CASE REPORT

Life-threatening haemorrhage in patients without pulmonary embolism who received anticoagulants

Huub van den Oever,¹ John W G M Schreurs,² Menno Huisman³¹Department of Intensive Care, Deventer Hospital, Deventer, The Netherlands²Department of Internal Medicine, University Medical Centre Groningen, Groningen, The Netherlands³Department of Haemostasis and Thrombosis, Leiden University, Leiden, The Netherlands**Correspondence to**

Dr Huub van den Oever, h.vandenoever@dz.nl

Accepted 15 November 2015

SUMMARY

Local and international guidelines recommend that anticoagulation should be initiated before diagnostic work up has been completed, in patients with high clinical probability of pulmonary embolism (PE). However, many patients receiving anticoagulants for suspected PE do not have this disease. We present three cases of life-threatening bleeding complications after treatment with low-molecular-weight heparins for suspected PE. A 35-year-old woman had acute chest pain and died of a ruptured thoracic aneurysm. A man with herpes encephalitis developed acute dyspnoea, and died of intracerebral haemorrhage. And a woman with mild chest trauma had a complicated recovery after life-threatening intrapleural haemorrhage. Neither of these patients had PE. These cases emphasise that delaying diagnostics may pose a risk in patients with acute chest symptoms. An early CT scan may avoid unnecessary anticoagulation in patients without PE, and may help to direct attention to the actual cause.

BACKGROUND

When pulmonary embolism (PE) is suspected, many patients are started on anticoagulant therapy before the diagnosis has been confirmed. The major complication of anticoagulation is bleeding.¹ When PE is confirmed, the expected benefit of anticoagulant treatment generally outweighs the risk. However, for a patient without PE, there is no benefit; hence only bleeding risk remains.

It might be expected that haemorrhagic complications following empiric PE treatment are common, but we found no reports of such cases in the literature.

In this report, three cases of life-threatening haemorrhage, following a single dose of low-molecular-weight heparin (LMWH) for suspected PE, in patients who did not have pulmonary emboli, are presented.

CASE PRESENTATION

Patient A, a 35-year-old woman, presented to our emergency ward around noon, with thoracic pain, dyspnoea and cough, which had started several days earlier and were progressive despite antibiotic therapy. Her blood pressure and pulse were normal, breathing was quiet and her oxygen saturation was 96%. Chest radiograph showed no abnormalities. Wells' score was 3 (no alternative diagnosis) and D-dimers were 1440 µg/L. She was admitted to the pulmonology ward and treated with 5700 IU nadroparin for suspected PE, while awaiting CT of the pulmonary arteries (CTPA).

One hour later, she was found gasping. When the resuscitation team arrived, she had sinus tachycardia with electromechanical dissociation. During cardiopulmonary resuscitation (CPR), 100 mg of alteplase was administered blindly, because of presumed massive PE. When spontaneous circulation did not return, CPR was stopped. At autopsy, a dissection of the thoracoabdominal aorta was found, starting at the aortic root, with blood in the pericardial and abdominal cavities. The pathologist noticed signs of Marfan syndrome, which was confirmed histologically. The cause of death was haemorrhagic shock with cardiac tamponade.

Patient B, a 63-year-old man, treated for myelodysplastic syndrome with lenalidomide, was admitted to the neurology ward, with herpes encephalitis, and treated with acyclovir. One week into treatment, he developed diplopia. An MRI scan of the brain showed an area with abnormal signal intensity and mass effect in the right hemisphere, which was interpreted as an encephalitic focus. There was no blood in the brain. The following night, he developed dyspnoea. The respiratory rate was 20 breaths/min, SpO₂ was 96% on room air, pulse was 80/min and blood pressure was 130/80 mm Hg. PE was suspected and physical examination and chest radiography did not support an alternative diagnosis. Because Wells' score was 4.5 (no alternative diagnosis and immobilisation), nadroparin 5700 IU was given subcutaneously, and CTPA was requested for the following day. Ten hours later, headache, restlessness, ataxia and dysarthria developed. CT scan of the brain showed intracerebral haemorrhage expanding into the ventricles. The patient lost consciousness and died of cerebral herniation. At autopsy, no pulmonary emboli were found.

Patient C, a 56-year-old woman with type 2 diabetes, hypertension and chronic obstructive pulmonary disease, arrived at our emergency department around midnight, with acute left-sided thoracic pain. Three weeks earlier, she had taken paracetamol for back pain subsequent to a fall, for which she had not sought medical attention. Her blood pressure was 150/103 mm Hg, pulse was 120/min and oxygenation was normal. Chest X-ray revealed a small subpulmonic effusion on the left side, and no rib fractures. The differential diagnosis included PE. Wells' score was 3 (tachycardia and immobilisation), but PE could not be ruled out because of elevated D-dimers. The patient was treated with 7600 IU nadroparin subcutaneously and admitted to pulmonology while awaiting CTPA. The next morning, she was admitted to the ICU with imminent

CrossMark

To cite: van den Oever H, Schreurs JWGM, Huisman M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211140

haemorrhagic shock. Her haemoglobin had dropped from 8.0 to 5.4 mmol/L. CTPA did not reveal PE, but did show left-sided rib fractures and haemothorax. The anticoagulants were antagonised with protamine and tranexamic acid, and a thoracic tube was placed. The clinical course was complicated by secondary infection of the pleura. The patient underwent thoracoscopic drainage followed by a prolonged surgical admission.

DISCUSSION

When PE is suspected, a clinical decision algorithm (Wells' score combined with a D-dimer test) is used to exclude PE. If one of the two elements is positive, PE cannot be ruled out, and further testing is required. At that point, only 30% of patients turn out to have PE.²

When CTPA cannot be obtained immediately, guidelines recommend empirical treatment with LMWH, while awaiting further testing (American College of Chest Physicians grade 2C).³ This recommendation is based on expert opinion, and lacks a high level of evidence, as no studies have addressed this question specifically.³ The cases reported expose two pitfalls of this approach.

First, even if the decision algorithm indicates that PE is likely, most patients do not have PE. Our cases illustrate that patients may have occult bleeding foci, especially in combination with elevated D-dimers. When such patients are exposed to anticoagulants, harm may be done.¹ Timely CTPA would have excluded PE in our patients, and no anticoagulants would have been given.

Second, the algorithm is a decision rule to increase pretest probability, and should not be seen as a diagnostic tool. When patients are admitted under a false working diagnosis of PE, the true cause of their symptoms may not be addressed appropriately, and may possibly deteriorate. From this perspective, it is easy to understand that as much as 20% of scans made for suspected PE yield an alternative diagnosis.² CT scan might have revealed the real diagnoses in our patients.

It is important that alternative diagnoses, including those that are also associated with increased risk of bleeding, such as trauma, pericarditis or intrathoracic neoplasms, are considered in the Wells' score in all cases of suspected PE, since they will lower the pretest probability of PE.⁴ Inclusion of alternative diagnoses will therefore increase the threshold to start anticoagulant treatment while awaiting additional imaging.

The cases presented here suggest that it has become common practice to start empirical treatment in some patients with suspected PE, even when radiological services would have been available. However, no formal investigation has ever shown that this is safe. Furthermore, there is no logic in implying that CT scanning can be comfortably postponed once LMWH has been given.

Patient's perspective

- ▶ We came to the hospital hoping to get better, not worse. When it was explained to me that blood thinners had contributed to my (...) death, I felt shocked, but still, we all know that every drug can have side effects, we need to accept that.
- ▶ When the specialist explained that, in hindsight, these blood thinners had been unnecessary, that they were given for a wrong, hypothetical reason, I mainly felt....confused. I still can't understand why this medicine was given. Nobody should be given dangerous drugs for no good reason, not even if it is protocol.

Learning points

- ▶ The bleeding risk associated with systemic anticoagulants given for pulmonary embolism (PE) is not negligible, and such bleeding may be life-threatening.
- ▶ When patients are treated with low-molecular-weight heparins on the basis of suspected PE, without first confirming the diagnosis, bleeding complications may occur. In this situation, harm may be done with no actual benefit.
- ▶ CT of the pulmonary arteries without delay should be considered when the clinical algorithm does not exclude PE, this may help to avoid anticoagulant treatment in patients without PE.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Schulman S, Beyth RJ, Kearon C, *et al.* American College of Chest Physicians. Hemorrhagic complications of anticoagulant and thrombolytic treatment: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133(6 Suppl):257S–98S.
- 2 van Belle A, Buller HR, Huisman MV, *et al.* Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 2006;295:172–9.
- 3 Kearon C, Akl EA, Comerota AJ, *et al.* Antithrombotic therapy for VTE disease: antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl):e419S–94S.
- 4 Testuz A, Le Gal G, Righini M, *et al.* Influence of specific alternative diagnoses on the probability of pulmonary embolism. *Thromb Haemost* 2006;95:958–62.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow