CASE REPORT

A case of panic to pulmonary embolism

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SUMMARY

Pulmonary embolism (PE) is a rare paediatric diagnosis, but its presence is likely to be underestimated due to the subtle and non-specific nature of its symptoms. Common clinical features of PE include shortness of breath, pleuritic chest pain and acute cardiovascular collapse. Less common symptoms can include persistent unexplained tachycardia, fever or deep vein thrombosis. Rarely do patients present with abdominal pain and self-resolving shortness of breath; symptoms our patient experienced. However, in contrast to popular belief, having normal vital signs does not necessarily lower the probability of PE. D-dimer, a specific fibrin degradation product, has a good negative predictive value for venous thromboembolism diagnosis but its use in children is less clear, with up to 40% of children with PE having a normal D-dimer level. CT pulmonary angiography remains the gold standard in diagnosis.

BACKGROUND

In children, the diagnosis of pulmonary embolism (PE), can be a major challenge due to the following reasons. First, paediatric venous thrombosis, particularly PE, is rare, with the estimated incidence at 0.07/10 000 children, which is lower than the 2–5% incidence reported in adults.¹ Second, a child's signs and symptoms are often non-specific and inconsistent, resulting in failure to even consider thrombosis as a differential diagnosis. At post-mortems, even when clinically significant embolisms have been found, only half of the patients had documented signs and symptoms, and of these in less than a third was PE considered a diagnosis.² This shows the importance of clinical suspicion, especially in high-risk patients. Further, laboratory investigations are often unhelpful and the gold standard for diagnosis of PE involves high doses of radiation.

This case report is written to illustrate this paediatric diagnostic challenge with the aim to make the reader consider PE in any child who has risk factors for thrombosis, to avoid delay in diagnosis in other cases.

CASE PRESENTATION

A 15-year-old, anxious Caucasian girl was admitted to our district general hospital on 20 June 2013. She had received a diagnosis of stage IV Hodgkin's Lymphoma in May 2013. Owing to bulky mediastinal and abdominal disease, a peripherally inserted central catheter line (PICC) was placed in the unusual position of the groin for venous access. Prior to her diagnosis she had been taking Microgynon contraceptive pills for menorrhagia for

over 6 months but switched to leuporelin depot injections on 17 June 2013.

Postinsertion of the PICC line, the patient had described several short, self-limiting episodes of breathing difficulties, which settled without any intervention. These were attributed to stress-induced panic attacks. On one of these episodes, the breathlessness lasted for over 1 h and she was brought to hospital for review of her shortness of breath, chest tightness and some abdominal pain. This was of sudden onset after standing up from sitting position. There was no calf pain or tenderness.

On examination, the patient was alert, afebrile and speaking in full sentences. Her respiratory rate was 20 breaths/min, oxygen saturations were 94% in air, there was no evidence of respiratory distress but there was some reduced air entry at the right lung base. Her heart rate was 104 bpm, blood pressure 126/91 mm Hg and she was peripherally well perfused. Her abdomen was soft and non-tender with a 1 cm liver edge but no splenomegaly. A right-sided supraclavicular mass was palpable.

INVESTIGATIONS

On admission, blood tests showed haemoglobin 113 g/L, white cell count $0.36 \times 10^9/L$, neutrophils $0.12 \times 10^9/L$, platelets $161 \times 10^9/L$ and C reactive protein <1 mg/L. ECG was normal at the time, with no tachycardia. Chest X-ray showed no effusion, but there was a bulky mediastinum in keeping with the underlying Hodgkin's lymphoma. Capillary blood gas showed pH 7.52, pCO_2 4.1 kPa, base excess 2.8 mmol/L, HCO_3^- 27 mmol/L, lactate 2.5 mmol/L. The patient's coagulation

Figure 1 CT pulmonary angiography showing large-volume bilateral pulmonary emboli in the distal right pulmonary artery extending to the upper, middle and lower lobes. On the left, there is extensive lower lobe thromboembolic disease.

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screen was normal but D-dimer test was raised at 456 ng/mL (range 0–243 ng/mL). After discussion with a tertiary oncology centre, the patient underwent CT pulmonary angiography (CTPA) scan. This showed large-volume bilateral pulmonary emboli in the distal right pulmonary artery extending to the upper, middle and lower lobes. On the left, there was extensive lower lobe thromboembolic disease (figure 1).

OUTCOME AND FOLLOW-UP

After the diagnosis, the patient was started on subcutaneous dalteparin 12 500 units once-a-day. There was subsequent multidisciplinary adult and paediatric team involvement. Being haemodynamically stable, she was not considered for thrombolysis. In view of the PICC line, she had an ultrasound of her left leg, which showed the tip of her PICC line sitting in the left common femoral vein, but the ultrasound failed to demonstrate thrombus in either leg. Despite this, her PICC line was removed immediately.

She attended her tertiary oncology centre for her routine chemotherapy, where her anticoagulant was changed to subcutaneous tinzaparin 10 000 units. It was decided the patient would remain on a heparin-based anticoagulant, not be given further leuprorelin and not have the PICC line reinserted. She was treated with tinzaparin for 6 months and her thrombophilia screen 6 months postcompletion of treatment was normal. Currently, she remains in remission.

DISCUSSION

The risk factors for venous thrombosis are related to Virchow's triad of endothelial injury, blood stasis and hypercoagulability. Over 90% of paediatric venous thrombosis is related to underlying medical or surgical risk factors,³ while idiopathic venous thrombosis is rare. The most common conditions causing thrombosis are congenital heart disease, malignancy, trauma, surgery, nephrotic syndrome and systemic lupus erythematosus.^{4 5} However, the single most important risk factor for the development of venous thrombosis is the presence of a central venous catheter (CVC), often necessary for the administration of chemotherapy, total parenteral nutrition and drugs.⁴

In children who have multiple risk factors, it is important to consider venous thrombosis even when symptoms are non-specific and there are other likely diagnoses. In this case, the major risk factors were lymphoma with a large mediastinal mass, the presence of a CVC and recent use of the combined oral contraceptive pill.

Common clinical features of PE include shortness of breath, pleuritic chest pain and acute cardiovascular collapse.⁴ Less common symptoms can include persistent unexplained tachycardia, fever or deep vein thrombosis. Rarely do patients present with abdominal pain,^{6 7} and there are no case reports documenting self-limiting breathlessness, which in this case was mistaken for panic attacks. However, in contrast to popular belief, having normal vital signs does not necessarily lower the probability of PE.⁸

D-dimer, a specific fibrin degradation product, has a good negative predictive value for venous thromboembolism diagnosis,⁹ but its use in children is less clear, with up to 40% of children with PE having a normal D-dimer.¹⁰ Levels may vary in children, and therefore be difficult to interpret.¹¹ While CTPA is the gold standard in diagnosis,⁵ yielding fewer ambiguous results in children than in adults, it carries with it the burden of radiation, which is a concern in young children.

ECG changes in PE are well described in adults. Typical abnormalities include right axis shift, right bundle branch block,

T-wave inversion in leads III, aVF, V1–5 and sinus tachycardia.^{12 13} However, in children, the changes are less clear-cut and not reliable.^{14 15} Similarly, chest X-ray is not used to diagnose PE, but it can be useful in excluding other diagnoses such as pneumonia and pneumothorax.¹⁶

There are different types of anticoagulation available for the treatment of PE in children; unfractionated heparin, thrombolytic agents, thrombectomy, vitamin K antagonists and low-molecular-weight heparin (LMWH), with the latter two the most commonly used. There are few paediatric-specific evidence-based guidelines for treatment, and therefore the risks and benefits of different treatments need to be considered in each case. Initiation of treatment usually involves LMWH followed by warfarin, with duration of treatment recommendations extrapolated from adult data.^{14 17} Occasionally, it is preferable for LMWH to be continued in children with complex coexisting problems.¹⁸

In the Canadian registry, the mortality rate caused by venous thromboembolism is 2.2%,¹⁹ although in small studies, the mortality rate for PE is around 10%.^{4 14 20} The cause of death in paediatric patients with PE is usually related to the underlying disease process, although congenital heart disease and malignancy confer a poorer prognosis.⁴ The recurrence rate for venous thromboembolism ranges from 6% to 21%,⁵ although this does not necessarily reflect the risk of PE alone. Predictably, an underlying prothrombotic state is associated with a higher recurrence rate.⁴

In conclusion, PE is a rare paediatric diagnosis, but its presence is likely to be underestimated due to the subtle and non-specific nature of its symptoms. Because children with complex medical conditions and malignancy are surviving for longer, PE is an important consideration when listing differential diagnoses. Better guidelines indicating diagnostic investigations and appropriate management are required to improve the care and outcomes in children.

Learning points

- ▶ Pulmonary embolism (PE) is a rare paediatric diagnosis.
- ▶ Consider PE as a diagnosis in any child who has risk factors for thromboembolic events, even if the symptoms are variable and vague.
- ▶ Coagulation studies with D-dimer should be sent early, when suspecting PE.
- ▶ Uncommon and rare problems do occur in general paediatric practice. Doctors should have an open mind for the unexpected and search for alternative explanations for their patient's complaint.

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