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Spontaneous rectal sheath bleed while on DOAC anticoagulation

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SUMMARY

A man in his 80s was transferred from his nursing home residence with sudden onset right-sided abdominal pain. The nursing home staff reported that he was walking to the bathroom when he became diaphoretic, reported he was feeling unwell, then sat on the ground and was reluctant to move. Past medical history was significant for longstanding atrial fibrillation for which he was taking apixaban 2.5 mg twice daily. A CT scan of the abdomen and pelvis was performed which showed a 21×11 cm rectus sheath haematoma on the right extending into the lumbar region. Surgical review advised no invasive intervention. Two units of red cell concentrate were transfused and he was monitored for 5 days before being transferred back to the nursing home.

BACKGROUND

For the past decade, direct oral anticoagulants (DOACs) have provided a convenient, efficacious and safe alternative to vitamin K antagonists. The prevalent choice in many cardiovascular conditions, the role of DOACs has been expanding since their approval in 2010. With few drug–drug interactions, a rapid onset of action, a relatively short half-life and no regular monitoring requirement, DOACs are an attractive choice in preventing thrombotic events.[1 2] Four DOACs are currently licensed and in common use in modern practice: apixaban, dabigatran, edoxaban and rivaroxaban. However, as with all anticoagulant therapy, they have a not insignificant risk of bleeding, both provoked and spontaneous.[3–5] While reversal agents such as idarucizumab and, more recentl,y andexanet alfa have been licensed for reversal of DOAC anticoagulation, the short half-life of these agents means that only a conservative approach is often indicated.[6] While risk stratification tools such as HAS-BLED[7] and HEMORR$_2$HAGES[8] have been developed, the decision to start anticoagulation will still require clinical judgement. We report a case of spontaneous moderate bleeding in a patient on DOAC therapy who was treated conservatively.

CASE PRESENTATION

A man in his 80s was transferred from his nursing home residence to the emergency department with moderately severe right-sided abdominal pain. The patient reported no fever, loss of appetite, nausea or vomiting. The pain was colicky in nature, confined to the right side of his abdomen and did not radiate. The nursing home staff reported that he had a longstanding history of constipation but had passed a small amount of hard stool the previous night and was passing flatus regularly. The staff reported no history of trauma and noted that he was walking to the bathroom when he became increasingly diaphoretic and notified a caregiver that he felt unwell. He then sat on the floor. There was no loss of consciousness, presyncopal symptoms or loss of power in his lower limbs. On examination his blood pressure was 103/62 mmHg, heart rate 56 bpm, oxygen saturation 95% breathing room air and respiratory rate 18/min. His abdomen was visibly distended and tender in the right hypochondriac, lumbar and iliac fossa regions with a palpable mass in the same area. Examination was otherwise unremarkable.

Relevant past medical history included moderate cognitive impairment from Alzheimer's disease, heart failure from ischaemic heart disease (ejection fraction 20–29%), coronary artery bypass graft and atrial fibrillation, for which he had been started treatment with apixaban 4 years previously.

INVESTIGATIONS

A CT scan of the abdomen and pelvis was performed which showed a 21×11 cm rectus sheath haematoma extending to the lumbar region (figures 1–3). No clear major artery was identified as the source of the bleed. On admission the haemoglobin concentration was 9.1 g/dL. Haemaglobin measured 1 year previously during an admission for decompensated heart failure was 12.2 g/dL. Coagulation studies showed an international normalised ratio of 1.2, prothrombin time of 16.5 s and an activated partial thromboplastin time of 26.6 s. Creatinine was raised at 158 µmol/L and the estimated glomerular filtration rate (eGFR) was 35 mL/min. His eGFR had been steadily declining from his first contact with the hospital in 2016 and was felt to be related to his heart failure. The neutrophil count was mildly raised at 11.21×10^9/L and C-reactive protein was 6.5 mg/L. A full blood count, renal profile and liver chemistry were otherwise within normal limits.

TREATMENT

The patient was reviewed by the general surgical team on call who advised no surgical intervention at that time. The apixaban was held and his vital signs and haemoglobin concentration were monitored at regular intervals. After 24 hours, his haemoglobin had fallen to 7.7 g/dL and he was subsequently transfused with 2 units of red cell concentrate, after which the haemoglobin returned to 8.7 g/dL. His vital signs remained stable throughout the admission. It is notable that the pulse rate may have been lowered by his beta-blocker therapy. On the third

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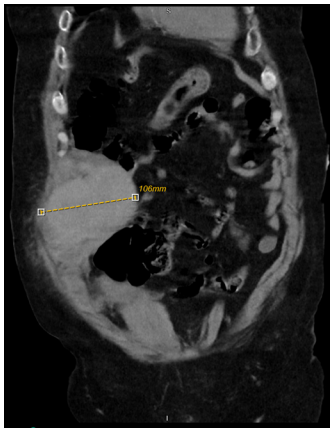

Figure 1 Anteroposterior CT scan coronal view, slice 19/63.

day of admission the medical team noted extensive ecchymosis on the posterior right abdomen (figure 4). His haemoglobin concentration did not fall significantly during the rest of the admission.

OUTCOME AND FOLLOW-UP

The patient was monitored in hospital for 5 days, after which he was considered fit for discharge back to the nursing home. His anticoagulation was held pending review of the haematoma in 6 weeks, and the thrombotic and bleeding risks were explained

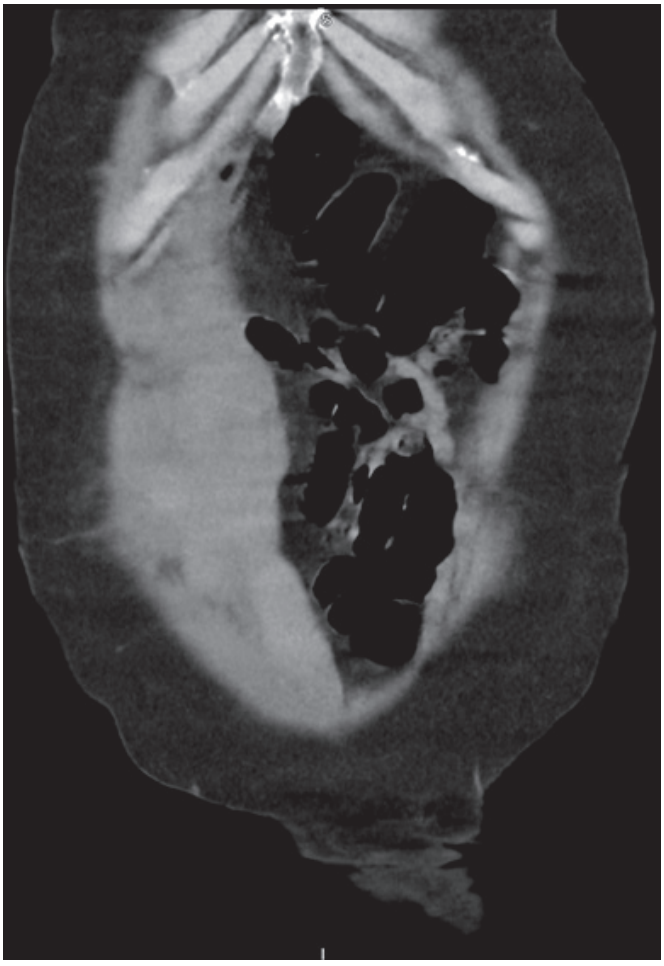

Figure 2 Anteroposterior CT scan coronal view, slice 15/63.

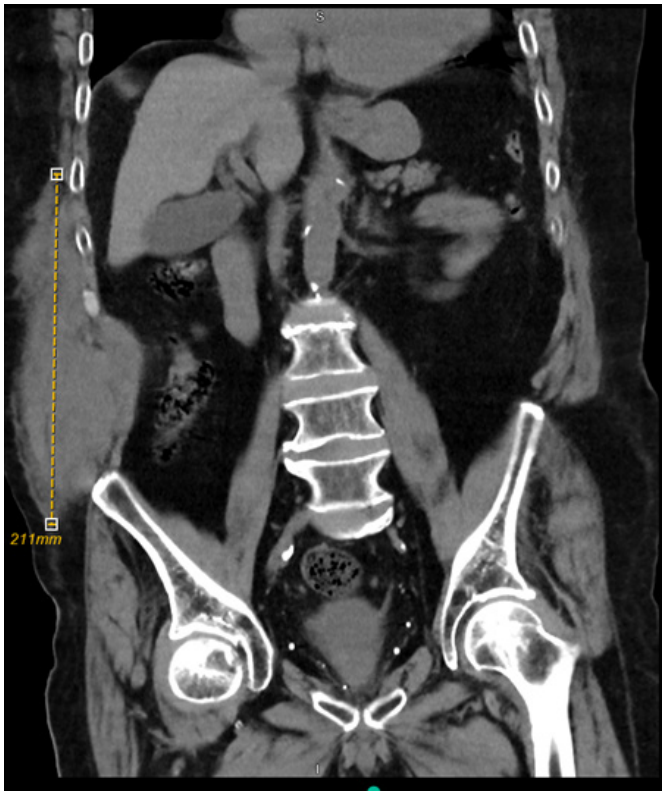

Figure 3 Anteroposterior CT scan coronal view, slice 34/63.

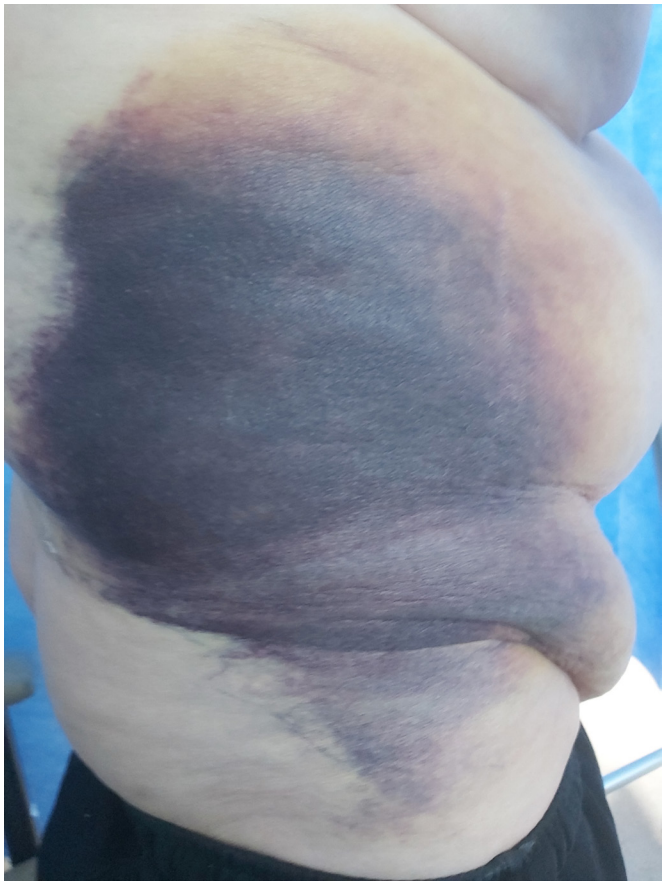

Figure 4 Photograph of ecchymosis on admission day 3.

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to the patient and his next of kin. He was booked for a repeat full blood count 1 week later.

DISCUSSION

DOACs are becoming increasingly prescribed. According to the American Agency for Healthcare Research and Quality, apixaban was the 48th most commonly prescribed drug in 2020, higher than both warfarin and rivaroxaban.[9] They have been shown to be more efficacious, better tolerated and safer than previous anticoagulants in the treatment of venous thromboembolism and prevention of stroke.[10–12] They have a rapid onset of action, short half-life, do not require monitoring, and have fewer drug and dietary interactions than vitamin K antagonists. New antidotes for the reversal of acute major bleeding continue to be developed,[13] further mitigating the risk of severe complications. As their prevalence continues to grow, so does the incidence of their uncommon but significant adverse effects.

Despite their favourable safety profile when compared with vitamin K antagonists, the risk of haemorrhage is nevertheless increased in prolonged anticoagulation, particularly in those with comorbid renal failure, liver failure, malignancies or thrombocytopenia. Bleeding is the most common adverse effect of DOAC therapy, including an increased risk of major gastrointestinal bleeding,[14] intracerebral haemorrhage[15] clinically relevant non-major bleeding,[16] as well as possibly increasing the risk when used in patients with trauma with pre-injury.[17] A number of incidents of serious bleeds have been reported, many with no history of trauma.[18–20] Spontaneous internal bleeding is difficult to diagnose quickly given its lack of signs and symptoms until the bleed has progressed significantly. Management of DOAC-induced haemorrhage can also be challenging as conventional methods including vitamin K and prothrombin complex concentrate may not be effective and the reversal agents are expensive and often not readily available. Immediate cessation of the offending agent and concurrent antiplatelet agents together with supportive care is often recommended in non-life-threatening bleeds. In the case of minor bleeds such as epistaxis, it may be appropriate to continue treatment if the risk of thrombosis outweighs any clinical benefit of withholding the DOAC.

Following resolution of the bleeding, the decision as to whether and when to restart anticoagulation can be challenging and is often complicated by the presence of extensive comorbidities, the degree of stroke risk, circumstances around the initial bleed and patient preference. Generally, it is reasonable to restart DOAC therapy 1–2 weeks after most mild to moderate gastrointestinal bleeding.[21] The American Stroke Association recommends an interval of at least 4 weeks before restarting treatment after spontaneous intracerebral haemorrhage,[22] but no definitive guidelines have currently been agreed for situations such as the one discussed here. Given the potential for life-threatening complications with both under- and over-treatment, the decision is often difficult.

With the expanding role of DOAC therapy in modern practice, clinicians should be cognisant of the potential risks that accompany what is often a prolonged course of anticoagulation, particularly in patients with multiple comorbidities. Reversal agents are licensed and effective but are also costly and may be prothrombotic.[23] Prompt recognition and early intervention can sometimes greatly improve outcomes. Supportive care only is indicated if a bleed is minor. Finally, whether and when it is appropriate to restart anticoagulation is a challenging decision with the potential for profound consequences. Further research is needed in order to construct substantive guidelines.

Learning points

- The incidence of adverse effects is lower with DOAC therapy than with vitamin K antagonists. However, the increased risk of haemorrhage—both provoked and spontaneous—is still present.
- While reversal agents are licensed for DOAC therapy, a supportive approach may be appropriate.
- The decision as to whether anticoagulation is appropriate should be reviewed on a regular basis as the patient's clinical condition changes.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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