A complicated case of anticoagulation

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SUMMARY

In this case of complex anticoagulation, a 60-year-old woman was treated with low-molecular-weight heparin for pulmonary embolism. As a result of anticoagulation, she then developed an acute subdural haemorrhage identified on CT brain scan requiring craniectomy. Subsequently, while continuing anticoagulation for treatment for pulmonary embolism, she additionally had a large intra-abdominal bleed within and around the psoas muscle identified on abdominal CT scan. Although the increased risk of bleeding is known with anticoagulation therapy, the case of both an intracerebral and intra-abdominal bleed is rare. However, the case does highlight how each individual has a unique physiological response to anticoagulation, in some cases more severe than others.

BACKGROUND

This case was presented as it highlighted the real risk of bleeding with anticoagulation. In this patient's case her diagnosis of pulmonary embolism required treatment however, as a consequence of this suffered from two life-threatening events, an acute subdural haematoma and an intra-abdominal bleed. Therefore, not only should a risk benefit analysis of anticoagulation be considered prior to starting anticoagulation but also while being on anticoagulation therapy. Although the risks of bleeding are known while on anticoagulation, the incidence of both an intracerebral and intra-abdominal bleed while on anticoagulation is rare.

CASE PRESENTATION

A 60-year-old woman with a background of bipolar disorder requiring treatment with 10 mg olanzapine, was an inpatient in a psychiatric ward in a hospital. Of note, one of the known side effects of olanzapine, an atypical antipsychotic drug, is thrombocytopenia. During her admission, she developed urosepsis and her care was transferred to the medical team for further management and she was started on antibiotic therapy. A day later, she began to feel unwell, was hypoxic, tachycardic and felt short of breath. A d-dimer blood test was performed which was positive and a CT pulmonary angiogram was performed. This revealed pulmonary emboli in all pulmonary arteries and therefore, she was started on treatment dose enoxaparin for this at 0.5 mg/kg with a total dose of 120 mg being prescribed.

Two days after being started on enoxaparin, the patient became 'unresponsive' with a GCS of 4 of 15. This deterioration in GCS occurred after a 3 h period with a gradual drop in GCS from 13 to 4. An urgent CT brain scan was performed which showed a large acute on chronic subdural haematoma. There was significant mass effect and

effacement of the underlying sulci and right basal ventricle as well as midline shift and early contralateral hydrocephalus. These were new changes compared with a CT of the brain previously performed 2 years ago, which showed no significant abnormalities but did show small vessel disease consistent with the patient's age. The cause of this new acute subdural was not clear although being on anticoagulation therapy certainly contributed to this pathology. Her case was discussed with the neurosurgeons and she was accepted as a candidate for an urgent high-risk craniectomy despite the fact that she was anticoagulated for treatment of her pulmonary embolism. Prior to craniectomy she was given 50 mg of protamine to reverse the anticoagulation effect. Therefore, a right craniectomy and evacuation of the acute subdural haematoma was performed with burying of her bone flap in the abdominal wall. There were no significant intraoperative complications. Postoperatively she was transferred to neurointensive care where she was kept ventilated and sedated, requiring inotropic support. Her enoxaparin was withheld.

24 h post craniectomy, her sedation was withheld and subsequently for the next 5 days, she had a fluctuating GCS of between 6 and 10. On day post craniectomy, the haematology team were contacted for advice regarding anticoagulation treatment of her pulmonary emboli. The treatment plan suggested was that of an unfractionated heparin infusion maintaining an APTT ratio of 2–2.5. In view of her intracerebral bleed, she was not loaded with unfractionated heparin as an intravenous bolus injection but was started on 18 units/kg per hour, with a weight of 80 kg, this was 1.4 ml per h of 1000 units in a 1-ml concentration. After starting the infusion, her APTT was checked and showed her to be subtherapeutic with an APTT ratio of 1.2. Her infusion rate was therefore increased to 1.6 ml per h of 1000 units in a 1-ml concentration. Once she was started on this, her APTT was checked every 4 h and her platelets twice a day, and for the next 4 days her APTT ratio was maintained between 2 and 2.5 at this rate and her platelets were within normal limits.

Four days after the heparin infusion was started, there was again a drop in the patient's GCS. She no longer obeyed commands and had inappropriate speech. A CT brain scan was repeated which did not show any evidence of a new bleed but on examination the patient was noted to have abdominal distension. She was hypotensive and tachycardic and had a haemoglobin of 4 and a haematocrit of 0.14. This was a significant decrease in her admission haemoglobin which was 10.4 and her haematocrit which was 0.31. Her heparin infusion was stopped and she was resuscitated with 3 units of blood. Owing to poor respiratory effort, the patient was reintubated and a CT of chest,

To cite: Nathwani R. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007672

Figure 1 CT abdomen: 22×15×13 cm intra-abdominal haemorrhage.

abdomen and pelvis was arranged. As shown on her abdominal CT scan in figure 1, a large fluid collection within and lateral to the left psoas muscle area suggestive of a haemorrhage was found. This measured approximately 22×15×13 cm. The cause of her bleed was deemed secondary to anticoagulation for treatment of her pulmonary emboli despite maintaining a tight control in APTT ratio of between 2 and 2.5 and having normal clotting levels and a normal platelet count.

OUTCOME AND FOLLOW-UP

A repeat CT pulmonary angiogram was performed to elicit if there was still evidence of pulmonary emboli requiring anticoagulation. This was unremarkable showing normal calibre and patency of the pulmonary arterial tree with no evidence of pulmonary embolism. In view of these findings, anticoagulation was stopped and the patient's intra-abdominal haemorrhage was conservatively managed. Once extubated and stabilised off sedation, the patient was transferred to neuro-rehabilitation for continuing management.

DISCUSSION

Anticoagulation therapy is a common medical intervention and is the main form of treatment and prevention of venous thromboembolism. Bleeding is the main complication of anticoagulation even when therapeutic control is achieved. In the case of low-molecular-weight heparin products such as enoxaparin, approximately 60% of its anticoagulant effect can be reversed by protamine in the event of an acute bleed.¹ However, 40% of its anticoagulation effect still remains.

Meta-analysis of studies comparing the bleeding risk between low-molecular-weight heparin and unfractionated heparin

showed that there was no statistical difference in risk between unfractionated heparin use and low-molecular-weight heparin use for major bleeding (RR 0.63 (95% CI 0.37 to 1.05)) and minor bleeding (RR 1.18 (95% CI 0.87 to 1.61)). However, there was a statistically significant difference for risk of total mortality in favour of low-molecular-weight heparin use (RR 0.76 (95% CI 0.59 to 0.98)). These results are based on data taken from 13 studies.²

Two cases of retroperitoneal haematoma in elderly patients aged over 70 have been reported where two elderly men receiving 0.8 and 0.94 mg/kg of subcutaneous enoxaparin suffered retroperitoneal haematomas.³ However, no cases have been reported of intra-cerebral bleeding and intra-abdominal bleeding with low-molecular-weight heparin use as described in this case. Therefore, the addition of this case to the literature aims to highlight a possible risk of anticoagulation and unexplained decreases in haemoglobin levels.

Learning points

- ▶ Anticoagulation remains the main form of treatment for prevention and treatment of venous thromboembolism.
- ▶ Low-molecular-weight heparin use is associated with a reduced mortality risk compared with unfractionated heparin.
- ▶ 40% of the anticoagulation effect of low molecular weight remains despite reversal with protamine.
- ▶ An individual's physiological response to anticoagulation is unique.
- ▶ The risk and benefits of anticoagulation should not only be considered prior to starting treatment but also at regular intervals while receiving anticoagulation therapy.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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