Massive hemoptysis in a patient with pulmonary embolism, a real therapeutic conundrum

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A B S T R A C T

Massive Hemoptysis and pulmonary embolism are two very severe and potentially fatal pulmonary emergencies requiring completely different treatments. We present the case of a 45-year-old male transmitted to our Hospital for massive hemoptysis who at the same time was found to suffer from pulmonary embolism. Hemoptysis was treated with bronchial artery embolization which resulted in cessation of haemorrhage and allowed the administration of anticoagulant therapy a few days later. This case report gives an answer on how to manage a real therapeutic conundrum which is the coexistence of a massive hemoptysis and a concomitant pulmonary embolism.

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1. Case report

A 45-year-old non-smoker male patient presented to the emergency department of a territorial hospital complaining for hemoptysis. On the day of admission, he reported that he had expectorated approximately 50ml of bright red blood. He denied any other symptoms, including fever, cough, dyspnea or chest pain. On his medical history he reported a similar episode of hemoptysis 5 years ago the cause of which remained unknown despite clinical investigation which included computed tomography (CT) of the chest, immunologic examinations and fiberoptic bronchoscopy. The patient denied any other medical problem and was not receiving any medication.

On physical examination, he was a pleasant apparently healthy man with body temperature 36.8 °C, pulse rate 110 beats/min, blood pressure 130/80 mmHg, respiratory rate 21 breaths/min and oxygen saturation 95% on room air. Auscultation disclosed mild crackles in the right lower lobe. No other abnormal findings were found in the rest of the physical examination. In the laboratory tests, the patient's hemoglobin was 13.1g/dL, hematocrit: 40.7%, white blood cell count was 7410 cells/µL (77.6% neutrophils and 15.1% lymphocytes), and platelet count was 161 000/µL, D-Dimers: 436 µg/L (normal values up to 500 µg/L) while the values for urea nitrogen, creatinine and electrolytes were within the normal range. Immunologic tests revealed only slightly increased Antinuclear Antibodies (ANA) (1:160). Sputum Gram stain, cultures for common bacteria and examination for M Tuberculosis were negative. ECG was normal.

The patient's chest x-ray on admission, revealed an area of consolidation in the middle lobe. Computed tomography of the chest revealed some bronchiectasis along with an area of consolidation in the middle lobe. The patient was admitted and received oxygen therapy, intravenous amoxyclavine-clavulanic acid and intravenous tranexamic acid at a dose of 1 g four times daily.

During the following days, the patient continued to experience streaks of blood in his sputum on a daily basis sometimes accompanied by dyspnea and tachypnea, and 2 days later, a new episode of massive hemoptysis occurred, and the patient was transmitted to our hospital for further evaluation and treatment. On admission to our hospital the patient underwent a CT angiography of the thoracic aorta and its branches (including bronchial arteries) which revealed some mild anatomical abnormalities in the bronchial...
arteries supplying the right lower lobe and ground glass opacities in the middle and right lower lobe, without showing a specific bleeding origin (Fig. 1). Although the examination was not sensitive enough, it also gave the impression of a thrombus in the left main artery. Thus, a CT pulmonary angiography was performed which revealed a large thrombus on the left main artery involving the pulmonary arteries for the left upper, the lingual, and the left lower lobe (Fig. 2). An ultrasonography was performed and the presence of a thrombus in the lower extremities and the pelvis was excluded. Echocardiography did not reveal any cardiac abnormalities. Although the leg and pelvis ultrasonography was negative, an inferior vena cava temporary filter (ALN Optional Vena Cava Filter, ALN, France) was placed via femoral approach since anticoagulant treatment was contraindicated. Tranexamic acid was discontinued.

A few hours later the patient experienced a new episode of massive hemoptysis and became severely dyspneic. On clinical examination he was found to be tachypneic, tachycardic and hypotensive. Oxygen saturation had dropped to 78% on room air. An emergency angiography was performed with the aim of embolizing any potential sources of bleeding from the bronchial circulation. Selective angiography from the right bronchial artery revealed extravasation of contrast from three different branches of the middle lobe and embolization was performed using a microcatheter (Progreat®, Terumo, Japan) and N-butyl-2-cyanoacrylate (NBCA; Histoacryl®) diluted in a 1:3 ratio, with oily X-ray contrast agent Lipiodol®. Final angiogram demonstrated complete occlusion of the target vessels without any sign of bleeding (Fig. 3). Following this procedure, the patient was stabilized and returned to the ward. Hemoptysis has been ceased.

However, the patient became febrile and developed chest pain in the right hemithorax together with cough and expectoration of dark bloody sputum. Post-procedural chest CT revealed a consolidation of the right lower lobe suggestive of a pneumonia (Fig. 4). High-flow oxygen was administered to achieve target saturation of 94–98%. Blood cultures were collected (their result was available a few days later and they were negative) and antimicrobial therapy was changed to meropenem and linezolide. 3 days after bronchial embolization, the patient's symptoms improved and hemoptysis was completely settled down. The patient received treatment with subcutaneous fondaparinux (in a dose of 7.5mg administered subcutaneous once daily) and underwent monitoring of anti-Xa activity twice a week. The patient was discharged a few days later with the advice to continue treatment with fondaparinux and to return 3 months later for the removal of the inferior vena cava filter. By that time his symptoms had disappeared and he had remained free of hemoptysis. Follow up chest CT demonstrated complete resolution of the consolidation and no other signs of parenchyma disease.

2. Discussion

This patient was a real therapeutic conundrum since he had developed at the same time two very severe and potentially fatal pulmonary emergencies: persistent major hemoptysis and concurrent acute pulmonary embolism (PE). Anticoagulation is required to prevent further thrombosis while, simultaneously anticoagulation is contraindicated in the case of hemoptysis since it increases the risk of bleeding.

Hemoptysis might be the presenting symptom in numerous diseases with an associated mortality 7–30% [1]. Massive hemoptysis, (defined as the expectoration of blood volumes 100–1000 ml per day in different studies) is a potentially fatal complication mainly due to obstruction of the airways, as the anatomical dead space of the major airways is approximately 100–200ml. Bleeding from the bronchial arteries is the most usual origin [90% of cases] of massive hemoptysis as it is a circulation at systemic pressure [1]. The main causes of hemoptysis are reported on Table 1 [1]. The precise localization of the bleeding site is essential for the decision and direction of definitive treatment. Imaging studies such as Chest X-Ray (CXR) and CT scans are very useful in the identification of possible causative lesions of massive hemoptysis. The use of contrast may also help to identify possible vascular malformations. CT angiography is very useful for the detection of the site of hemorrhage and the detection of the possible causes related with hemoptysis. The investigation should be performed in deep inspiration and coverage should include the area between the lung apices to the hilum of the kidneys, from the supra-aortic vessels to
the origin of the inferior diaphragmatic arteries [2]. CT angiography can also demonstrate a cause and/or signs of alveolar or bronchial flooding with intraluminal clots [2]. However, despite all investigative procedures, the aetiology of hemoptysis may remain unknown in up to 5–10% of patients as in the first episode which our patient had experienced 5 years ago.

The oral antifibrinolytic agent tranexamic acid, an inhibitor of plasminogen activation, is frequently used in clinical practice in order to control recurrent hemoptysis, although, evidence supporting its use is limited [1]. Although the aetiology of hemoptysis, the length of treatment, and the prescribed dosage and form of tranexamic acid significantly varies between the studies, there is still evidence that tranexamic acid may reduce both the duration and volume of bleeding with some concerns regarding the risk of short-term thromboembolic complications [3,4]. Our patient received treatment with intravenous tranexamic acid and this might possibly be related to the development of pulmonary embolism. The fact that on his first admission the D-Dimers testing was negative, further supports the hypothesis that pulmonary embolism occurred later during his hospitalization and management of hemoptysis.

Bronchial angiography, an invasive diagnostic procedure that is considered the gold standard for the localization of the source of hemoptysis and provides the opportunity to proceed to transcatheter bronchial artery embolization if indicated [1]. During selective bronchial artery cannulation, it is possible to identify the site of bleeding, and perform embolization using a variety of permanent (micro-particles, isobutyl-2-cyanoacrylate, metallic coils or absorbable (gelatin pledgets) embolic materials within the feeding vessel as to achieve haemostasis. Hemoptysis control ranges from 65 to 92% [2]. In this case NBCA was used. According to the literature, both NBCA and microspheres result in satisfactory technical success rates without any significant difference in complication rates, if used following super-selective catheterization by experienced Interventional Radiologists [5].

Technical failure of BAE can occur mainly due to inability to catheterize small calibre bronchial arteries, recanalization of

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**Fig. 3.** (a) Selective catheterization and initial digital subtracted angiography (DSA) of the right bronchial artery. (b) Super-selective distal catheterization of the right bronchial artery with a micro-catheter demonstrating blushing and extravasation of contrast at the distal arterial segment (circle). (c) Super-selective DSA following embolization. Note the opacification of the occluded vessels created by the embolic material (arrows). (d) Final DSA from the origin of the right bronchial artery, demonstrating patency of bronchial branches of the upper and lower right lobe and complete occlusion of the bronchial branches of the middle lobe with no signs of bleeding.

**Fig. 4.** Post-procedural chest CT demonstrating consolidation of the right lower lobe at the area of embolization. Note the embolic material (glue) within the consolidation (white arrows).
Table 1
Causes of massive hemoptysis (reproduced from Ref. [1] after permission).

| Category            | Causes                                                                 |
|---------------------|------------------------------------------------------------------------|
| Infections          | Mycobacteria, particularly tuberculosis                                |
|                     | Fungal infections (mycetoma)                                           |
|                     | Lung abscess                                                           |
|                     | Necrotising pneumonia (Klebsiella, Staphylococcus, Legionella)         |
| Spurious            | Epistaxis                                                              |
|                     | Haematemesis                                                           |
| Iatrogenic          | Swan-Ganz catheterization                                              |
|                     | Bronchoscopy                                                           |
|                     | Transbronchial biopsy                                                  |
|                     | Transtracheal aspirate                                                 |
| Parasitic           | Hydatid cyst                                                           |
|                     | Paragonimiasis                                                        |
| Trauma              | Blunt/penetrating injury                                               |
|                     | Suction ulcers                                                         |
|                     | Tracheoarterial fistula                                                |
| Neoplasm            | Bronchogenic carcinoma                                                |
|                     | Bronchial adenoma                                                      |
|                     | Pulmonary metastases                                                   |
|                     | Sarcoma                                                                |
| Haemoptysis in children | Bronchial adenoma                                                      |
|                     | Foreign body aspiration                                                |
|                     | Vascular anomalies                                                     |
| Vascular            | Pulmonary infarct, embolism                                            |
|                     | Mitral stenosis                                                        |
|                     | Arteriobronchial fistula                                               |
|                     | Arteriovenous malformations                                            |
|                     | Bronchial telangiectasia                                               |
|                     | Left ventricular failure                                               |
| Coagulopathy        | Von Willebrand’s disease                                               |
|                     | Haemophilia                                                            |
|                     | Anticoagulant therapy                                                  |
|                     | Thrombocytopenia                                                       |
|                     | Platelet dysfunction                                                   |
|                     | Disseminated intravascular coagulation                                 |
| Vasculitis           | Behcet’s disease                                                       |
|                     | Wegener’s granulomatosis                                               |
| Pulmonary           | Bronchiectasis (including cystic fibrosis)                             |
|                     | Chronic bronchitis                                                     |
|                     | Emphysematous bullae                                                   |
| Miscellaneous       | Pneumoniosis                                                           |
|                     | Broncholith                                                             |
|                     | Idiopathic                                                             |
|                     | Lymphangioleiomatosis                                                  |
|                     | Catamenial (endometriosis)                                             |

embolized vessels, incomplete embolization, revascularization of the target lesion by collateral supply, or non-recognition of systemic supply of the lesion such as the phrenic, intercostal, mammary, or subclavian arteries [6]. The most common complication of BAe is chest pain, which is usually transient and is attributed to mild post-embolization ischemia. Less common but more significant complications include dysphagia, bronchial necrosis and the most fearful event of spinal cord ischemia due to embolization of spinal branches, with reported prevalence ranging from 1.4 to 6.5%. Super-selective, more distal embolization has been proposed as to avoid non-targeted embolization of spinal branches [5].

Our patient presented in our hospital, not only with hemoptysis but also with acute PE. Anticoagulation is the treatment of choice in patients with PE as it is known to prevent both early death and recurrent symptomatic or fatal VTE [7]. However, anticoagulation is contraindicated in patients with severe hemoptysis since it might lead to fatal haemorrhage in the airways. retrievable IVC filter insertion in acute PE should be performed if anticoagulation is contraindicated [8] as in the case of our patient. Non-permanent filters are preferred to be used in cases where VTE is related to a transient risk factor [8]. The IVC filter protects from PE recurrence but should be removed when the anticoagulation can be re-administered since unretrieved removable IVC filters may carry significant long-term risks [9]. We have decided to remove the IVC filter 3 months after the episode of PE and hemoptysis since according to our opinion there was risk of recurrence of hemoptysis which might force us to discontinue the anticoagulant treatment. Furthermore, although the American College of Chest Physicians guidelines recommend against an IVC filter unless the patient cannot tolerate anticoagulants [10] we have decided to insert a IVC filter in our patient even without there was no obvious vein thrombosis was observed in the ultrasound of the lower extremities.

Intravenous unfractionated heparin with close monitoring of the activated partial thromboplastin time (aPTT) is the anticoagulation of choice when there is a risk of significant haemorrhage because it can be quickly discontinued in the event of a lifethreatening bleeding [7]. However, this method requires repeated monitoring of the activated partial thromboplastin time, in order to achieve the required therapeutic values, which is sometimes difficult, time consuming and often results in under- or overtreatment (especially during the first hours of admission). For these reasons, in the case of our patient we decided to administer anticoagulant therapy with fondaparinux when the haemorrhage was ceased. Fondaparinux, is a pentasaccharide synthetic derivative of unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) [11]. It possesses increased affinity to inhibit factor Xa compared with UFH and LMWHs. It is administered once daily by subcutaneous injection at weight-adjusted doses, without the need for monitoring and has not been related to proven cases of Heparin Induced Thrombocytopenia (HIT) while its reported bleeding rates are similar to those obtained with intravenous UFH [12,13]. Monitoring is not generally recommended except in special patient populations, i.e. pediatric, obese, or pregnant patients or patients with renal failure, and increased danger of bleeding like our patient [11]. Since the assay methodology with appropriate fondaparinux calibrators is very similar to the standard anti-factor Xa curves for LMWH or UFH, when monitoring is necessary, anti-factor Xa concentrations can be assessed based on local existing LMWH curves to adjust the patient’s dosing until a fondaparinux-specific curve could be established [14]. Since in our lab there is no available special assay for the monitoring of fondaparinux anti-factor Xa anticoagulant activity, a commercial available assay for the monitoring of the activity of unfractionated and low molecular heparins (using and automated chromogenic assay, HEMOSIL Liquid anti-Xa) was used. However, we have to admit that the anti-factor Xa for LMWH and fondaparinux assays are not equivalent and fondaparinux concentrations determined using the UFH or LMWH curves might be overestimated [14].

The development of PE in a patient with massive hemoptysis is a highly challenging clinical condition and can be related to numerous respiratory diseases such as patients with lung cancer, aspergillosis, cystic fibrosis or vascular malformations as in the case of our patient. In this case it is extremely possible that the use of the tranexamic acid contributed to the development of venous thrombo-embolism although the role of such prothrombotic agents requires further investigation. Bronchial artery catheterization and embolization is the management of choice in patients with massive and life threatening hemoptysis.
Sources of support

None.

Conflict of interest

All authors declare that they have no conflict of interest related to the present manuscript.

Authors’ contributions

All authors have been involved in the care of the patient. YH, AIP, AK, EM, IT, VA and SP, were involved in the patient’s care and treatment. LR and EB were involved in the interpretation of radiographic studies, the performance of embolization and prepared all artwork. YH, AIP SP, LR and EB wrote the manuscript. All authors read and approved the final manuscript.

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