Chapter 2

Hemoptysis

Elif Guliyev[1]

Abstract

Composed of two Greek words ("heima"-blood and "ptysis"-spitting), hemoptysis is a symptom that alarms the patient. If the hemoptysis is not massive, there is time to investigate the underlying disease. Massive hemoptysis is life-threatening. It has serious mortality and morbidity. In this article, the latest developments in the hemoptysis approach will be discussed.

Hemoptysis is the expectoration of blood or mixed secretions from the lower respiratory tract. The amount may be small or in amounts that can cause death. Sputum mixed with mucus, thick, sticky, blackish, and sour, is called bloody sputum (hemopteic krasha).

Life-threatening bleeding is defined as massive hemoptysis. Massive hemoptysis, which constitutes 5-15% of all hemoptysis, requires urgent intervention. For massive bleeding, different amounts are reported as 200-1000 ml bleeding in 24 hours, more than 200 ml in 2 hours, and more than 600 ml in 24 hours in different sources. Definitions for this non-standardized amount of bleeding do not always reflect the clinical characteristics of the patient. For example, the acute situation caused by 200 mL blood expectoration in the last 10 minutes, and 200 mL expectoration spread throughout the day cause different clinical pictures and require different interventions. For this reason, today, the definition is made by considering the clinical characteristics of the patient.

Any amount of hemoptysis leading to a life-threatening condition such as respiratory failure or hypotension is recommended to be defined as massive hemoptysis (life-threatening hemoptysis).

1 Dr., Kocaeli University, Faculty of Medicine, Department of Pulmonary Diseases, elifkrsl@gmail.com, Orcid: 0000-0002-1501-3360

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Pathophysiology

Perfusion of the lungs; 95% is supplied from the pulmonary arteries (right ventricle) and 5% from the bronchial arteries (the descending aorta between T3-T8, most often from the T5-T6 level (80%), phrenic arteries, subclavian arteries, intercostal arteries). 95% of pulmonary blood circulation is provided by the pulmonary artery (functional role) and its branches, which have a low-pressure system.

Since the bronchial arteries (nutritional role) are supplied with blood from the systemic arteries, blood pressure is high and this high pressure increases the risk of massive bleeding. At the same time, the bronchial arteries are the vessels that supply the airways and are affected by airway lesions. Often (40%) there is one bronchial artery on the right and two on the left. Various anatomical variations have been described in normal healthy individuals (Figure-1). They may also have aberrant origins from other systemic arteries (20%)

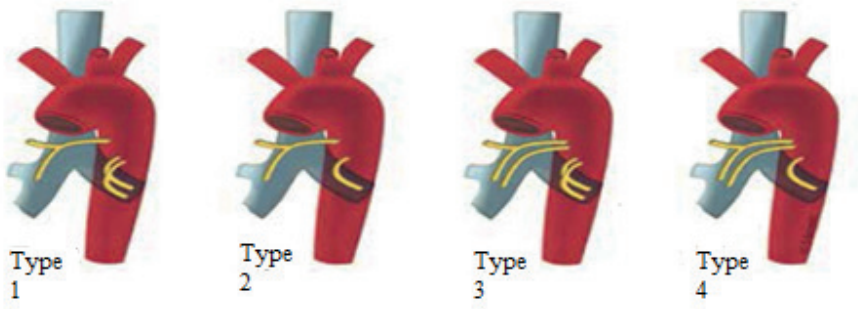

Figure 1- Bronchial artery variations

Type 1: 1 right Bronchial artery 2 left Bronchial arteries of the same origin

Type 2: 1 right Bronchial artery and 1 left Bronchial artery of the same origin

Type 3: 2 right Bronchial arteries and 2 left Bronchial arteries of the same origin

Type 4: 2 right Bronchial arteries of the same origin and 1 left Bronchial artery,

Bleeding in patients presenting with the complaint of hemoptysis; originates from 90% bronchial arteries, 5% pulmonary arteries, 5% non-bronchial systemic arteries, and very rarely pulmonary-bronchial veins and

capillaries. Pulmonary venous bleeding is usually mild and may occur in left heart failure, mainly due to pulmonary venous hypertension.

Bleeding due to the bronchial venous system can occur with proliferating submucosal bronchial veins, often as a complication of mitral stenosis, may be life-threatening, and may constitute an indication for surgical intervention.

Hemoptysis occurs with the formation of capillary anastomoses between the pulmonary artery and systemic bronchial arteries, pulmonary thromboembolism, vasculitis, suppression of pulmonary circulation due to hypoxic vasoconstriction, and an increase in bronchial flow. Hemoptysis develops as a result of the widening of the vessels and thinning of their walls due to excessive flow increase in these anastomoses. On the other hand, the change in vascular anatomy as a result of chronic inflammatory lung diseases causes the bronchial arteries to expand and fold, and new collaterals are formed with the clarification of normal anastomoses between the bronchial arteries and pulmonary veins, and the release of angiogenic growth factors, supporting neovascularization and pulmonary vascular remodeling. Hemoptysis develops as a result of an increase in collaterals and enlargement and fragility of vessels.

Causes of Hemoptysis

The vast majority of cases of hemoptysis occur in adults. Although the average age varies according to the underlying cause, hemoptysis due to lung cancer is usually seen between the ages of 40-60. It is seen twice as often in men than in women.

The most common causes of hemoptysis are pulmonary tuberculosis, bronchial cancer, bronchiectasis, pneumonia, vasculitic syndromes, and pulmonary infarction. In our country, Fidan et al. and Ünsal et al., bronchiectasis, tuberculosis, and lung cancer were reported as the three most common causes. On the other hand, up to 50% of cases of unknown-cryptogenic hemoptysis are reported worldwide.

In pulmonary tuberculosis, massive bleeding may occur with the rupture of Rasmussen aneurysms in the cavity wall. Aspergillus infection is the most common fungal agent that settles in the cavity wall and causes hemoptysis in our country. In pulmonary edema; The patient has hemoptysis in the form of pink foamy sputum, and the patient has severe dyspnea, orthopnea, and heart failure findings. The causes of hemoptysis are listed in Table 1.

Bleeding seen in bronchiectasis originates from the bronchial artery and can be serious. It can also be traumatic or iatrogenic hemoptysis. In

alveolar hemorrhages; While hemoptysis is seen immunologically, periodic hemoptysis "catamenial hemoptysis" may occur in the menstrual cycle due to ectopic endometrium in women. Despite all possibilities, the cause of hemoptysis cannot be determined in 50% of the cases. The prognosis is generally good in idiopathic hemoptysis, but it may recur.

Table 1- Conditions causing hemoptysis

Infections:	**Neoplasm:**	**Vascular/itis:**
Tuberculosis	Bronchogenic carcinoma	Pulmonary embolism
Fungal infections	Pulmonary metastases	AV malformations
Lung abscess	Carcinoid	Wegener's granulomatosis
Bronchiectasis/Bronchitis	Medication (VEGF etc.)	Left heart failure
Coagulopathy:	**Iatrogenic:**	**Cardiac**
Anticoagulant therapy	Endoscopic biopsy	Mitral stenosis
Platelet dysfunction	CT guided biopsy	left heart failure
Hemophilia	Swan Ganz catheterization	Tricuspid endocarditis
DIC		
Medicines	**Trauma**	**Other**
Aspirin	Thoracic traumas	foreign body
Anticoagulation	bronchial rupture	broncho-lithiasis
penicillamine	fat embolism	bronchopleural fistula
Solvents	Tracheal-innominate artery fistula	Bronchial telangiectasia
Cocaine		amyloidosis
		pneumoconiosis
		Catamenial hemoptysis

Diagnosis / Differential Diagnosis

An important step in diagnosis; is to distinguish whether the hemoptysis is a true hemoptysis or a pseudo hemoptysis. Pseudohemoptysis, that is, non-pulmonary blood expectoration, is considered as bleeding from the upper respiratory tract, esophagus, or stomach. Table 2 shows the distinction between hemoptysis and pseudo hemoptysis.

Upper respiratory tract bleeding usually originates from the nose, nasopharynx, throat, and mouth. In this type of bleeding, inhalations of bloody secretions cause a cough reflex and may give the impression of hemoptysis in the form of coughing up blood. Intraoral bleeding is usually caused by psoriasis of the gums. Here the blood is mixed with saliva.

Since hemoptysis and pseudo hemoptysis are not always easily differentiated, a detailed history should be taken from all patients and a careful physical examination should be performed.

Table 2- Hemoptysis-pseudo-hemoptysis distinction

Clinical feature	**HEMOPTYSIS**	**PSEUDHEMOPTYSIS**
origin of blood	Respiratory tract	Oral cavity, larynx, esophagus, stomach,
Cough	More often	less often
respiratory symptoms	More often	less often
Esophagogastric symptoms	less often	More often
Alcohol use, liver disease	less often	More often
nausea, vomiting	less often	More often
Hematemesis, melena	less often	More often
The color of expectorated blood	bright red	brown or black
Intensity of expectoration	clotted or liquid	coffee grounds
Foaminess of expectoration	Generally	rare or absent
pH	alkaline	Acid
alveolar macrophage in sputum	yes	None
Food particles in the expectorator	None	Var

How much bleeding was in the anamnesis, is the bleeding fresh red, mixed with sputum, is it the first time or has it happened before, is there any bleeding from the nose, or gingival, are there signs of infection such as fever, at night sweats, weight loss, joint pain Do you have signs of chronic and/or systemic disease such as blood in the urine, rash, smoking, history of pulmonary, cardiac, renal or rheumatic disease, family or own hematological disease, history of tuberculosis, use of anticoagulant and antiplatelet drugs history, cocaine or other substance use, history of deep vein thrombosis or pulmonary embolism and risk factors, chemical exposure should be questioned.

In the physical examination, signs of respiratory failure such as tachypnea, cyanosis, and use of accessory respiratory muscles should be evaluated first.

Vital signs, condition of the patient, signs of bleeding in the upper respiratory tract, skin bruising, rash and telangiectasia (hereditary hemorrhagic telangiectasia or vasculitis, etc.), venous engorgement, peripheral edema, liver congestion, cachexia, lymphadenomegaly, abnormal heart sounds on auscultation, wheezing, rales should be examined for localized rhonchi.

Diagnostic tests;

- Radiological Imaging
  - Chest X-ray - Computed tomography
- Complete blood count, platelet
- Complete urine
- Renal functions
- Looking for ARB
- Serological tests
- Ventilation perfusion scintigraphy
- Echocardiography
- Bronchial arteriography
- Pulmonary angiography
- Bronchoscopy (Fiberoptic, Rigid)

Bidirectional chest radiography is the first examination to be requested. Lung X-ray; 33-82% may indicate the localization of bleeding, and 35% may indicate the underlying cause (tuberculosis or tumor). If the etiology cannot be identified, contrast-enhanced CT should be performed. Compared to traditional angiography, it is a more accurate choice if multidetector CT can distinguish bronchial and non-bronchial systemic arteries more accurately.

According to whole blood, coagulation, and inflammation parameters, routine biochemistry, and patient findings, tests such as d-dimer and autoantibodies should be requested. In case of insufficient thoracic CT, bronchoscopy should be performed. If there is no abnormality in CT, recurrent hemoptysis, or high-risk malignancy is suspected, if there is CT abnormality, therapeutic bronchoscopy should be performed to stop bleeding as well as for diagnostic purposes. Rigid bronchoscopy has advantages such as superior imaging, airway safety, adequate aspiration or cleaning of blood, clots, and debris, and better use of various therapeutic intervention devices. On the other hand, the fiberoptic bronchoscope is easy to find, can be used at the bedside, and can be easily applied to the intubated patient.

Treatment

Treatment management in hemoptysis is based on the amount of bleeding and the vital stability of the patient. Massive hemoptysis is a medical emergency that needs immediate evaluation and treatment. Death from hemoptysis is usually due to asphyxia, not blood loss. In addition to the severity of bleeding, lung reserve also plays a role in hemoptysis to such an extent that it obstructs the conductive airways of the patient and causes asphyxia and respiratory failure. Even a small amount of hemoptysis can cause asphyxia in a patient with chronic lung disease and limited lung reserve.

In the first evaluation; Whether there is a life-threatening situation or a life-threatening situation at any time, comorbidities and treatments that may be associated with hemoptysis should be evaluated.

First things to do in massive hemoptysis;

1. To prevent aspiration into the unaffected lung,

2. To stop the bleeding,

3. To treat the disease that causes bleeding.

In massive hemorrhages, the cases should be followed up in the intensive care unit. In order to prevent aspiration into the unaffected lung, the patient should be laid on his side with the bleeding side down, oxygen support should be provided, vital parameters should be monitored (saturation, blood pressure, arterial, etc.), and vascular access should be established.

All blood and secretions expected by the patient should be collected in order to monitor the patient's vital and hematological findings and determine the rate of blood and volume lost.

Volume loss should be completed and corrected if there is a coagulation disorder (blood, fresh frozen plasma transfusion, etc.).

Medical treatment;

-Tranexamic acid (transamine); is a synthetic lysine derivative that inhibits plasmin activation. Although it does not contribute to clot formation, it prevents clot disintegration. It is commercially available in 250 mg IV and 250-500 mg oral forms. It is used as 3X1 1 g IV, 3X500 mg orally, and 3X500 mg nebules with 5 cc saline. It is used in hepatic insufficiency, but the dose should be adjusted in renal insufficiency.

-codeine sulfate; 30-60 mg IM every 4-6 hours can be administered to suppress the cough reflex.

- In cases with high anxiety and agitation, midazolam 2-4 mg iv or 5 mg diazepam every 6 hours may be useful for sedation.

intubation;

If bleeding continues and asphyxia develops; The patient is intubated with an 8.5 mm or larger tube so that a bronchoscopy can be performed when necessary.

- If the lesion is in the trachea, selective intubation is performed.

- While left single-lumen intubation is recommended for right system bleeding,

- In left system bleeding, right single lumen intubation is not recommended as it will prevent right upper lobe aeration. In cases of left system bleeding, placement of the endotracheal tube in the trachea and obstruction of the left main bronchus with a balloon catheter from the outer part of the endotracheal tube or through the tube in front of the vocal cords are recommended.

bronchoscopy;

-Rigid bronchoscopy is preferred. Because with rigid bronchoscopy, aspiration of blood and clots can be achieved better, it also helps localization of the bleeding site, the major airways can be seen better and adequate ventilation can be provided. The disadvantage is that it requires general anesthesia.

-Fiberoptic bronchoscopy, which can be performed at the bedside in lower grade bleeding, can be selected to evaluate subsegment anatomy and especially upper lobe orifices.

Recently, it has been stated that while the patient is intubated with a double-lumen endotracheal tube and oxygenation is provided from one lumen of the tube using fiberoptic bronchoscopy, the bleeding site can be detected with FOB from the other lumen, and aspiration can be performed if necessary. This view has not found much support today.

If the chest X-ray is normal or if the bleeding side cannot be determined due to aspiration to the other side, an emergency bronchoscopy can be performed;

1- The bleeding site is determined

2- The formed coagulum is cleaned

3-Bleeding can be controlled by irrigating the bleeding area with adrenaline or cold water.

If the blood comes from the right bronchial system, single lung intubation can be performed on the healthy side with a Fogarty catheter under the guidance of a bronchoscope. This type of application is not recommended on the right side as it may obstruct the upper lobe bronchus. Wrong-side intubation or slippage of the tube can result in death.

Repetitive bronchial lavage with cold (+40 °C) isotonic liquid, administered topically with a bronchoscope, can stimulate local vasoconstriction and accelerate hemostasis. Adrenaline in 1/20.000 dilution (1 ml adrenaline + 19 ml saline), thrombin, and thrombin/fibrinogen solutions are also applied topically.

When bleeding cannot be stopped with these measures;

1- If the bleeding site is known; When the balloon-buffered catheter pushed through the bronchoscope with the endobronchial balloon tamponade method is inflated and fixed in the proximal part of the bleeding segment or subsegment bronchus, aspiration into the intact lung areas is prevented. The balloon should be deflated after 24 hours to prevent complications such as ischemia and post-obstructive pneumonia.

2- If the bleeding site is unknown; Bleeding should be tried to be controlled by performing unilateral lung ventilation with double-lumen catheters.

In intubated patients with massive hemoptysis, electrocautery, argon plasma coagulation, and Nd-YAG laser therapy, as well as photo resection and vaporization, can control bleeding and intervene in the endobronchial lesion.

However, in practice, bleeding can be controlled by irrigation of the bleeding segment with adrenaline solution or cold water without the need for many of these methods. The methods used in the treatment of massive hemoptysis are shown in Table 3.

Table 3- Bronchoscopic methods in massive hemoptysis

Topical treatments	Endobronchial treatments
Washing with cold saline (40) Adrenaline lavage (1:20,000 1-2 ml) Tranexamic acid Vasopressin Ornipressin, Terlipressin Thrombin-fibrinogen complex Oxidized regenerated cellulose	Fogarty balloon tamponade Endobronchial blocker Silicone plugs The thermal ablative technique (laser, APC, Electrocautery, cryotherapy) Endotracheal intubation

Bronchial Artery Embolization (BAE);

It is a minimally invasive and effective method. Especially in hemoptysis due to bronchial artery bleeding, bronchial artery embolization with polyvinyl alcohol, particles N-butyl cyanoacrylate glue, gelatin sponges, triacryl gelatin microspheres, and metallic coils selectively to the bleeding site is recommended. The full anatomy of the bronchial circulation should be determined by performing pulmonary angiography before the procedure.

6.5% spinal artery ischemia is the most important complication. Due to the recurrence risk of up to 30%;

1- In hemoptysis that cannot be stopped by conventional methods,

2- In those with bilateral disease,

3- It is applied in cases with limited respiratory functions and who cannot tolerate surgery.

Since massive hemoptysis mostly originates from the bronchial arteries, it is not recommended for bleeding originating from the pulmonary artery.

Radiotherapy;

-Compression due to edema in the perivascular tissue,

- Vascular thrombosis-forming effect is utilized.

It may be an option when surgical resection is contraindicated and BAE cannot be performed. It may be particularly useful in hemoptysis caused by tumors such as pulmonary angiosarcoma or hemangioendothelioma.

Surgical;

Indications

If the cause of massive hemoptysis is a localized lesion

• If complete resection is possible

• Failure to perform BAE or the continuation of bleeding despite being performed

• If it is thought that it would be a waste of time to try excessive bleeding and embolization that will disrupt hemodynamics.

• These are types of hemoptysis in which embolization is ineffective, such as pulmonary artery rupture and mycetoma.

Segmentectomy, lobectomy, or pneumonectomy can be performed by surgical thoracotomy. Up to 50% mortality has been reported in cases undergoing surgical intervention due to massive hemoptysis.

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