The British Student Doctor, 2019;3(1):51-56
doi: 10.18573/bsdj.33
Education

The radiology of the complications of Warfarin therapy - a pictorial review

EDUCATION

AUTHOR

Matthew Renwick
Swansea University School of Medicine

Address for Correspondence:

Matthew Renwick
Swansea University Medical School, Grove Building, Swansea University, Singleton Park, Swansea, SA2 8PP

Email: 820094@swansea.ac.uk

No conflicts of interest to declare

Accepted for Publication:
08.10.2018

ABSTRACT

Summary

This article aims to teach about the complications of warfarin therapy through radiological imaging and highlight the importance of radiology in diagnosing challenging cases.

Relevance

Warfarin is the most widely used anticoagulant worldwide and is vital in the treatment of many conditions. However, the use of warfarin increases one's risk of bleeding which can have potentially fatal consequences. It is vital that the complications of warfarin use are considered as part of the differential diagnosis when a patient presents with unexplained symptoms, as quickly diagnosing an acute bleed will improve outcomes.

Take Home Messages

Complications of warfarin therapy can present in a variety of ways, not always associated with trauma, with potentially dangerous consequences. Radiological investigations are one of the best ways to confirm the diagnosis and so should always be considered to aid diagnosis and treatment.

INTRODUCTION

Warfarin is the most widely used oral anticoagulant in the world. (1) In the UK alone, it is thought that around 1% of the total population and 8% of those over 80 are taking warfarin. (2) Originally developed as a rat poison, it is now recommended by the National Institute for Health and Care Excellence (NICE) in the treatment of conditions such as atrial fibrillation (AF), deep vein thrombosis (DVT) and stroke prophylaxis. More rarely, it is given to those who have had a myocardial infarction. (3-6) These conditions primarily affect the elderly population and with the average age increasing in the UK, anticoagulant use is likely to increase.

Warfarin blocks vitamin K reductase which normally activates vitamin K and, consequently, the clotting ability of factors II, VII, IX and X are reduced. (7) It usually takes a few days, depending on the patient's physiology, for warfarin to start having a therapeutic effect, therefore concurrent heparin therapy is needed until warfarin is effective. Warfarin has a narrow therapeutic range and, once started on warfarin, the patient must be closely monitored to ensure the dose is correct. Too low and the patient will be at risk of blood clots forming, too high and the patient is at risk of bleeding complications. (8) Monitoring is done via regular blood testing measuring the patient's international normalised ratio (INR). Due to warfarin's therapeutic range and differing physiology between patients it can be difficult to get a patient stabilised on a regular dose. Indeed, one study of over 6000 patients taking warfarin for AF showed that for nearly 50% of the time, the INR was outside the target range. (9) Warfarin has many potential drug interactions which can destabilise the INR (e.g. alcohol can increase the INR putting the patient at risk of bleeding).

A major drawback with warfarin therapy is its side effects, including the increased risk of bleeding. These bleeds can range from something as insignificant as a simple cut on the hand taking longer to clot to an uncontrollable, potentially fatal, haemorrhage in the brain. In terms of hospital admissions related to drug therapy, warfarin ranks 3rd on the list, with the clear majority of these admissions being due to a bleeding event. (10)

One of the issues with warfarin related bleeding is that it may be of insidious onset, or not immediately apparent that bleeding is the cause of the patient's symptoms, and it can also mimic other conditions. In these cases, after taking a full history and examination, further investigation is needed including radiological input. It is often here that the bleeding is identified or confirmed. Other rare but serious complications of warfarin treatment such as osteoporosis or calcification of blood vessels may also be identified by radiological investigation.

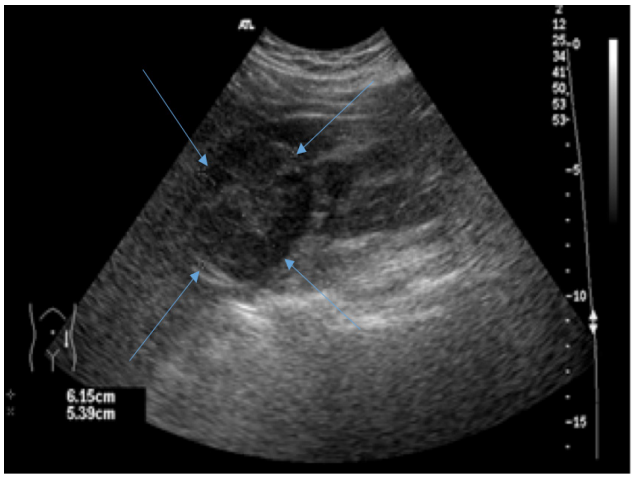
This review will demonstrate warfarin related haemorrhage in all parts of the body using different imaging modalities, and it will demonstrate how some difficulties in clinical diagnosis were aided by radiological investigation.

Cases – Diagnostic Challenges

The first section of this pictorial review will focus on those cases which presented a diagnostic challenge and the diagnosis was assisted greatly with radiological investigation. The first three images are all from different patients. However, all had a similar presentation.

Image one shows an example of a haematoma located in the psoas muscle. The patient presented with an acutely painful abdomen. The pain had started acutely that day and had been growing worse in severity. The patient was otherwise well and had no other symptoms. On examination the abdomen was soft but tender in the left flank, particularly when balloting for the kidneys, and rectal examination was normal. Acute abdomen has a broad differential diagnosis. Infection, bowel or ureteric obstruction, renal stones and ectopic pregnancy must all be considered. However, the patient was not of child bearing age, had no urinary or bowel symptoms and had been otherwise well making these causes less likely and further investigation was needed.

Figure 1 - Left psoas haematoma



An abdominal radiograph did not show any acute pathology, so an ultrasound was requested, given the tenderness over the left kidney. The bleed was spontaneous and difficult to diagnose through history and examination alone. In this case, it was only through using ultrasound that the cause and source of the pain could be identified.

Similar scenarios are shown in images two and three, with the patients suffering from an intramuscular bleed and presenting with

acute pain and no history of trauma. Ultrasound investigation was again needed in aiding diagnosis and treatment.

Figure 2 - Left sided retroperitoneal haematoma, possibly in psoas muscle

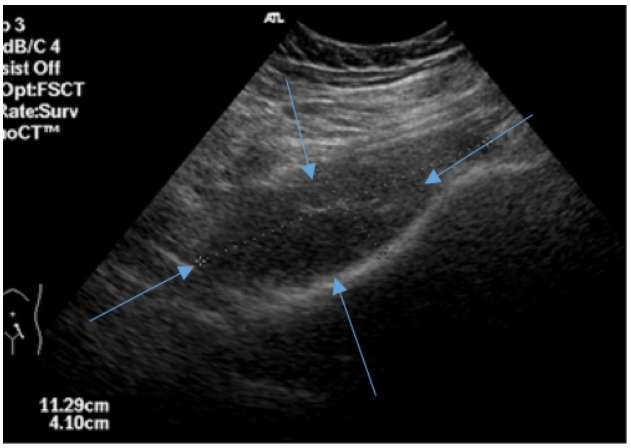
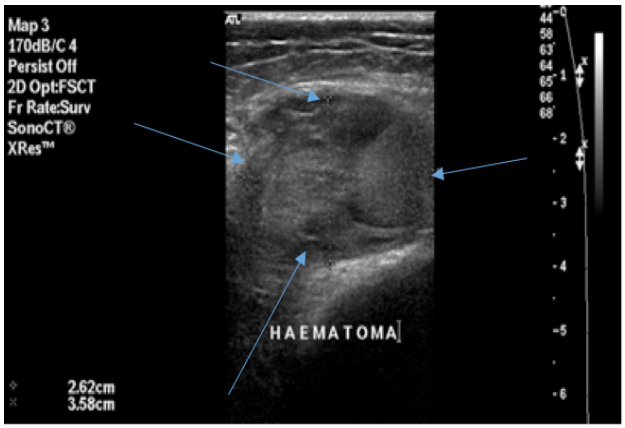


Figure 3 - Quadriceps haematoma



Both images four and five show examples of a spontaneous haemothorax in the absence of significant trauma. Both patients presented with gradually increasing breathlessness over several hours. Examination revealed reduced breath sounds and dullness to percussion of the affected areas. A pleural effusion was suspected, and a chest radiograph confirmed this but did not show a likely cause. CT thorax was requested which revealed a haemothorax. Chest drains were required in both cases.

Figure 4 - Chest wall haematoma with haemothorax. The denser area indicates a fresher bleed

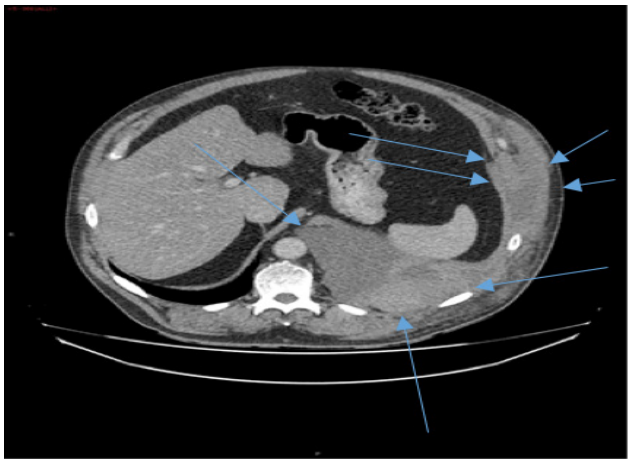


Figure 5 - Left sided haemothorax. In this case the denser area within the fluid is collapsed

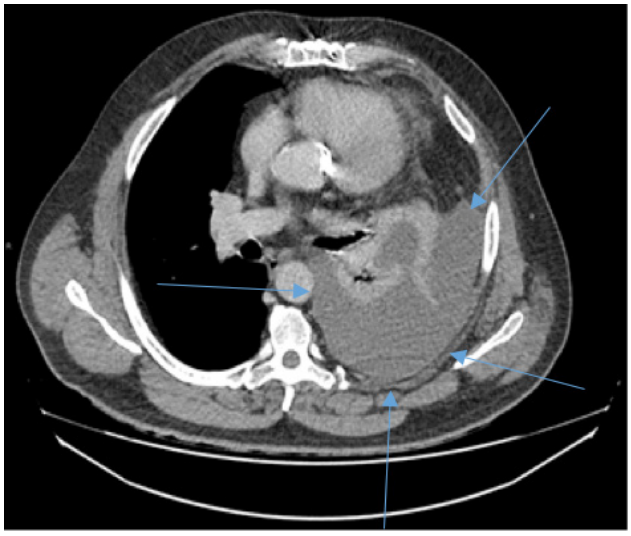


Image six shows a subtle subdural haemorrhage. The elderly patient presented with confusion which had been getting gradually worse over several days. This is a very non-specific yet common presentation.

Figure 6 - Subdural haemorrhage visible in the falx

Confusion in the in the elderly is often caused by infection (classically a urinary tract infection, UTI), dementia or injury to the brain such as a stroke or bleed.

The urine dipstick was negative, and the short duration of the symptoms made dementia unlikely. It is vital to always consider the possibility of a spontaneous bleed in the brain in patients on warfarin therapy, and CT head is needed to rule this out even in the absence of trauma. In this patient's case, the CT head revealed a small subdural haemorrhage in the falx. Due to its small size, treatment was conservative, and the patient recovered.

Cases- Fatalities and Emergencies

This section will focus on the more serious, life-threatening complications of warfarin therapy. In all cases, there was no history of a significant trauma.

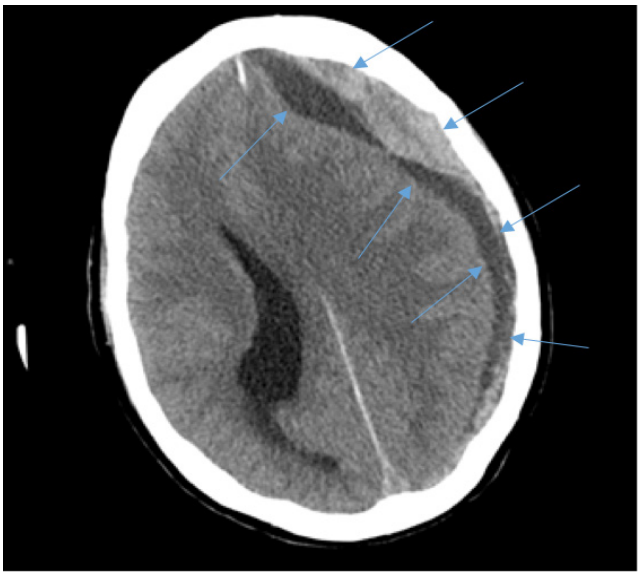
Image seven shows an acute left sided subdural haemorrhage. When a patient is on anticoagulant medication and presents with an acute drop in conscious level, intercranial haemorrhage must always be considered. Differential diagnosis in this case include infections such as meningitis or an ischaemic event. Due to their anticoagulation status the patient was sent for a CT head to enable a quick diagnosis.

Figure 7 - Subdural haemorrhage with fresh blood visible in the sylvian fissure

There is mass effect visible as a shift of the midline of the brain to the right is present, and there is blood visible in the sylvian fissure. In this case, the bleed is still in the acute stage and may resolve spontaneously, therefore depending on the condition of the patient treatment may be conservative.

Image eight shows an acute-on-chronic left sided subdural haemorrhage. The patient presented similarly to the patient in image seven, however, in this case there has been a long-term bleed, which is the low-density area between the brain and the skull, then on top of this there has been a fresh bleed which is the high-density area lying more superficially. If the rate of bleeding is slow, it is not uncommon for it to go unnoticed for a long time and only present when the patient acutely decompensates. Unfortunately, this is what happened in this case. A CT head showed that there is a huge mass effect visible and the loss of sulci suggests a very tight, oedematous brain. In this case, due to the swelling, the patient coned and did not survive.

Figure 8 - Acute on chronic subdural haemorrhage



Haemorrhage within the abdomen: Image nine shows a large haematoma with active haemorrhage in the liver which has ruptured into the peritoneum. The patient did not survive. Image ten shows a large retroperitoneal bleed in front of the aortic bifurcation, again fatal.

Figure 9 - Liver haematoma with retroperitoneal haemorrhage

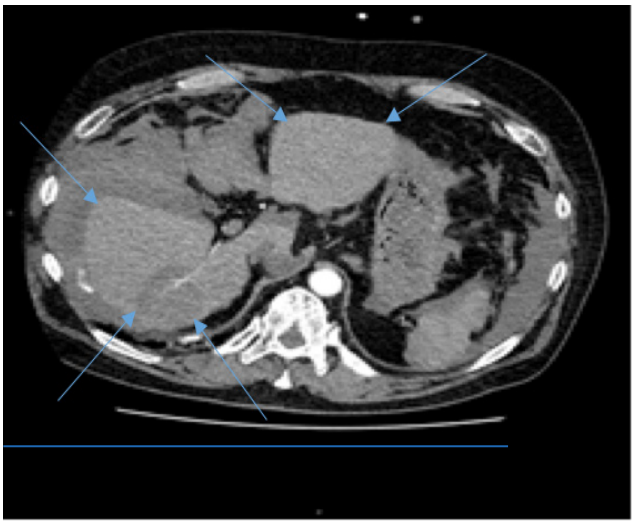
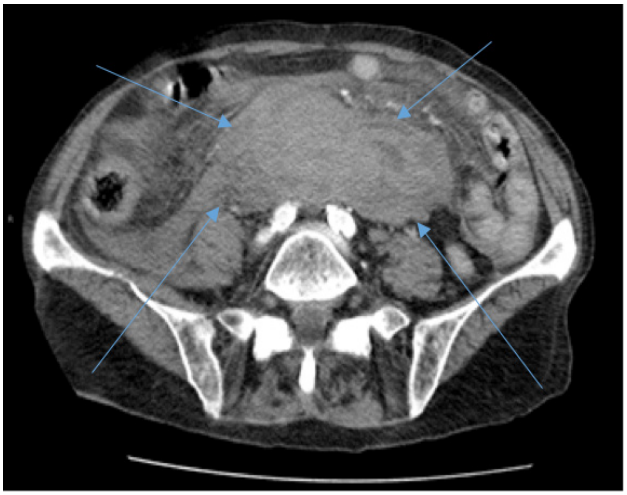


Figure 10 - Retroperitoneal haemorrhage



SUMMARY AND THE FUTURE

Warfarin has been an incredibly reliable and effective medication for the past fifty years. However, as has been previously discussed, the combination of constant monitoring and side effects means it has never been the perfect treatment. Direct oral anticoagulation (DOAC) drugs such as Rivaroxaban, Edoxaban and Dabigatran have all been shown to work as well as, if not better, than warfarin whilst having fewer side effects and no need for constant monitoring. (11-13) As time and medical research advances, warfarin may be coming to the end of its domination of anticoagulation.

This review aims to highlight the potential dangers of using warfarin. The images included are just examples of a larger number of cases which unfortunately are not uncommon in clinical practice.

Note: All the images in this report were taken at York Teaching Hospital in Scarborough. All identifying factors have been removed from the images to preserve patient confidentiality and were used with permission from the responsible consultant radiologist at the hospital. Further details such as warfarin dose and concurrent medications at the time were unavailable.

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Journal DOI
10.18573/issn.2514-3174

Issue DOI
10.18573/bsdj.v3i1

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