Risk factors and recurrence patterns in 203 patients with hemoptysis

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ÖZET

Hemoptizili 203 hastada risk faktörleri ve nüks olasılıkları

Hemoptizili hastanın tedavisi, özellikle masif hemoptizi gibi hayatı ciddi olarak tehdit eden durumlarda, hastanın stabilizasyonunu ve ivedi teşhisi gerektirir. Bu retrospektif çalışmada, hemoptizili hastalardaki etyolojilerin dağılımı, fiberoptik bronkoskopi (FOB)'nin bir teşhis aracı olarak yerini, masif hemoptiziyi ve hemoptizi nüksünü tahmin ettirecek potansiyel risk faktörleri irdelendi. Kliniğimize yatırılarak tetkik edilen 181'i erkek, 22'si kadın toplam 203 hemoptizili hasta retrospektif olarak irdelendi. Hemoptizili hastalarda en sık saptanan etyoloji 89 (%43.8) hasta ile tüberküloz iken, bunu 44 (%21.7) hasta ile akciğer kanseri, 11 (%5.5) hasta ile kronik bronşit izledi. Her ne kadar FOB hastaların çoğunda tanı sağlayabildi ise de, 31 (%15.3) hastada herhangi bir endobronşiyal patoloji saptanmadı. Toplam 29 (%14.3) hastada nüks hemoptizi saptandı ve ilk hemoptizinin beş günden fazla sürmesi, ikinci hemoptizinin oluşması için bir risk faktörü olarak belirlendi (p= 0.02). Çoklu değişkenli analiz sonucu, akciğer kanseri varlığı, hemoptizinin tekrarlaması için negatif bir belirleyici olarak bulundu (p= 0.034). Toplam 22 (%10.8) hastada ağır hemoptizi gelişti ve bu olgular medikal olarak tedavi edilebildi. Tüberküloz, akciğer kanseri ve ağır sigara içiciliği, hemoptizi gelişimi açısından bağımsız risk faktörleri olarak belirlendi (p= 0.016, 0.001, 0.041). Hemoptizi, her zaman kanama yerini ve etyolojiyi belirlemek için FOB ile inceleme gerektiren önemli ve sık görülen bir semptomdur. Beş günden fazla süren ve akciğer kanseri nedeniyle oluşan hemoptizi nüks kanamayı işaret eder, daha sık ve yakından takip gerektirir.

Anahtar Kelimeler: *Hemoptizi, tıbbi tedavi, nüks, akciğer kanseri, tüberküloz.*

SUMMARY

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Management of hemoptysis requires prompt diagnosis and patient stabilization especially in massive hemoptysis as a potentially life-threatening condition. This retrospective study was designed to determine the etiologic distribution of hemoptysis, the role of the fiberoptic bronchoscopy (FOB) as a diagnostic tool, and to clarify potential risk factors for massive hemoptysis and recurrences. A total of 203 patients (181 male, 22 female) with hemoptysis admitted to our hospital were evaluated retrospectively. Tuberculosis was the leading cause of hemoptysis (n= 89; 43.8%) followed by lung cancer (21.7%) and chronic bronchitis (n= 11; 5.5%). FOB plays an essential role for localization of bleeding and diagnosis, although no bronchoscopic abnormality was found in our 31 patients (15.3%). Twenty-nine of the patients (14.3%) had recurrent hemoptysis and hemoptysis lasting longer than five days was found as a risk factor for recurrences (p= 0.02). Having lung cancer was an independent negative risk factor for recurrent hemoptysis using multivariate analysis (n= 44; p= 0.034). Twenty two of the patients (10.8%) had severe hemoptysis and managed medically. In our study, tuberculosis, lung cancer and heavy cigarette smoking were revealed as independent predictors of massive hemoptysis (p= 0.016, 0.001, 0.041 respectively). Hemoptysis is a common respiratory symptom that always requires investigation by using FOB and radiography in order to determine exact site of bleeding and etiology. Hemoptysis continuing more than five days and lung cancer diagnosis may indicate recurrent bleeding and need more attention.

Key Words: *Hemoptysis, medical management, recurrence, lung cancer, tuberculosis.*

In the beginning of last century, hemoptysis was patognomonic of advanced pulmonary disease (1,2). Nowadays, lung cancer and tuberculosis are the most frequent causes in our country (3). For majority of the patients, blood spitting or blood present in the sputum constitutes a worrying symptom rarely taken lightly. When it is massive, patient's life is threatened and emergency admission in intensive care unit must be achieved. In order to reduce mortality and morbidity rates, a multidisciplinary approach associating the endoscopic pneumologist, the interventional radiologist and thoracic surgeon is of utmost importance.

Although, conservative and surgical approaches have been defined and discussed in the literature in detail, there is little information regarding relationships between clinical and pathological parameters in hemoptysis patients which could help to navigate through appropriate management in a patients with hemoptysis (4-7).

MATERIALS and METHODS

We evaluated 203 consecutive patients presenting with hemoptysis from 2000 to 2005. Workup and results were reviewed. All patients underwent chest radiography. A chest computerized tomography (CT) and bronchoscopy were performed at the discretion of the evaluating pulmonary physician. All bronchoscopic examinations were performed with a fiberoptic instrument in standard fashion. Endobronchial and transbronchial biopsies were performed when indicated, and all specimens were routinely examined for cytology and microbiology. Hemoptysis of unknown origin was defined as endoscopic examination and imaging study findings and no significant abnormalities found on all submitted specimens.

According to amount of hemoptysis per day, the patients were divided into four groups: 1. "mild": only streaking of sputum or less than two tablespoons (< 30 mL); 2. "moderate": 30-100 mL; 3. "severe": 100-600 mL; 4. "massive": > 600 mL (3).

Patients' assessment was conducted using the same procedure but was guided by seriousness of the situation. The main objectives of treatment were to prevent asphyxiation, to localize the site of bleeding, to stop the hemorrhage, to examine the etiology of hemoptysis, to treat the underlying pathology, and to avoid the recurrence of hemoptysis indefinitely. Therapeutic means used were: Pulmonary isolation, diagnostic bronchoscopy, arterial embolization, surgical treatment and medical treatment. Those means were adopted to the cause of the hemoptysis, which was supposed by the past medical history and clinical examination of the patients and confirmed by chest roentgenogram, fiberoptic bronchoscopy (FOB) and chest CT. Medical treatment included rest in bed, insertion of a wide bore intravenous cannula, monitoring oxygen saturation, antitussives (qid), aminocaproic (qid) acid in all patients. Baseline hematology, biochemistry, and clotting test were obtained. Collected sputa were stained for bacteria and acid-fast bacilli.

Arterial embolization was performed by a Seldinger technique through femoral access. An emergency surgical treatment was applied when the site of bleeding was localized, the indication of pulmonary resection justified and the other means of treatment having failed. The surgical treatment was postponed as far as possible after cessation of bleeding using the other means of treatment. It was only considered when the patient had sufficient pulmonary reserve and when the bleeding source was clearly identified. When the surgical treatment was not possible (poor pulmonary function or diffuse lesions), the patient was informed about the possible recurrence of hemoptysis even after a successful arterial embolization.

In case of massive acute bleeding, isolation of the bleeding lung from the healthy one was achieved by the use of rigid bronchoscope done at the thoracic surgery unit. In that case, the choice between operation and non-surgical treatment was taken after clinical and radiologic evaluation. Informed consent was not required because it was an retrospective observational study. The variables including age, sex, total cigarette smoking (pack.year), amount of hemoptysis, duration of hemoptysis, number of episodes of hemoptysis, findings on chest CT, bronchoscopic findings, duration (days) between first hemoptysis and bronchoscopy were evaluated.

Data were expressed as mean, number or percentages. Data analyses were made using SPSS software for Windows 10.0 packages (SPSS, Chicago, IL, USA). The Pearson Chi-squared test was used to ascertain the significance of association between two categorical variables. Potential risk factors for a complication were identified by univariate logistic regression analysis. The cut-off level for statistical significance was $p< 0.05$.

RESULTS

Within the reviewed period, 203 patients were evaluated for hemoptysis and all charts were available for reviewed. One hundred eighty-one (89.2%) patients were male, and 22 (10.8%) patients were female (Table 1). The mean age was 45.5 years (SD, 17.0, ranging from 16 to 81 years). Most patients (n= 131; 64.5%) had mild hemoptysis followed by severe hemoptysis (n= 32; 15.8%) (Table 1). Twenty-nine patients (14.3%) had a previous episode of hemoptysis. The majority of previous attacks of hemoptysis were mild. These attacks were managed medically.

Table 1. Demographic features of the patients with hemoptysis.

Features	Data
Male/female	181/22
Mean age (SD) years	45.5 (17.0)
Smokers, No (%)	162 (79.8)
Amount of hemoptysis No (%)	
Mild	131 (64.5)
Moderate	31 (15.3)
Severe	32 (15.8)
Massive	9 (4.4)
Episode of hemoptysis No (%)	
1	174 (85.7)
2	29 (14.3)
Mean duration of hemoptysis (SD) days	6.7 (5.4)

In 190 patients (93.6%) a source and etiology for bleeding could be identified using after diagnostic workup (Figure 1). Tuberculosis was found to be the most frequent cause of hemoptysis. Table 2 showed the roentgenographic findings of the patients. Most patients (n= 46; 22.7%) were found to have cavity. However, 15 patients showed no abnormality on radiographies.

One hundred twelve patients (55.2%) underwent FOB. Table 3 showed bronchoscopic findings of the patients. The most frequent bronchoscopic finding was endobronchial lesion recorded in 32 patients (28.6%). However, no endoscopic abnormality was seen in 31 patients (27.7%). In these patients, a diagnosis was made using sputum examination (i.e., acid-fast bacillus and/or culture for *Mycobacterium tuberculosis*, cytologic examination of sputum) or trans-thoracic fine needle aspiration or transbronchial fine needle aspiration.

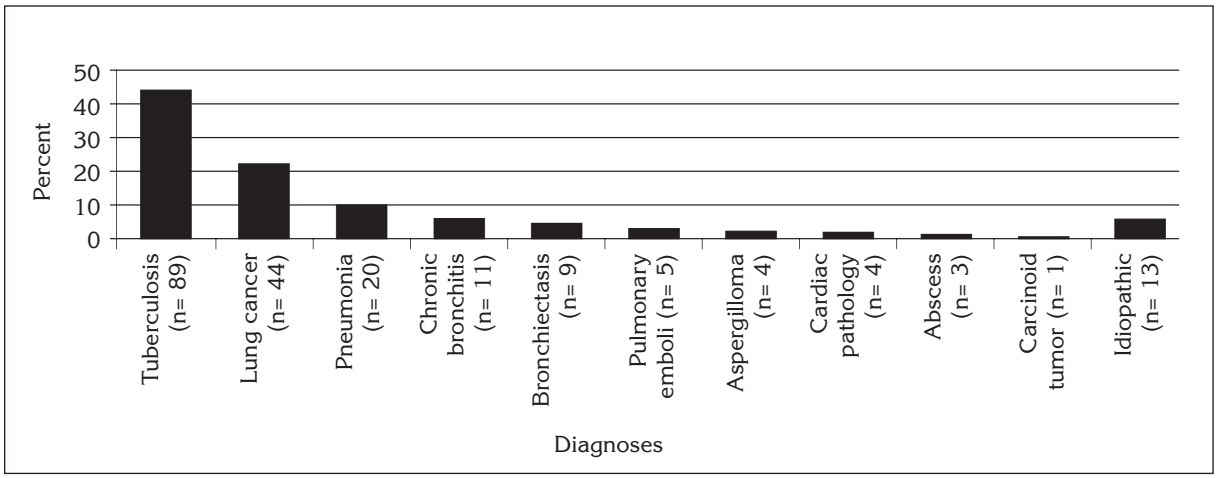

Figure 1. Diagnoses in patients with hemoptysis (n= 203).

Table 2. Roentgenographic findings is 203 patients.

Radiographic feature	Number (%)
Cavity	46 (22.7)
Patchy infiltration	32 (15.8)
Mass	31 (15.3)
Consolidation	18 (8.9)
Interstitial fibrosis	14 (6.9)
Bronchiectasis	10 (4.9)
Hydrothorax	8 (3.9)
Atelectasis	5 (2.5)
Cavity with fungus ball	2 (1.0)
Ground-glass opacity	1 (0.5)
Normal	15 (17.2)

Table 3. Bronchoscopic features of patients (n= 112).

Findings	Number (%)
Endobronchial lesion	32 (28.6)
Hyperemic bronchus	16 (14.3)
Bleeding into bronchus	14 (12.5)
Circumferential narrowing	7 (6.3)
Endobronchial coagulum	5 (4.5)
Fragile bronchus	4 (3.6)
Endobronchial mass	1 (1)
External compression to bronchus	1 (1)
No endoscopic abnormality	31 (27.7)

Multivariate analysis using forward logistic regression identified tuberculosis, pulmonary carcinoma and heavy cigarette smoking (> 40 pack.year) as independent predictors of massive hemoptysis (p= 0.016, 0.001, 0.041 respectively). Other parameters had no predictive power on massive hemoptysis.

There were 29 patients (14.2%) who developed recurrent hemoptysis. Having lung cancer was an independent negative risk factor for recurrent hemoptysis using multivariate analysis (p= 0.034). Univariate analysis indicted that, hemoptysis lasting more than five days has a statistically significant predictive power for second hemoptysis(p= 0.02). Figure 2 showed the diagnoses of the patients with recurrent hemoptysis.

Twenty patients had normal radiographic evaluation(i.e., plain radiography and CT). In these patients, bleeding site was discovered via bronchoscopy in 16 patients (80%). A total of 116 patients underwent a FOB examination. No pathologic finding was noted in 32 patients (27.6%). A subset analysis of these patients indicated that, there was no radiologic abnormality in 8 patients (25%). Four patients were referred to bronchial arterial embolization. The procedure was done as described in Methods section.

DISCUSSION

Hemoptysis remains a distressing symptom and, at times, a challenging diagnostic problem. Clear guidelines for the initial work-up in pati-

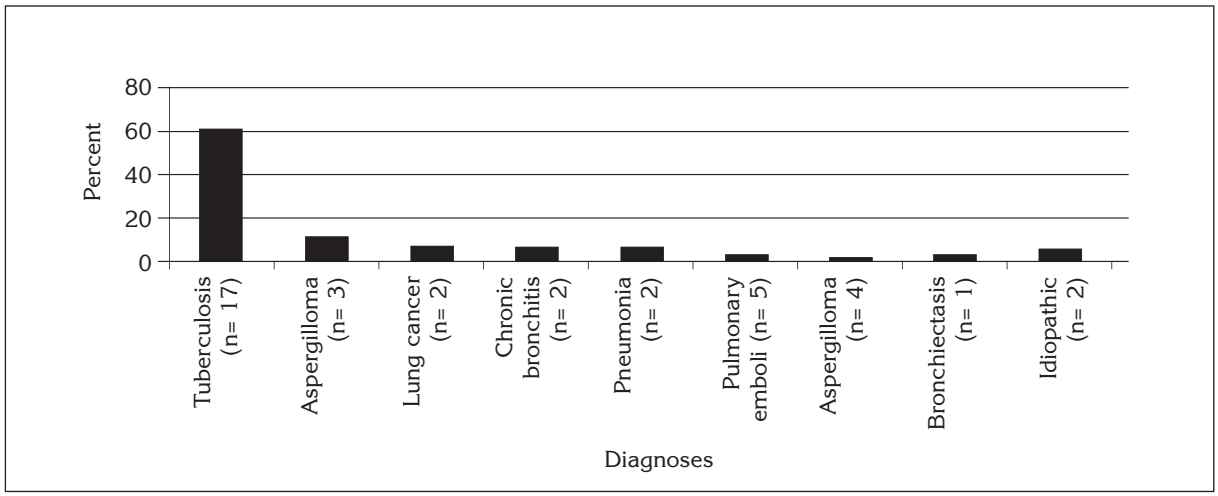

Figure 2. Diagnoses in patients with recurrent hemoptysis (n= 29).

ents without a definitive diagnosis are missing. The etiology for hemoptysis may vary depending on geographic location, and infections such as tuberculosis play a significant role in developing countries (5-7).

Hemoptysis occurs as a presenting symptom in 9 to 57% of patients with lung cancer (6,8,9). Since massive bleeding is caused by erosion of the tumor into a major vessel, such as the pulmonary artery or even the aorta, it was reported that approximately 50% of patients with massive hemoptysis due to lung cancer died compared to 28% from other causes (10).

Bronchoscopy plays an integral part in managing massive hemoptysis in diagnosis and treatment. In our study, only patients with confirmed active pulmonary tuberculosis did not undergo fiberoptic bronchoscopy. Numerous bronchoscopic findings ranging from external compression to endobronchial vegetative lesion were noticed. However, no bronchoscopic abnormality was found in 31 patients (27%). For this reason, although, bronchoscopy plays a pivotal role in diagnosis of hemoptysis patients, other diagnostic tools could have diagnostic role in a considerable fraction of hemoptysis patients.

In our series, most patients with hemoptysis (n= 89; 43.8) had pulmonary tuberculosis. It was followed by lung cancer (n= 44; 21.7%) and chronic bronchitis (n= 11; 5.5%). Hirsberg and colleagues reported similar disease distribution whereas Callis stated that bronchiectasis was most frequent cause of hemoptysis (11,12).

In our study, we found that, tuberculosis, pulmonary carcinoma and heavy cigarette smoking (> 40 pack.year) as independent predictors of massive hemoptysis. Massive bleeding into the airways is an imminent threat to life because asphyxiation occurs as the tracheobronchial tree fills with blood. Exsanguination itself is rarely the cause of death (12). For this reason, prediction of massive hemoptysis could be helpful for adequate patient management. The patients with known tuberculosis, lung cancer or heavy smoker cases must be observed closely and interventional treatment such as embolization or surgical resection should be planned earlier. In the literature, no predictive data was given.

In 13 patients (6.3%) no etiology was found for hemoptysis by using FOB and radiographic examination. However, these patients did not underwent surgical resection and theoretically, a fraction of 'idiopathic' hemoptysis could have had undetermined occult pulmonary pathology. Herth and colleagues indicated that, lung cancer was diagnosed in the patients with hemoptysis of unknown origin (13). However, a number of patients remained undiagnosed despite all efforts and long-term follow-up. Interestingly, the entity 'pulmonary hemorrhage syndrome' was designated in a number of patients who underwent resectional surgery (14). However, the de-

finition of 'pulmonary hemorrhage' could be limited to the presence of blood in alveoli. Pathologically there was hemorrhagic alveolitis (14).

Hemoptysis lasting longer than five days was found to be risk factors for recurrent hemoptysis. For this reason, the patients with these factors must be followed more closely and invasive and/or non-invasive measure to prevent recurrence must be taken. However, patients with lung cancer less likely develop recurrent hemoptysis. It is probably attributable to dismal prognosis of these patients. It can be speculated that, they died before recurrent hemoptysis would develop because of advanced stage.

The exact site of bleeding is not always easy to find. No endobronchial pathology was found in 27.7% of the patients who underwent bronchoscopic examination. Of these, 25% of patients had no abnormality seen on CT or roentgenogram. We recommend following these patients closely.

FOB as an important diagnostic tool in hemoptysis patients showed various abnormalities in the bronchial system. 'Endobronchial lesion' was most frequent bronchoscopic pathology recorded in our patients (6,7,12,15). It was probable attributable the higher percentage of lung cancer patients in this series.

In conclusion, lung cancer and tuberculosis have been major causes of hemoptysis. Heavy smoking and these pathologies indicated a more profuse hemoptysis and the patients having these factors should be monitored closely and evaluated with surgical department when admitted. In addition, hemoptysis continuing more than five days and a diagnosis of lung cancer may indicate recurrent bleeding and deserves utmost attention.

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