Management of haemoptysis after cure of pulmonary tuberculosis

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Abstract:
Our case report concerns a young woman from Umuahia in eastern Nigeria who was managed for pulmonary tuberculosis (PTB), was declared cured, but later presented with haemoptysis and was referred to us as a possible case of drug-resistant TB.

A review of the literature on the pathogenesis, pathophysiology, differential diagnoses, diagnostic methods, and management of haemoptysis was carried out.

A diagnosis was made and appropriate treatment was instituted. Prompt response was observed with antibiotics and antifungal agent plus conservative management of the haemoptysis.

It was concluded that although PTB is a common cause of haemoptysis in most developing countries, all cases of haemoptysis are not due to PTB. The presence of haemoptysis should not warrant initiation of anti-TB drugs in a patient who had been cured of TB and does not show any clinico-radiological or bacterial evidence of active TB.

Introduction

Haemoptysis is the expectoration of blood from the respiratory tract.[1,2] It ranges from mildly insignificant to a massive life-threatening condition. Haemoptysis can occur in many clinical entities and does not only reflect underlying pulmonary tuberculosis (PTB).[1,3] Haemoptysis can occur during and after treatment of TB. Therefore a proper screening for the cause of the haemoptysis is required before initiating treatment.

We report on a 26-year-old female farmer who presented with haemoptysis after being cured for PTB and was referred as a possible case of drug-resistant TB.

Miss E U, was admitted via the Accident and Emergency (A & E) Department with a history of cough, weight loss of 3-months duration, fever of 6-weeks duration, and haemoptysis 3 weeks prior to presentation.

She had been treated for PTB 6 years previously with category two drugs [4] (rifampicin, isoniazid, ethambutol, and pyrazinamide, plus parenteral streptomycin) after 8 weeks of default following completion of intensive phase of category one treatment.[4] She was then declared cured after 8 months of treatment.

At presentation in the A & E department, she expectorated about 160 ml of blood daily and had dyspnoea and chest pain. She had no history of heartburn or reflux. She was not on any anticoagulant and had no history of bleeding from puncture sites. There was no history of malignancy or consumption of raw/poorly cooked crabs.

Clinical examination revealed a chronically ill-looking young woman, grossly wasted, afebrile (temperature 37°C), moderately pale, with grade one digital clubbing. She had no peripheral lymphadenopathy and no leg oedema. Chest examination showed a respiratory rate of 35 cycles/minute. Trachea was central; palpation showed equal chest excursion. Dull percussion notes were noted on the right mid and lower, left lower zones postero-laterally. Vocal fremitus and coarse crackles were heard in the same areas. Cardiovascular examination revealed a pulse rate of 100/minute, blood pressure of 100/60 mmHg. An abdominal examination showed mild hepato-splenomegally. Other systemic examinations were normal.

A provisional diagnosis of relapsed PTB was made with differential diagnoses of drug-resistant TB, chronic obstructive pulmonary disease (COPD) with acute exacerbation and pulmonary aspergillosis. The management plan was to investigate her and commence initial therapy with intranasal oxygen 4 litres/minute, intravenous cephtraxone 2 g daily, tablet vitamin C 1 g daily, intravenous normal saline, and haematenics. She was also placed on a high calorie and high protein diet.

Investigation results obtained showed a haemoglobin of 7.7 g/dl, a white blood count (WBC) of 11 000, a neutrophils count of 83%, lymphocytes of 16%, and eosinophil of 1%. The patient's platelet count was 536 000/mm and the erythrocyte sedimentation rate was 60 mm in the first hour (Westergreen method). Her HIV screening was negative and a chest X-ray showed homogenous opacities with background fibrocystic nodular changes in both lung fields, sparing the upper lobes. Sputum culture yielded heavy growth of pseudomonas species that was sensitive to ciprofloxacin, ofloxacin and cephtazidime, and cephtriaxone. Sputum microscopy revealed spores of aspergillus species while the Ziehl–Neelsen (ZN) stain for acid-fast bacteria (AFB) was negative. GeneXpert for *Mycobacterium tuberculosis* (MTB) was also negative.

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The patient's antibiotics were adjusted according to sensitivity result and tablet fluconazole 200 mg bid was given and was transfused with two units of blood. She improved within 2 weeks and was discharged home.

Discussion

Haemoptysis is defined as expectoration of blood from the respiratory tract, a spectrum that varies from blood-streaked sputum to coughing up of large amount of blood or massive haemoptysis (100 to 600 ml of blood in 24 hours).[1,2] It could be a marker for potentially serious disease (bronchogenic carcinoma), a life-threatening condition (massive haemoptysis), or a benign condition as in acute pneumonias.[1,5] Expectoration of even a relatively small amount of blood is an alarming symptom. Therefore, haemoptysis, no matter the amount involved, requires thorough investigation.

The lung has a dual circulation – bronchial and pulmonary. Bleeding in the lungs could be from the tracheobronchial tree, the lung parenchyma, or primarily from the pulmonary vasculature. When bleeding occurs in any of the three sites it irritates the sensory receptors which are innervated by the afferent limb of the cough reflex (cranial nerves v, xii, x and the superior laryngeal nerves). Through the efferent limb (recurrent laryngeal and spinal nerves) the blood is expectorated with or without other secretions.

Haemoptysis is a non-specific symptom and can occur in up to 100 clinical conditions.[1,3,6,7] In our environment and many other developing nations of the world haem-optysis is almost synonymous with PTB and many patients presenting with this symptom are started on anti-TB treatment without proper diagnosis.[3]

The differential diagnoses of haemoptysis include:[1]

- tracheo-bronchial source as in bronchiectasis;
- neoplasms;
- Kaposi's sarcoma;
- bronchial carcinoid;
- acute and chronic bronchitis;
- airway trauma;
- foreign body.

Bleeding from pulmonary parenchyma sources include:

- pneumonias (viral and bacterial);
- lung abscesses;
- aspergillosis;
- TB;
- actinomycosis;
- Goodpasteur's syndrome;
- Wegener's granulomatosis lupus pneumonitis;
- idiopathic pulmonary haemosiderosis;
- parasitic infections, such as hydatid cysts;
- paragonimiasis.

Other sources include:

- sarcoidosis;
- cystic fibrosis;
- HIV-associated pneumonitis;
- *Mycobacterium avium intercellulare* infection (MAI).

Bleeding from pulmonary vasculature can happen in pulmonary embolism, elevated pulmonary venous pressure (mitral stenosis, left ventricular failure, and aortic aneurysm). Other cases include polyarteritis nodosa, arteriovenous malformation, and pulmonary artery rupture following balloon-tip pulmonary artery catheter manipulation.

Miscellaneous, as well as rare, causes of haemoptysis include:

- pulmonary endometriosis;
- systemic coagulopathy, as in leukaemia;
- haemophilia;
- disseminated intravascular coagulation;
- thrombocytopenia;
- anticoagulant/thrombolytic agents.

Other rare causes include schistosomiasis and mixed cryoglobulinaemia due to hepatitis C viral infection.

Sources other than lower respiratory tract bleeding may be from upper airway bleed or upper gastro-intestinal tract.

Making the correct diagnosis depends on good history taking, clinical examination, and prompt targeted investigation.

A history of chronic cough, weight loss, drenching night sweats and contact with a TB patient may suggest a diagnosis of TB. In a setting of immunosuppression and HIV, TB, neoplasm, and Kaposi's sarcoma may be suspected. Acute onset with fever, cough, and chest pain would suggest a viral or bacterial pneumonia, while history of copious purulent sputum may suggest bronchiectasis or lung abscess. Pleuritic chest pain and calf tenderness may be a pointer to pulmonary infarction or embolism. Tobacco use may suggest bronchial cancer, chronic bronchitis, or other forms of COPD. Occupational history, for example exposure to asbestos, may suggest bronchial cancer. Dyspnoea on exertion, orthopnoea, or paroxysmal nocturnal dyspnoea with frothy pink sputum suggests heart failure or mitral stenosis. Travel history may suggest TB or parasitic infection while anticoagulant use may be a pointer to an iatrogenic cause. Nausea, vomiting, alcoholism or chronic non-steroidal anti-inflammatory (NSAID) use suggests upper gastro-intestinal drug bleeding rather than haemoptysis.

Clinical examination revealing cachexia, clubbing, hoarse voice, or Cushing's syndrome would suggest a lung malignancy. Digital clubbing is a pointer to bronchiectasis, lung abscess, or severe chronic lung disease. Fever, tachypnoea, hypoxia, barrel chest, pursed lips breathing, wheeze tympanitic percussion notes, and distal heart sounds would suggest acute exacerbation of chronic bronchitis. The finding of mulberry gingivitis, saddle nose and nasal septum perforation suggests Wegener's granulomatosis. Violaceous tumours on the skin are a pointer to Kaposi's sarcoma associated with HIV infection. Tachycardia, elevated jugular venous pressure (JVP), and S3 (third heart sound) gallop, heart murmurs, and bilateral fine rales suggest heart failure

or mitral stenosis. Tachycardial dyspnoea, fixed split S2, pleural friction rub, unilateral calf tenderness, and oedema suggest pulmonary embolism. Oropharyngeal and mucous membrane telangectasia and epistaxis suggest Osler-Weber-Rendu disease while dull percussion notes over lung apices and cachexia would suggest TB.

The common investigative procedure for haemoptysis in our environment is sputum culture, Gram stain, Ziehl–Neelsen stain for acid fast bacilli, and the use of chest X-ray. In a significant number of cases these will give the diagnosis. But when this fails to happen, as in our index patient, additional investigations need to be done. The old method of culture using Lewensen–Jensen medium takes at least 12 weeks. The newer method – Bactec 460[1] – will take about 6 weeks; and the patient cannot wait this long for definitive treatment to take place. Hence, the introduction of the Gene Xpert machine[8,9] for the diagnosis of TB and drug-resistant TB is a laudable approach as it was able to rule out TB as the cause of haemoptysis in our index patient. The Gene Xpert machine uses polymerase chain reaction (PCR) for the rapid diagnosis of TB. It is able to make the diagnosis within 90 minutes with a sensitivity of 92%, 96%, and 98% for one, two, and three sputum specimens respectively.[8,9] The specificity on non-TB cases was 99% with one sample, declining marginally to 98% with three sputum samples. The disadvantage is the high cost. Sometimes invasive approaches such as bronchoscopy, bronchial lavage, and lung biopsy may be necessary for diagnosis of neoplasm and other conditions. Pulmonary angiogram may be required for a diagnosis of pulmonary embolism while computerised tomography may be necessary for diagnosis of bronchiectasis.

The overall management of patients with haemoptysis is aspiration prevention, bleeding cessation, and treatment of the underlying cause. Most of the patients with mild-to-moderate haemoptysis (as in our index patient) will be managed conservatively. This involved absolute bed rest, the use of cough suppressants such as codeine, mild sedation, and treating the underlying disease with antibiotics and antifungal agents. In one series of patients, bleeding stopped in 91.8% of the patients who were managed conservatively with death attributable to haemoptysis in only 5.3% and these were patients with massive haemoptysis.[3] Many of the patients with massive haemoptysis will require surgical intervention and prompt appropriate intervention will improve survival in these patients.[1]

Conclusion

Although PTB is a common cause of haemoptysis in most developing countries, all cases of haemoptysis are not due to PTB. The presence of haemoptysis should not warrant initiation of anti-TB drugs in a patient who had been cured of TB and does not show any clinico-radiological or bacterial evidence of active TB.

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