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# Rivaroxaban-induced acute pancreatitis

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## ABSTRACT

Rivaroxaban is a direct factor Xa inhibitor and has been safely used since 2008. It is used for the detection of atrial fibrillation and venous thromboembolism. Pancreatitis is one of the rare but dangerous side effects of rivaroxaban. The case of a 53-year-old female patient that developed in the third month of drug usage was evaluated, and it was confirmed after a full analysis was conducted that excluded all other factors, such as biliary calculus, alcohol usage, hypertriglyceridemia, biochemical parameters, ultrasonography and computed tomography that the patient's condition was caused by the use of Rivaroxaban. The aim of this case presentation is to indicate that awareness should be increased regarding the risks of using the drug Rivaroxaban, as it could lead to drug-induced pancreatitis, even though this is rare.

**Keywords:** drug-induced pancreatitis, rivaroxaban, drug safety

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Acute pancreatitis is an important disease that can cause morbidity. Approximately 80% of cases progress mildly, while severe pancreatitis is seen in 20% of cases. The most frequent causes are biliary calculus and alcohol, followed byhypertriglyceridemia and drugs [1]. Approximately 4%-5.3% of the condition is drug-induced pancreatitis and they generally progress in a mild form. It is argued that drugs may be a direct cause of pancreatitis by the way of idiosyncratic, direct toxic or angioedema [2].

Rivaroxaban direct factor Xa inhibitor began to be used in 2008 after it was approved by the FDA. It is used for atrial fibrillation, seizure prophylaxis and venous thromboembolic prophylaxis. According to FDA reports, 81,217 side effects were reported since its inception, of which 81 of these side effects were pancreatitis. Furthermore, 60.87% of the cases that developed pancreatitis showed symptoms of the disease in the first month, while 21.74% occurred between the first and sixth month of usage. A total of 49.3% of the patients were female and 50.7% were male. More than 50% of the patients were over the age of 60 [3].

## CASE PRESENTATION

A 53-year-old female patient consulted the emergency service complaining of painthat had started suddenly after eating and had spread to the rear of the epigastric region. In her physical examination, sensitivity in the epigastric area and rebound were present. In her laboratory tests, the alanine aminotransferase, aspartate aminotransferase, gamma

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glutamyl transferase, bilirubin levels were all normal. Amylase was observed at 3,000 mg/dl. Kidney functions were normal. Gall bladder and biliary tracts were observed to be normal in the ultrasonography of the patient that was suspected of having pancreatitis. Oedematous pancreatitis findings were present in the contrast enhancement computed tomography (CT), while the gall bladder and biliary tracts had normal appearance (Figure 1). The patient had no history of alcohol or smoking. Triglyceride and calcium levels were normal. She had no abdominal trauma history. The patient had no suggestion of autoimmunity in either her family history or clinical findings. It was determined that she had been taking metoprolol 25 mg once per day for valvular heart disease for approximately 5 years, cytolopram 5 mg per day for anxiety disorder and had started to take 20 mg/a day of Rivaroxaban for paroxysmal atrial fibrillation diagnosis 3 months prior to the onset of the symptoms. Based on the existing findings, it was thought that she had acute pancreatitis. There were no biliary calculus findings in ultrasonography and CT scan, the gall bladder and biliary tracts were normal, no herbal medication had been consumed, there had been no alcohol use and the normal triglyceride level Indicated a high likelihood that the patient had drug-induced pancreatitis. As the patient had used metoprolol and cytolapram for 5 years with no symptoms of pancreatitis during this timeand had then started using Rivaroxaban 3 months prior to experiencing pain, this suggested that pancreatitis was associated with theRivaroxaban. The oral intake and current medications of the patient were stopped, and appropriate fluid replacement and analgesia was performed. Anticoagulation was provided with LMAH. On the third day of treatment, the patient had no pain complaints and oral intake started. On the fifth day, metopropol and cytolapram treatment started again. In accordance with the cardiology consultation, Apixaban 2×5 mg treatment started for the patient instead of Rivaroxaban. No complications developed and no further complaints were reported by the patient.

## DISCUSSION

Rivaroxaban is an anticoagulant that has been safely used and is being increasingly utilised. According to FDA data, 81,271 patients experienced side effects to date and of these, only 81 experienced Acute Pancreatitis [2]. This is the 82nd case that was reported and the first in 2017. Drug-induced

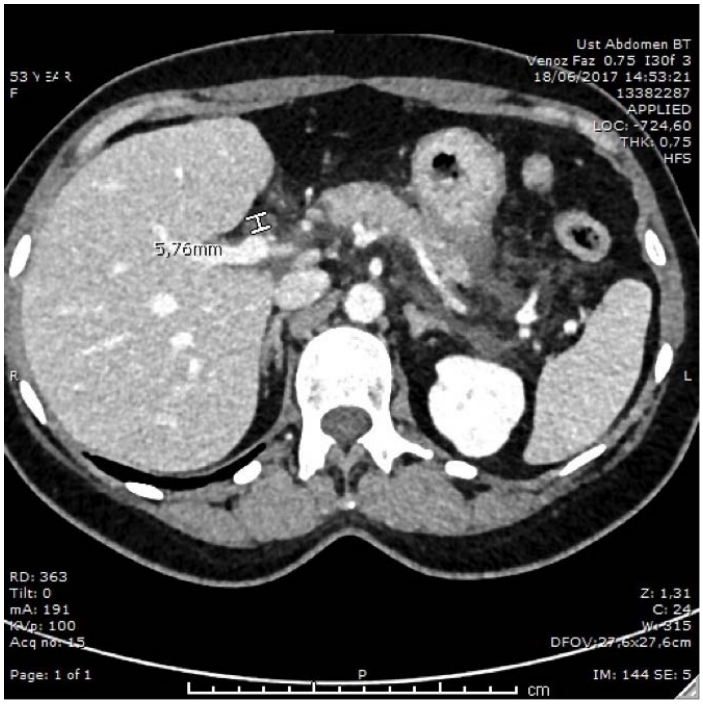


**Figure 1.** Abdominal computered tomography

pancreatitis is generally diagnosed according to four criteria: a) Pancreatitis development while using medication; b) Recovery of the patient by stopping the medication; c) Repetition of complaints by repeating usage of the medication; d) Exclusion of other pancreatitis causes [4, 5]. In this case, the symptoms developed while the patient was using the medication and complaints reduced when the patient stopped the medication; therefore, all other possibilities were excluded and the medication was not given again [4, 5]. Because the patient required the use of an anticoagulant, Apixaban treatment was started and there were no complaints or findings that would suggest pancreatitis in the follow-up. We started abixaban because it will provide enough anticoagulant effect and currently noabixaban induced pancreatitis reported yet. Pancreatitis conditions were light while under medication and the patient's complaints were rectified with supportive care by the fifth day and the patient was subsequently discharged. Drug-induced pancreatitis incidence has been reported in only 5.3% of patients with pancreatitis, although it is difficult to confirm this, as many patients do not provide honest answers on questionnaires [1]. In this case, it was evaluated that it was highly likely that the pancreatitis was related to Rivaroxaban as a idiosyncratic reaction. Because other reasons were excluded after proper examinations and the patient had not consumed alcohol and had no history of smoking, autoimmunity, hypercalcaemia history, herbal medication usage and had started to use Rivaroxaban recently. In the declared rivaroxaban related pancreatitis cases until today, 60.87% were observed to develop in the first month and 21.74% within 1-6 months. In the present case, pancreatitis developed in the third month.

## CONCLUSION

In the drug-induced pancreatitis etiology, Rivaroxaban should be considered to be one of the causative factors and treatment should include stopping the medication. If anticoagulation is necessary, the other new oral anticoagulants like apixaban or dabigatran may be used during the treatment period however, they may cause pancreatitis.

*Informed consent*

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

*Conflict of interest*

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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