebral vasculitis. Pulse steroid therapy with methylprednisolone was performed for 3 days, with improvement of the condition. In 7 days patient was evolved with pain in limbs. Doppler ultrasound showed deep venous thrombosis. Rivaroxaban was started in a therapeutic dose. In 2 days, she started to lose consciousness level and left hemiplegia also appeared. Brain CT showing intraparenchymal hematoma on the right, being submitted to craniotomy for drainage of intracranial hematoma. After 9 days it evolved with low consciousness level again, CT showing subfalcine herniation with midline deviation and ventricular compression, being submitted to decompressive craniectomy and ICP monitoring. The patient evolved without presenting new thrombotic and hemorrhagic events, with stability, clinical improvement and maintenance of neurological status. In a new Doppler ultrasonography of limbs, there was no evidence of thrombus and signs of significant axillary-subclavian stenosis on the left arm. After 81 days of hospitalization, the patient was discharged from the ICU.

Conclusion: Despite increased safety in clinical trials with rivaroxaban, anticoagulant effects can not be measured as in coumarin, which leads to a therapeutic dilemma and shows the need for further comparative studies

Keywords: Rivaroxaban; Intracranial Hemorrhage; Cerebral Vasculitis; Deep Venous Thrombosis; Cerebral Vasculitis

Introduction

Rivaroxaban is a direct, specific inhibitor of Factor Xa, which targets Factor Xa and Factor Xa free and coagulated in the prothrombinase complex. In the literature, rivaroxaban is described as having several characteristics that benefit patients who needs anticoagulation. One of the most important particularity is the lowest risk of bleeding. In patients treated with Rivaroxaban, the rate of intracranial hemorrhage was lower than in those treated with coumarins (0.5% vs. 0.7%, p=0.02). It is not known if this advantage actually happens in clinical practice, since it has only been tested in clinical trials.

Objective

To report a case of CNS rebleeding after using Rivaroxaban for treatment of DVT.

Methodology

Information was obtained in medical records, interview with the patient and literature review based on the diagnosis confirmed by imaging and laboratory tests.

Case Report

Patient, female, 45 years, 68 kg, BMI: 27.24, admitted to a neurological ICU, transferred from another hospital under mechanical ventilation due to lowering of consciousness level, headache and hemiparesis. She was extubated and presented right hemiparesis with muscular strength level 4. Patient reported headaches and dizziness during 10 days that preceded this event. Brain CT showed hemorrhagic stroke. Brain MRI and Angio-MRI showed acute ischemia and hemorrhages in different territories, with vascular stenosis, compatible with cerebral vasculitis. Pulse steroid therapy with methylprednisolone was performed for 3 days, with improvement of the condition. Prednisone was started and rheumatologic tests were requested: Anti-SM, FAN, PANCA and C-ANCA negative. VDRL and HIV non-reactive, C3, C4 and CH-50 cells normal. Anti-cardiolipin non-reactive IgG, IgA and IgM. She was using prophylactic heparin when developed an abrupt fall in platelets on the sixth day, and its use was suspended. She tested positive for anti-heparin antibody. Mechanical prophylaxis was started for thrombosis, but in 7 days patient was evolved with pain in limbs. Doppler ultrasound showed in superior limbs: occlusive acute thrombus in internal jugular, subclavian, axillary, brachialis, cephalic, basilic and medial elbow veins. Occlusive acute thrombus in distal radial artery up to 10 cm above the wrist. In left arm, acute occlusive thrombus in the cephalic and median veins of the elbow. In addition to subcutaneous edema. RIVAROXABAN was started in a therapeutic dose. Before starting treatment, the patient had the following rates: creatinine: 0.8 mg/dL, Creatinine Clearance: 95.33 mL/min, Platelets: 75.000, TTPa: 30s, AP: 70%, Hemogram: Hb: 11.5 VCM: 90 Leuc: 19200 Neut: 16,896 (bw: 08%) Ldf: 1344, K: 5.3, Na: 136. In 2 days, she started to lose consciousness level and left hemiplegia also appeared. Brain CT showing intraparenchymal hematoma on the right, being submitted to craniotomy for drainage of intracranial hematoma. At the event, rates were: creatinine: 0.63 mg/dL, Creatinine Clearance: 121.05 mL/min, Platelets: 120.000, INR: 1.02, TTPa: 30s, AP: 98% Hb: 12.5 Leuco: 22900. Urea: 22, K: 4.8 and Na: 140. After 9 days it evolved with low consciousness level again, CT showing subfalcine herniation with midline deviation and ventricular compression, being submitted to decompressive craniectomy and ICP monitoring. After surgical intervention, CT control showed transcalvarian herniation, with no evidence of hydrocephalus or residual hematomas (Figure 1-4). The possibility of using Fondaparinux as a transition to warfarin due to thrombosis was raised, but it was decided not to, because of the risk of further bleeding. Patient was submitted to placement of a vena cava filter, as prophylaxis and treatment. New brain CT presented no signs of worsening and discreet dilation of the lateral ventricles. The patient evolved without presenting new thrombotic and hemorrhagic events, with stability, clinical improvement and maintenance of neurological status. In a new Doppler ultrasonography of limbs, there was no evidence of thrombus and signs of significant axillary-subclavian stenosis on the left arm. After 81 days of hospitalization, the patient was discharged from the ICU.

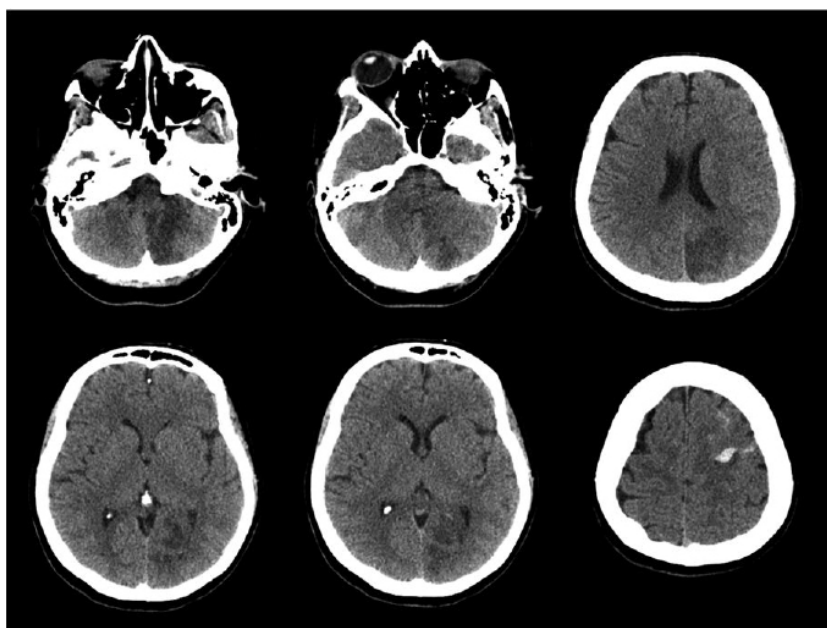


Figure 1: Computed tomography images without contrast of encephalus performed on the day of patient admission in the hospital, evidencing areas of hypoattenuating compromising the inferomedial portion of the left cerebellar hemisphere and the medial portion of the left occipital lobe, relates to subacute ischemic vascular injury. In addition to an intraparenchymal hemorrhagic focus in the left frontal gyrus (measuring 1.6 x 1.4 x 0.8 cm) associated with mild subarachnoid hemorrhage

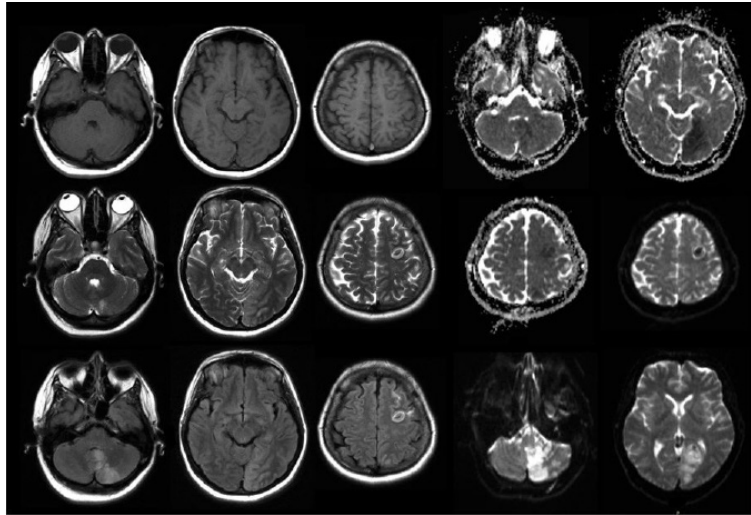


Figure 2: Nuclear magnetic resonance imaging performed on the 2nd day of hospitalization showing acute ischemic infarcts affecting the irrigation territory of the vertebra-basilar system involving the occipital lobes, larger left, left cerebellar hemisphere and left posterolateral bulbar region. Small acute lacunar infarction affecting left caudate nucleus head. Left frontal cortical-subcortical acute parenchymal hemorrhage, with mild subarachnoid haemorrhage associated



Figure 3: Images of Nuclear magnetic resonance angiography performed on the 2nd day of hospitalization showing tapering and irregularity of the left vertebral artery, with associated parietal thickening, being suggestive of vasculitis

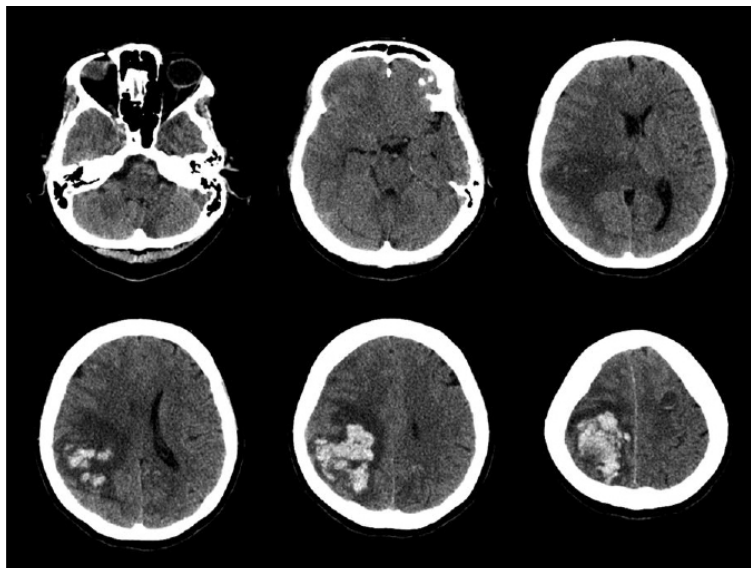


Figure 4: Computed tomography images without contrast of brain performed on the day of rebleeding after the use of Rivaroxaban for the treatment of deep venous thrombosis showing an area of heterogeneous intraparenchymal hemorrhage with irregular contours measuring about 5.5 x 4.4 x 4.0 cm, associated with vasogenic edema, located in the right parietal and frontal lobes

Conclusion

There is no specific antidote currently available for rivaroxaban for use in emergency situations, as with other direct oral anticoagulants. There have been reports of cases with severe intracranial hemorrhages associated with rivaroxaban in elderly patients with impaired renal function. Despite increased safety in clinical trials with rivaroxaban, anticoagulant effects cannot be measured as in coumarin, which leads to a therapeutic dilemma and shows the need for further comparative studies.

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