



Case report

Clinical characteristics and treatments for bronchial Dieulafoy's disease

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ABSTRACT

Background: Dieulafoy's disease of the bronchus is an arterial abnormality characterized by enlarged mucosal arterial branches that are susceptible to lethal bleeding. To date, this disease is rarely reported in the literature. We recently encountered three patients from February 2010 to March 2017, each with such a vascular anomaly in a bronchus with massive hemoptysis.

Aim: This paper describes the clinical characteristics and treatments for Dieulafoy's disease.

Methods: We report three cases with recurrent massive hemoptysis. Bronchoscopic examination was performed on two patients, one with a non-pulsating polypoid nodule and the other without. One patient had fatal bleeding after biopsy and could not withstand bronchial artery embolization or thoracotomy. Angiography and bronchial artery embolization on another two patients successfully stopped the bleeding. In addition, we retrospectively reviewed the literature on all reported cases with cryptogenic hemoptysis, obtained through PubMed and Chinese journal searches.

Results: The intervention with embolization was successful, and no new episodes of acute hemoptysis were observed.

Conclusion: Angiography can be used for diagnosis of Dieulafoy's disease of the bronchus, whereas bronchoscopy biopsy should be avoided. Interventions such as embolization or bronchial coagulation play an important role in patients with coughing with massive hemoptysis.

1. Introduction

Dieulafoy's disease of the bronchus is an extremely uncommon but potentially fatal cause of substantial bronchial bleeding. Dieulafoy lesions are rare in the bronchus and were first described in the gastrointestinal tract [1]. The disease is characterized by submucosal arterial dilatation or abnormal arterial rupture. Less than 50 cases of bronchial Dieulafoy's disease have been reported. In this article, we describe three cases treated in our hospital. To improve understanding of bronchial Dieulafoy's disease and more important to avoid lethal hemoptysis, the current state of diagnosis and treatment of bronchial Dieulafoy's disease is described.

2. Case report

2.1. Case 1

An 18-year-old female patient was admitted to our hospital on

March 9, 2017 after 3 days of hemoptysis. The patient had experienced frequent episodes of hemoptysis for 4 years prior to this. The patient denied a history of smoking and illicit drug use. Four years earlier, the patient had frequent but less severe episodes of hemoptysis, which typically ensued after an upper respiratory tract infection. Bronchoscopy showed a nodule at the entrance to RB10 (Fig. 1). We tried to make a biopsy but the nodule was easy to bleed. Endoscopic hemostatic, opening venous access and intravenous drug administration were rapidly performed, the blood from the nodule stopped. The total amount of bleeding was about 300 mL. Because of the massive hemoptysis, the pathological specimen is not ideal. The nodule were still taken into account for possible vascular malformation, however, the patient regretted the continued examination. The hemoptysis stopped spontaneously after anti-infection and hemostatic therapy.

However, the most recent episode had occurred after an upper respiratory tract infection 3 days earlier. The patient coughed up approximately 100 mL of fresh blood in an episode of hemoptysis, and this symptom was alleviated by anti-tussive and anti-infective treatment in

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Fig. 1. Bronchoscopy showed a nodule at the entrance to RB10.

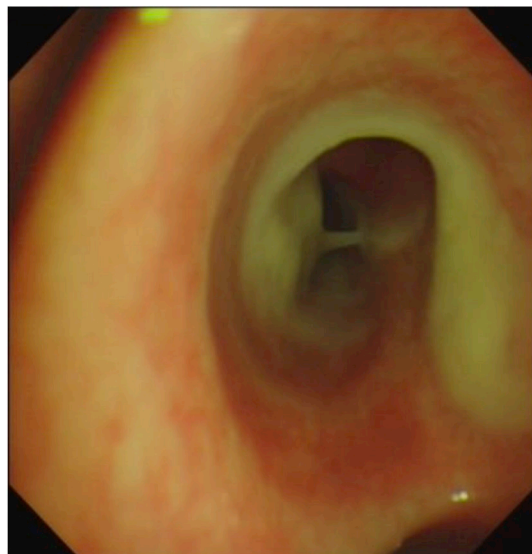


Fig. 3. Purulent yellow secretions in the right bronchus observed using bronchoscopy.

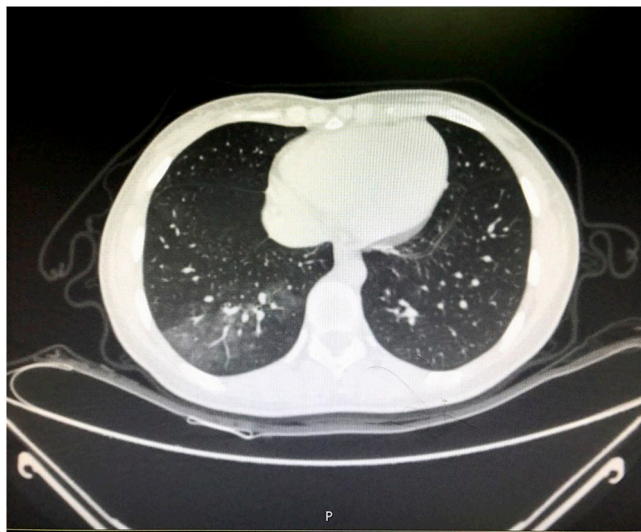


Fig. 2. CT scan showing ground-glass opacity at the lower lobe of the right lung.

another hospital. After the patient was admitted to our hospital, a physical examination revealed signs of rhonchi and reduced breath sounds. A diagnostic workup revealed no evidence of coagulopathy. Computed tomography (CT) scans revealed ground-glass opacity at the lower lobe of the right lung, combined with clinical manifestations of alveolar hemorrhage (Fig. 2). Bronchoscopy showed purulent yellow secretions without nodules in the right bronchus (Fig. 3). Because of a suspicion of Dieulafoy's disease of the bronchus, digital subtraction angiography (DSA) was performed, which demonstrated a tortuous right bronchial artery (Fig. 4). A diagnosis of Dieulafoy disease of the bronchus was considered. Because blood vessels are considered to be the culprit of hemoptysis, selective arterial embolization was performed. No new episodes of acute hemoptysis were observed, and the patient was still being followed up at the time of writing this report.

2.2. Case 2

Another case is a 72-year-old female, who presented with cough and abundant blood expectoration. In the previous years, the patient had frequent but less severe episodes of upper respiratory tract infections. CT scans showed right middle lung atelectasis and lower lobar bronchiectasis with infection (Fig. 5).

In the right lower lobe anterior basal branch, we observed a small uplifted mucosal lesion with a smooth surface without pulsation or any



Fig. 4. Right tortuous bronchial artery on DSA.

blood vessel shadows using bronchoscopy (Fig. 6). Because the submucosal nature was unknown, and we could not exclude submucosal tumor infiltration, biopsy specimens were taken. The patient immediately experienced massive bleeding during the biopsy. Endoscopic hemostatic, opening venous access and intravenous drug administration were rapidly performed, but the blood flow continued despite negative pressure suction. Because of restlessness, chest discomfort and self-extubation, the patient could not cooperate with the inspection, struggled to sit up and expectorated a large quantity of blood. The total amount of bleeding was expected to exceed 1000 mL. We immediately performed supine, bronchoscopic tracheal intubation and continued to draw blood.

After these treatments, the patient was sent to the intensive care unit (ICU). The results of repeated examination of the platelet count and coagulation factors were approximately normal. During the three-day hospitalization, the patient experienced rapid bleeding and finally died of respiratory failure. The main characteristics of the patient were a small bulge on the bronchial mucosa and fatal bleeding during bronchoscopic biopsy. Owing to the patient's critical condition,



Fig. 5. Right middle lung atelectasis and lower lobar bronchiectasis with infection on CT scan.

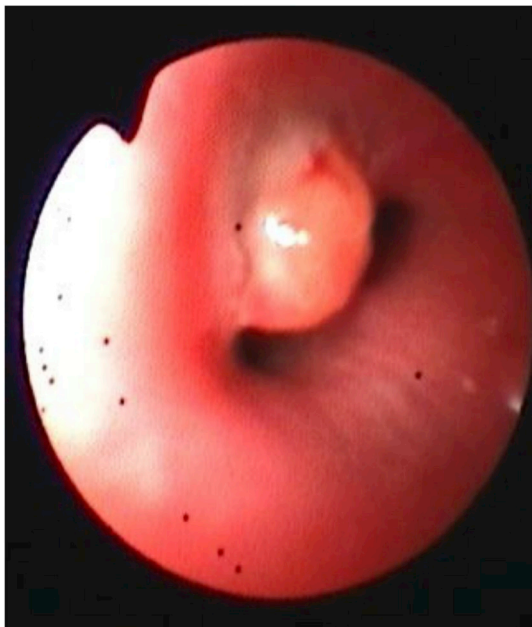


Fig. 6. A small uplifted mucosal lesion with a smooth surface without pulsation or any blood vessel shadow observed using bronchoscopy.

bronchial arteriography and thoracotomy were deemed intolerable and were not performed. However, according to the clinical features of this patient, Dieulafoy's disease was considered.

2.3. Case 3

A 38-year-old man presented with a 23-year history of recurrent hemoptysis. He had a history of hypertension. On the day of admission, he had coughed up approximately 400 mL of fresh blood and had recovered after hemostatic drug therapy in other hospital. He was a non-smoker and had been treated for left pulmonary bronchial artery malformation 10 years earlier. There were no other associated symptoms. At the time of admission, the clinical examination was normal. The patient's hemoglobin level was 123 g/L. A chest X-ray demonstrated left lobe opacities suggestive of pneumonia (Fig. 7). A CT scan of the chest showed diffuse grinding glass density in the left lung, thus suggesting a possibility of bleeding. The left main bronchus and its branches were not patent, possibly because of clots or secretions caused by blockage

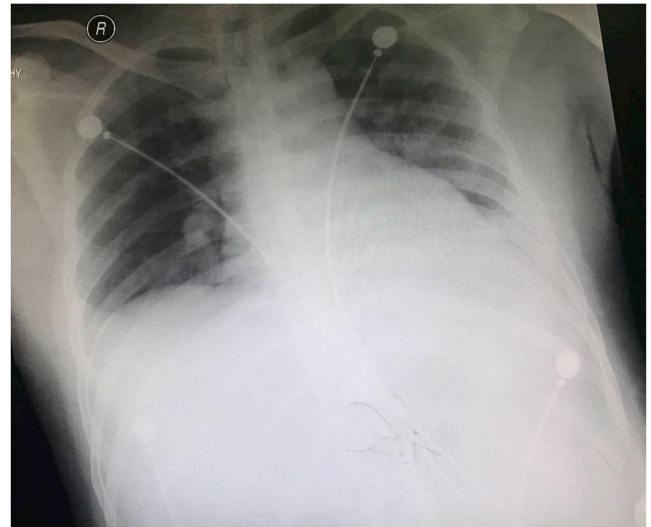


Fig. 7. Left lobe opacities suggestive of pneumonia using X-ray.

(Fig. 8). Moreover, the left bronchial artery was abnormal and uneven in thickness. A local tumor-like dilatation of the left bronchial artery was found (Fig. 9).

No fiber optic bronchoscopy biopsy was taken, because of the suspicion of Dieulafoy's disease and the risk of bleeding. We performed left bronchial artery embolization using microparticles, and it was successful (Fig. 10). No further episodes of acute hemoptysis occurred during the two-year follow up.

3. Discussion

3.1. Epidemiology

In 1898, Dieulafoy first reported a superficial gastric ulcer for vascular malformations that later became known as Dieulafoy's disease [2]. The disease commonly appears in the digestive tract, and Dieulafoy's disease of the bronchus has rarely been reported. Perhaps because of the difficulty of diagnosis, less than 50 cases have been reported (Table 1). In recent years, owing to an improved understanding of the disease and progress in examination technology, the reports increased

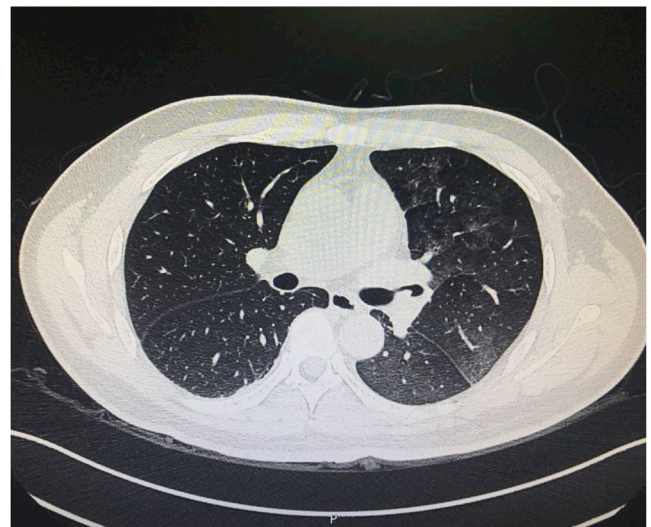


Fig. 8. CT scan showing diffuse grinding glass density in the left lung, suggesting the possibility of bleeding. The left main bronchus and its branches were not patent, thus suggesting clots or secretions caused by blockage.



Fig. 9. The left bronchial artery is abnormal and uneven in thickness. A local tumor-like dilatation of the left bronchial artery can be seen on the CT scan.

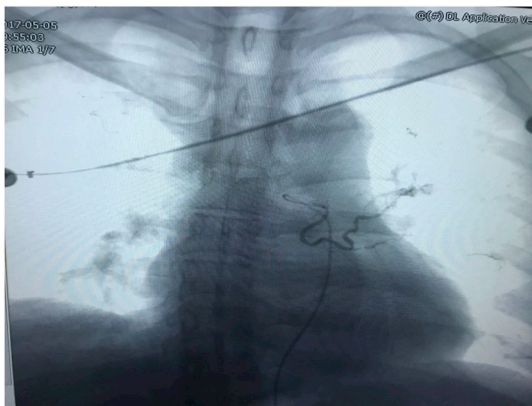


Fig. 10. Left tortuous bronchial artery observed using DSA.

annually. However, because most cases still require surgery or autopsy to be diagnosed, the incidence may still be underestimated.

3.2. Pathogenesis

At present, no systematic study on pathogenesis and the risk factors of Dieulafoy's disease has been reported [3]. The specific pathogenesis and risk factors remain inconclusive and may be related to congenital vascular malformation, chronic inflammation and injury.

There is limited literature on the pathogenesis of Dieulafoy's disease. Dieulafoy's disease of the bronchus is a bronchial artery

abnormality, and bronchial submucosa dilation or abnormal artery rupture hemorrhage are considered the pathological features of the disease. The blood supply arteries do not gradually become smaller and form capillaries when they enter the submucous membrane. Instead, their diameter remains unchanged, and they protrude into the lumen [3].

Acute massive bleeding is caused by rupture or spontaneous rupture due to external factors. A much debated question is whether hypertension, diabetes, cardiovascular disease or other confounding factors may be involved. The patients described in previous studies (Table 2) include 14 cases with smoking history, 5 cases with pulmonary tuberculosis, 2 cases with chronic obstructive pulmonary disease, 1 case with asthma, 1 case with renal failure, 1 case with ischemic stroke and 2 cases with hypertension. Hypertension and inflammation in the lungs seems to be associated with an elevated risk of morbidity and mortality in persons with Dieulafoy lesions. Under conditions of high blood pressure or inflammatory stimulation, twisted arteries with constant diameter are prone to sclerosis. Padilla-Serrano et al. have suggested that massive hemoptysis may be related to smoking history, because long-term tobacco consumption causes chronic airway inflammation [4]. With increasing patient age, the self-repair ability and the vascular wall compliance decrease. As a result, the blood vessels rupture more easily. However, these results were based on data from more than 30 years ago, and the associations between confounding factors and Dieulafoy lesions are difficult to trace.

3.3. Clinical features

According to our literature review, the main characteristics of the population ($n = 48$) are shown in Table 2. Most patients were male ($n = 28$), the age ranged from 13 to 72 years, and most patients had middle-age onset. Fourteen patients were current or ex-smokers. Most of the lesions appeared in the right airway ($n = 29$), especially the lower right lung ($n = 16$). Common clinical manifestations were hemoptysis, progressive dyspnea, chest pain, cough and fatigue.

3.4. Radiology

Conventional chest X-ray and CT examination can reveal hemorrhage. Liu Yanhong et al. have reported six cases, three of which demonstrated pulmonary effusion in the hemorrhagic lobes [5]. Bronchoscopic manifestations occur mainly in small mucosal protrusions several millimeters wide and high. As case 2 very clearly demonstrates, it is important to identify this kind of lesion. The top surface of the mucosa shows white visible protrusions and no pulsation. Such lesions are difficult to find, because the surrounding mucosa may be normal or slightly congested, or the airway cavity may be filled with blood, owing to the mucosa biopsy. Generally, we try to perform biopsy because of a suspicion of submucosal tumor invasion. Mucosal biopsy primarily reveals chronic inflammation but poses a great risk of fatal bleeding [6,7]. Angiography and thoracic vascular CTA (bronchial and pulmonary arterial remodeling) are helpful in lesion diagnosis and can reveal abundant blood vessels, artery dilation, malformation and hemorrhage.

3.5. Pathology

The diagnosis depends on pathological examination. Postoperative pathology or autopsy can indicate artery malformation in the bronchial mucosa. Gurioli et al. performed a biopsy to evaluate lesion pathology via rigid bronchoscopy with endobronchial ultrasound [8]. However, because of the high risk of biopsy bleeding, most cases do not have a definite pathological diagnosis. Bronchoscopy and bronchial-pulmonary angiography are important in diagnosis of this disease [9].

Table 1
Clinical features of bronchial Dieulafoy's disease.

Case	First Author	Age	History	Sex	Electrocautery	YAP laser	APC	Treatment			Follow up (month)	Location	Smoking History
								Embolization	Surgery	Medicine			
1	A. Padilla-Serrano	49	COPD	F	-	-	-	Success	-	-	-	RUL	Y
2	Savvas	47	-	M	-	-	-	Success	-	-	-	RLL	Y
3	Hadjiphilippou Oormila Ganganah	13	-	M	-	-	-	Failure	Success	-	3	RLB	N
4	Levent Dalar MD	28	-	M	-	-	Success	-	-	-	2	LUB	Y
5	Antoine Parrot	38–69	Tuberculosis	M	-	-	-	Failure	Success	-	-	-	Y
6	Antoine Parrot	38–70	Hypertension	M	-	-	-	Failure	Success	-	-	-	Y
7	Antoine Parrot	38–71	Hypertension	M	-	-	-	Failure	Success	-	-	-	Y
8	Antoine Parrot	38–72	Ischemic stroke	M	-	-	-	-	Success	-	-	-	Y
9	Antoine Parrot	38–73	-	M	-	-	-	-	Success	-	-	-	Y
10	Antoine Parrot	38–74	-	F	-	-	-	-	Success	-	-	-	Y
11	Antoine Parrot	38–75	-	F	-	-	-	-	Success	-	-	-	Y
12	Jianfeng Zhang	61	-	F	-	-	-	-	-	-	3	LUL	Unknow
13	Weijian Leng	63	-	F	-	-	-	Success	-	-	-	LP	Unknow
14	Ting Ge	64	-	F	-	-	-	Success	-	-	48	LP	Unknow
15	Ting Ge	45	-	F	-	-	-	Success	-	-	48	LP	Unknow
16	Baosong Xie	28	-	F	-	-	-	-	-	Success	60	LLL	Unknow
17	Yanhong Liu	18	-	F	-	-	-	Failure	Success	-	60	RLL	Unknow
18	Yanhong Liu	23	-	M	-	-	-	-	-	Success	-	LUL	Unknow
19	Yanhong Liu	31	-	M	-	-	-	Success	-	Failure	12	RLL	Unknow
20	Yanhong Liu	33	-	F	-	-	-	Success	-	Failure	13	RLL	Unknow
21	Yanhong Liu	36	-	F	-	-	-	Success	-	Failure	14	RLL	Unknow
22	Yanhong Liu	47	-	F	-	-	-	-	-	Success	31	RML	Unknow
23	Ruihong Yang	41	-	M	-	-	-	-	Success	-	6	RML	Unknow
24	Ruihong Yang	36	-	M	-	-	-	-	-	Failure	Death	RML	Unknow
25	Ruihong Yang	61	-	M	-	-	-	-	Success	-	60	RUL	Unknow
26	Wei Wan	19	-	M	-	-	-	Success	-	-	12	RML	Unknow
27	Jianyong Zhu	23	-	M	-	-	-	Success	-	-	6	RLL	Unknow
28	Haiyang Hu	62	-	M	-	-	-	-	Success	-	-	RML	Unknow
29	Dong Ding	70	-	M	-	-	-	Success	-	-	6	RLL	Unknow
30	Sheth HS	51	Alagille syndrome/CKD 4	F	-	Success	-	-	-	-	24	LLL	N
31	Sheth HS	72	Follicular thyroid carcinoma	M	-	Failure	-	First time fail, another success	-	-	6	RMB	Y
32	Stoopen E	51	Paravertebral neurilemoma	M	Failure	-	-	-	Success	-	-	RML	Unknow
33	Wadji MB	16	-	F	-	-	-	-	Success	-	9	RLL	N
34	Danrong Yang	60	-	F	-	-	-	Success	-	-	12	Trachea	Unknow
35	Karan Madan	26	-	M	-	-	Success	-	-	-	6	RLL	N
36	Ben Smith	30	-	M	-	-	-	-	Success	-	22	RLL	N
37	Praveen Bhatia	42	Tuberculosis	M	-	-	-	Success	-	-	24	RUL/LUL	Y
38	T S van der Werf	70	Tuberculosis/ COPD/pneumonia	M	-	-	-	-	-	Failure	Death	LUL	Unknow
39	Yu Fang	15	-	M	-	-	-	Failure	Success	-	5	RLL	N
40	Emanuela E Barisione	57	-	F	-	-	-	Success	-	-	-	RMB	N
41	M Sweerts	35	Upper respiratory tract infection	F	-	-	-	Failure	Success	-	4	RLL	N
42	M Sweerts	59	-	M	-	-	-	-	Success	-	-	RLL	Y
43	Francesca D'Souza	63	-	F	-	-	-	Success	-	-	Death	RMB	Unknow
44	Yeh Rim Kang	74	-	M	-	-	-	Failure	Success	-	-	RLL	Unknow
45	C. Gurioli	65	Asthma/prostatic cancer	M	-	-	-	-	-	Success	-	RLL	Y
46	In Je Kim	69	Tuberculosis	F	-	-	-	-	Success	-	-	RUL	Unknow
47	Jinhua Zhou	66	Tuberculosis	F	-	-	-	Failure	Success	-	7	RML/RLL	Unknow
48	Ruirong Yang	65	COPD	M	-	-	-	-	Success	-	12	LUL	Unknow

3.6. Treatment

The bleeding occurs from the artery system, sometimes quite rapidly, and is difficult to stop through medical treatment. Sheth et al. (2018) attempted Dieulafoy lesion ablation with an Nd:YAP laser in two cases [3], and the first case was successfully ablated. Selecting a vessel that is visible and accessible to ablative energy is crucial. Other ablative tools also have been successful in ablation of Dieulafoy lesions of the bronchus, such as argon plasma coagulation (APC) [10,11]. The mechanism of APC is that the blood is quickly coagulated locally at the

proximal end of the bleeding bronchus, so that the immediate hemostatic effect could be achieved. In case 2, by reconsideration, the patients could be given a unilateral lung intubation using a standard endotracheal tube to ensure ventilation and oxygenation. Blood and secretions in the airway could be cleared by rigid bronchoscopy and then treated with APC. Our hospital does not have the APC, but the hospitals with APC are suggested to have a try. Madan K et al. suggested that rigid bronchoscopy was useful in the management of massive hemoptysis and it can be difficult to control a massively bleeding airway with flexible bronchoscopy [12]. Compared with soft bronchoscopy,

Table 2
Patient characteristics.

Characteristics	No. of patients (n = 48)
Male sex	28
Smoking history	14
Hypertension	2
COPD	2
Asthma	1
CKD4	1
Ischemic stroke	1
Tuberculosis	5
Right airway	30
Left airway	10

rigid bronchoscopy is helpful to keep the airway unobstructed, the treatment of massive hemoptysis, the shorter time of interventional therapy and the acquisition of large biopsy specimens. However, for patients admitted to hospital because of massive hemoptysis, or who had not previously foreseen the possibility of massive hemoptysis, sometimes they were already in a bleeding state and could not be introduced into rigid bronchoscopy in an emergency due to unclear vision by blood immersion. With active treatment of massive hemostasis, the general negative pressure suction should be performed first to clear the blood, and a unilateral lung intubation to ensure ventilation and oxygenation of the unilateral healthy lung should be performed as soon as possible. Selective bronchial artery embolization is recommended for the culprit vessel in Dieulafoy disease of the bronchus. We also carried out successful selective arterial embolization, and to date no recurrent episodes of hemoptysis have been observed in the patient. Most reported cases have demonstrated the effects of embolization on Dieulafoy lesions of the bronchus [13–21]. Ge Ting et al. have reported that in patients with a known anomalous artery source, embolization may be promptly used to avoid lethal massive hemoptysis [16]. If embolization fails, surgery is another possibility [22–32]. Data from several cases diagnosed by Parrot et al. suggest that surgery can achieve radical cure [33]. The field of interventional respiratory diseases has been very active in recent years. Using minimally invasive techniques has widened the field between traditional respiratory science and surgery. Interventional techniques such as bronchial embolization via blood vessels and endoscopic intervention such as ablation both play an important and crucial role in the diagnosis and treatment of Dieulafoy disease. However, many controversies remain about the indications for different treatment methods, and we believe that understanding will be improved gradually in the future.

4. Conclusions

In Dieulafoy's disease, hemoptysis, which can erupt spontaneously and repeatedly, is common, and biopsy may cause fatal bleeding. Most malformed arteries originate from the bronchial artery, whereas only a few originate from the pulmonary artery. The disease etiology is still unknown and may relate to congenital vascular malformation, chronic inflammation or injury.

Although the current report involved a small sample of participants, the findings suggest that angiography can be used for diagnosis of Dieulafoy's disease of the bronchus, whereas bronchoscopy biopsy should be avoided. Interventions such as embolization or bronchial coagulation play an important role for patients with coughing with massive hemoptysis.

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RUL: right upper lobar; RLL: right lower lobar; RLB: right lower

bronchus; RML: right middle lobar; RMB: right main bronchus; LUB: left upper bronchus; LUL: left upper lobar; LP: left lung; LLL: left lower lobar.

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