European Journal of Case Reports in Internal Medicine

The Clot Thickens: Diagnosing Acute Pulmonary Embolism as a Trigger for Chronic Obstructive Pulmonary Disease Exacerbation in the Setting of Anticoagulation Failure

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Doi: 10.12890/2020_001884 - European Journal of Case Reports in Internal Medicine - © EFIM 2020

Received: 12/07/2020
Accepted: 04/08/2020
Published: 23/09/2020

How to cite this article: Saleh SN, Mansi IA. The clot thickens: diagnosing acute pulmonary embolism as a trigger for chronic obstructive pulmonary disease exacerbation in the setting of anticoagulation failure. *EJCRIM* 2020;**7**: doi:10.12890/2020_001884.

Conflicts of Interests: The Authors declare that there are no competing interests.

ABSTRACT

Chronic obstructive pulmonary disease (COPD) exacerbations are most commonly triggered by infections, but up to 25% of those that require hospitalization are thought to be triggered by acute pulmonary embolism. We present the case of a 71-year-old patient with a history of unprovoked pulmonary embolisms on anticoagulation therapy hospitalized for a COPD exacerbation. The exacerbation was triggered by an acute pulmonary embolism, representing anticoagulation failure.

LEARNING POINTS

- Pulmonary embolism (PE) is an important trigger of COPD exacerbations and should be considered, especially when there is an unexplained abrupt or recurrent increase in the frequency or severity of exacerbations.
- Therapeutic anticoagulation does not preclude the presence of PE.
- Clinical risk stratification is a crucial component of medical decision-making.

KEYWORDS

COPD exacerbation, pulmonary embolism, anticoagulation, anticoagulation failure, enoxaparin

CASE DESCRIPTION

A 71-year-old man with severe chronic obstructive pulmonary disease (COPD) on 3 litres per minute (l/min) of home oxygen and a distant history of unprovoked pulmonary embolisms (PEs) currently on warfarin presented to the emergency room with an overnight history of increased dyspnoea with blood-streaked sputum production and oxygen desaturation. He denied fevers, chills or sputum purulence. Over the previous few months, he had an increase in the frequency of COPD exacerbations resulting in 5 admissions, all thought to be triggered by viral respiratory infection.

On examination, he had tachycardia of 130 beats per minute, tachypnoea of 25 breaths per minute and oxygen saturation of 90% at rest and 80% with conversation on 4 l/min of oxygen. He was afebrile and normotensive. Pulmonary examination revealed diffuse wheezing and bronchial breath sounds in the right upper lobe.

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He had a white blood cell count of 10.5 K/µl, stable haemoglobin around 10 g/dl, creatinine of 0.89 mg/dl and an INR of 2.11. A week earlier, his INR was 3.27. Arterial blood gas (ABG) analysis showed a pH of 7.42, PCO_2 of 41.8 mmHg and PO_2 of 53.7 mmHg on 4 l/min of oxygen supplementation. A chest x-ray was unrevealing.

Methods and Procedures

The patient was admitted to a step-down unit and started on oral corticosteroids, nebulized bronchodilators and antibiotics. Searching for an explanation for the recent increase in his COPD exacerbation readmissions, chest computed tomography (CT) angiography was pursued, which revealed an acute-on-chronic right upper lobe segmental PE. A Doppler ultrasound revealed an acute left popliteal deep venous thrombosis despite the lack of symptoms or signs. The patient was treated with enoxaparin with significant improvement. Given warfarin failure despite a therapeutic INR level, the patient was evaluated for causes of thrombophilia and was discharged on enoxaparin.

DISCUSSION

COPD exacerbations are often reflexively managed with corticosteroids, bronchodilators, antimicrobials, oxygen and, if necessary, noninvasive mechanical ventilation. Although respiratory infections trigger approximately 50 to 70% of COPD exacerbation cases[1], it is imperative that alternative diagnoses and precipitants are considered. PE, which can often have similar symptoms of cough and dyspnoea, is an important trigger in nearly 25% of hospitalized COPD exacerbations[2]. Left untreated, a PE has a high case fatality rate and morbidity burden, especially in COPD patients where the risk of mortality nearly doubles[2]. It is important to have a high index of suspicion and to evaluate pre-test probability to guide testing.

The pre-test probability for our patient was relatively high. Risk factors in our patient that raised suspicion of PE included a sedentary lifestyle, a history of advanced COPD, a history of multiple PEs, repeated unexplained COPD readmissions and clinical presentation with dyspnoea, hypoxia and significant sinus tachycardia. Of note, his Geneva score was 11 points, which is high risk with greater than 60% incidence of PE[3]. While the fact that this patient was therapeutically anticoagulated on presentation decreased his pre-test probability of PE, it certainly did not rule out its possibility. Approximately 2% of patients on anticoagulation therapy (treated with direct oral anticoagulants; DOACs, or warfarin) experience a recurrence, which is a poor prognostic factor[4]. There was no significant difference in the recurrence of venous thromboembolism between treatment with DOACs and warfarin (relative risk; RR 0.90, 95% confidence interval; CI 0.77–1.06), but treatment with a DOAC was associated with a significantly reduced risk of major bleeding (RR 0.61, 95% CI 0.45–0.83)[4]. There is no clear evidence that allows evaluation of the effectiveness of DOACs when there is true warfarin anticoagulation failure and limited evidence guides the current standard of practice to switch to low molecular weight heparin[5].

In those patients with anticoagulation failure, it is important to consider the aetiology and distinguish between true failure and pseudo-failure due to subtherapeutic anticoagulation (that is, adherence, drug–drug interactions and malabsorption). Given our patient's therapeutic INR on admission and 1 week prior, this coincides with true failure. Important considerations for true failure include underlying malignancies (specifically, myeloproliferative neoplasms), antiphospholipid syndrome, heparin-induced thrombocytopenia and inherited thrombotic disorders[5]. However, none of these conditions were identified in our patient.

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