

Bronchial stump aspergillosis, an unusual cause of hemoptysis, and review of the literature

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Aspergillus species are ubiquitous dimorphic molds found in an environment. Of the 250 species, few of them are pathogenic to human and can cause various lung involvements, tracheobronchial being one of the variant. Bronchial stumps and anastomosis are prone for fungal infection and can present with cough, hemoptysis, central airway obstruction and bronchopleural fistula with its highest incidence in patients with lung transplantation. Its occurrence in other types of lung surgery is very rare and 20 cases have been described in English medical literature till date since first published in 1969. We present a case of recurrent hemoptysis caused by bronchial stump aspergillosis, first reporting from India, and systematically analyze the literature for all the reported cases of bronchial stump and anastomosis aspergillosis in patients with lung surgery other than transplantation.

Introduction

Aspergillus spp. are ubiquitous dimorphic molds found in soil, various types of decaying organic debris, water, stored hay and grains, and indoor environments [1]. Of the 250 species, few of them are pathogenic to humans and can cause various lung involvements, tracheobronchial being one of the variants, albeit low in incidence [2]. Bronchial stumps and anastomosis are prone for fungal infection and can present with cough, hemoptysis, central airway obstruction, and bronchopleural fistula with its highest incidence in patients with lung transplantation. Its occurrence otherwise is rare and 20 cases have been described in English medical literature to date, since first published in 1969. We present a case of recurrent hemoptysis caused by bronchial stump aspergillosis (BSA) and systematically analyze the literature for all reported cases of bronchial stump and anastomosis aspergillosis in patients with lung surgery other than transplantation.

Case report

A 59-year-old housewife underwent enucleation of the right middle lobe with ruptured hydatid cyst in 2003 at our institute and had uneventful recovery. She was doing fine until 3 years ago when she started complaining of intermittent episodes of streaky hemoptysis that used to subside with short course of antibiotics. The complaints lasted for about 2 years, and then she had spontaneous resolution a year back when she again had recurrence of hemoptysis, which was more frequent and large in quantity without relief with short courses of antibiotics. However, she denied

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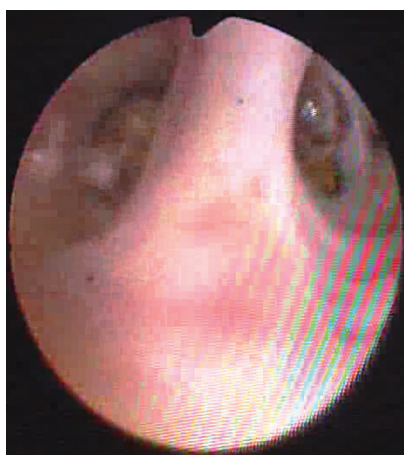
fever, chest pain, mucopurulent sputum, loss of appetite, and weight loss. A sputum examination was negative for acid fast bacilli. Chest radiography showed consolidation silhouette right cardiac border, and computed tomography thoracic angiography revealed mildly hypertrophied right bronchial artery and subsegmental consolidation in the right middle lobe and the apical segment of the right lower lobe. Fiberoptic bronchoscopy showed foreign body-like hard material in the subsegment of the right middle lobe. Suture granulation versus organized secretions was considered and biopsy was performed [3] (Fig. 1). Histopathology revealed multiple fragments of suture material, necrotic tissue, and septated fungal hyphae with acute angle branching resembling the morphology of *Aspergillus* spp. (Figs. 3 and 4). BSA was diagnosed and she was started on oral itraconazole 200 mg twice daily for 8 weeks, followed by 100 mg twice daily for another 8 weeks. She did not have hemoptysis following treatment subsequently, and repeat bronchoscopy performed after 16 weeks of therapy revealed the presence of excess secretion but no evidence of BSA (Fig. 2).

Discussion

BSA and bronchial anastomosis aspergillosis occurs infrequently in immunocompetent host after lung

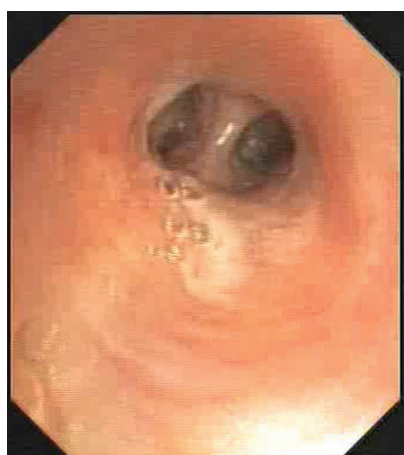
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Figure 1



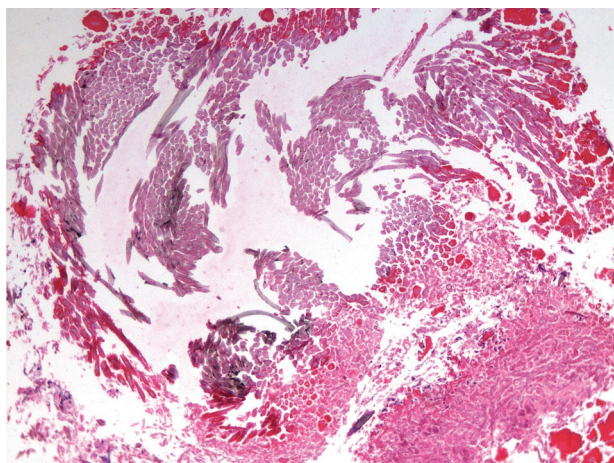
Bronchoscopic image shows golden brownish foreign body like hard material in subsegment of right middle lobe.

Figure 2



Post treatment bronchoscopic image showing disappearance of stump aspergillosis.

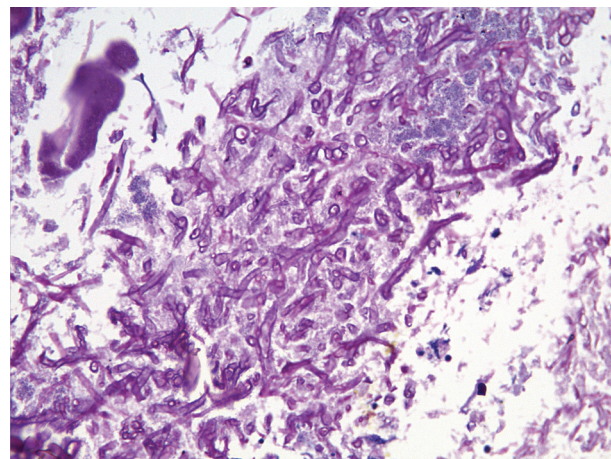
Figure 3



H&E stain shows multiple fragments of suture material (prolene), necrotic tissue and septated fungal hyphae.

surgery. Bronchial stump/anastomosis aspergillosis occurs due to colonization of endobronchial suture and infection of the surrounding granulation tissue by *Aspergillus* spp. It is considered as a saprophytic

Figure 4



Silver stain showing multiple septated fungal hyphae in hpf.

Table 1 Baseline characteristics and treatment of bronchial stump/anastomoses aspergillosis

Variables	Results
Total cases	21
Age (mean±SD) (years)	44.67±15.23)
Sex (male : female)	13 : 8
Types of surgery	
Segmentectomy	2
Lobectomy	14
Pneumonectomy	4
Enucleation	1
Sutures	
Silk	14
Nylon	2
Prolene	2
Staple	2
Not described	1
Onset of symptoms (mean±SD) (months)	36.43±26.19
Symptoms	
Hemoptysis	10
Expectoration of fungal mass and/or sutures	7
Cough with or without purulent expectoration	6
Exacerbation of asthma	1
Dyspnea	2
Methods of diagnosis	
Culture only	7
HPE only	6
Both	8
Treatment modality	
Removal of infected tissue and/or suture materials	
Local application and/or inhalation of antifungal agents	
Oral or parenteral antifungal agents	
Surgery	2

Table 2 Clinical presentations and bronchoscopic findings

Case no.	Age (years)	Sex	Primary disease	Operation	Suture used	Symptoms	Postoperative period (months)	Chest radiography finding	Bronchoscopic finding	
									At discharge	At onset of disease
1	25	Male	PTB	RLL lobectomy	Silk	Expectoration of fungus mass and suture thread	12	-	Normal	Mycelial layerSilk thread [3]
2	27	Female	PTB	Segmentectomy	Silk	Hemoptysis, expectoration of fungal mass and suture thread	38	-	-	-
3	33	Male	PTB	Segmentectomy	Silk	Putrid sputum	9	Residual cavity	-	Putrid layerSilk thread [3]
4	36	Male	PTB	RUL lobectomy	Silk	Hemoptysis	6	-	-	Mucosal erythemaSilk thread [3]
5	37	Male	PTB	RUL lobectomy	Silk	CoughExpectoration of fungal mass	10	-	-	Mycelial layerSilk thread [3]
6	31	Female	PTB	RLL lobectomy	Silk	Expectoration of fungus mass and suture thread	14	-	-	Normal [3]
7	31	Male	PTB	RUL lobectomy	Silk	Hemoptysis	26	-	-	Mycelia layerSilk thread [3]
8	22	Male	PTB	RUL lobectomy	Silk	Expectoration of fungal mass	13	-	-	Mycelial layer [3]
9	33	Male	PTB	RUL lobectomy	Silk	Putrid sputum, hemoptysis, expectoration of fungal mass	12	-	-	Mycelial layerSilk thread [3]
10	69	Male	Lung cancer	Left pneumonectomy	Silk	Fever, cough, chest painLeft pyopneumothorax	72	-	-	Purulent exudatesSilk thread [6]
11	38	Male	Lung cancer (epidermoid tumor)	RUL lobectomy	Silk	CoughHemoptysis	48	-	-	Silk thread with surrounding granulation tissue [7]
12	61	Female	Lung cancer	LLL lobectomy	Silk	Acute exacerbation of asthma	48	-	-	Silk thread with surrounding white necrotic tissue [8]
13	58	Male	Lung cancer	Right pneumonectomy	Silk	Hemoptysis	84	-	-	Hemorrhagic granulation tissue with silk thread [8]
14	39	Male	Lung cancer	LUL lobectomy	Silk	Hemoptysis	72	LUZ mycetoma	-	Hemorrhagic necrotic tissue with silk suture [8]
15	47	Male	Lung cancer	Right pneumonectomy	Nylon	-	60	-	-	Granulation mass on stump with visible nylon thread [4]
16	56	Female	Lung cancer	Right pneumonectomy	Nylon	Acute dyspnea	72	-	-	Fungal massNylon thread [4]
17	44	Male	Carcinoid tumor	LLL sleeve resection	Prolene	Cough with expectorationDyspnea	48	-	-	Mass occluding 90% of the left main bronchus [5]
18	58	Female	Lung cancer	LUL lobectomy	Synthetic thread	Asymptomatic (PET uptake in left hilum)	24	-	-	Necrotic lesion in bronchial stump [9]
19	70	Female	Lung cancer	LUL lobectomy	Staple	Hemoptysis	1	-	-	Necrotic mass in bronchial stump with visible staple [10]

(Continued)

Table 2 (Continued)

Case no.	Age (years)	Sex	Primary disease	Operation	Suture used	Symptoms	Postoperative period (months)	Chest radiography finding	Bronchoscopic finding	
									At discharge	At onset of disease
20	64	Female	Lung cancer	LUL lobectomy	Staple	Hemoptysis and expectoration of necrotic tissue	60	-	-	Necrotic mass in bronchial stump with visible staple [10]
21	59	Female	RML hydatid cyst	Enucleation	Prolene	Hemoptysis	36	RML consolidation/cavitation	-	Foreign body-like hard material in subsegment of RML

LLL, left lower lobe; LUL, left upper lobe; PET, positron emission computed tomography; PTB, pulmonary tuberculosis; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

form of tracheobronchial aspergillosis [2]. We performed systematic search in PubMed using the key words BSA and bronchial anastomosis aspergillosis and came across a total of 20 cases published to date; since first published in 1969. This is the first case reported from India and the first case of BSA after enucleation surgery. The baseline characteristics of these patients are shown in Table 1; and details of clinical presentation and bronchoscopy findings are tabulated in Table 2. The mean age was 44.67 years. A total of 14 patients had undergone lobectomy. Silk was the most commonly used suture for stump closure. Hemoptysis was the most common presentation after surgery with a mean±SD time of 36.43 ±26.19 months. Many cases received multimodal treatment; which included removal of infected tissues and sutures; local application or inhalation of antifungal agent; and or use of systemic antifungal agents. Two cases required surgery to cure it. Each case management and outcome is tabulated in Table 3.

Sawasaki *et al.* [3] first described BSA as a specific clinical entity in English medical literature. In their landmark study, they demonstrated that the use of silk suture was the main reason for developing BSA. Out of 495 pulmonary resections with silk thread suture, nine (1.6%) cases developed BSA, whereas in 140 pulmonary resections using nylon monofilament, none developed this complication. Silk suture produced more local inflammation (24.6%) compared with nylon monofilament (5.7%), which was also proven experimentally. It was shown that, in addition to its irritative quality, silk thread has inherent capillarity and nutritive value that can act as a nidus for fungal growth. This study led to the replacement of silk as a suture material in sewing bronchial stumps. However, there are few cases described with these new suture materials (nylon [4], prolene [5], synthetic thread [9], and titanium staple [10]).

Patients with BSA usually present with hemoptysis that can mimic recurrence of lung cancer. They can present with cough and expectoration of putrid sputum as well as fungal mass and suture material. Interestingly, there are case reports of BSA presenting with *Aspergillus empyemas* [6], central airway obstruction [4,5], and increased fluorodeoxyglucose uptake in positron emission computed tomography in an asymptomatic patient after lung cancer resection [9]. The onset of symptoms is variable, presenting as early as 1 month and as late as 7 years [7,10]. Bronchoscopic examination of the bronchial stump can be normal or show suture thread with

Table 3 Treatment and outcome of bronchial stump aspergillosis

Case no.	Age (years)	Sex	Fungal characteristics		Histopathology	Treatment		Outcome
			Sputum			Method	Duration (months)	
			Fungal characteristics	Lesion				
1	25	Male	-	<i>P. citreum</i> A. <i>oryzae</i> A. <i>nigra</i> A. <i>fumigatus</i> A. <i>cheval</i>	-	Removal of threadApplication of iodine tincture x10	20	Cured [3]
2	27	Female	<i>P. casei</i> <i>C. albicans</i>	<i>A. versicolor</i>	-	LLL lobectomyMycostatin inhalation	-	Cured [3]
3	33	Male	-	-	<i>Aspergillus</i> spp. in specimen	RUL lobectomy	-	Cured [3]
4	36	Male	-	<i>A. tamarii</i>	-	Removal of threadApplication of iodine tincture x7Mycostatin inhalation	5	Cured [3]
5	37	Male	-	<i>A. tamarii</i>	-	Removal of threadApplication of iodine tincture x2, phenylacetic silver x1Mycostatinhalation	21	Cured [3]
6	31	Female	<i>A. oryzae</i>	<i>A. oryzae</i>	-	Application of iodine tincture x2, phenylacetic quick silver x5Mycostat inhalation	7	Cured [3]
7	31	Male	-	-	<i>Aspergillus</i> spp.	Removal of threadApplication of phenylacetic quicksilver x4Mycostat inhalation	2	Cured [3]
8	22	Male	-	<i>A. oryzae</i>	-	Application of iodine tinctureMycostatin inhalation	3	Cured [3]
9	33	Male	-	<i>A. oryzae</i>	-	Removal of threadApplication of iodine tincture x2, phenylacetic quick silver x1Mycostat inhalation	2	Cured [3]
10	69	Male	-	-	<i>A. fumigatus</i>	Removal of sutureIntraleural amphotericin instillation x2	1	Cured [6]
11	38	Male	-	-	<i>Aspergillus</i> spp.	Removal of suture	1	Cured [7]
12	61	Female	-	<i>A. fumigatus</i>	Fungal hyphae and spores with bronchial mucosal ulceration	Oral itraconazole 200 mg b.i.d	1	Cured [8]
13	58	Male	-	<i>A. fumigatus</i>	Lymphoplasmacytic infiltration with fungal spores and hyphae	First time: oral itraconazole 200 mg b.i.d.Second time: Nd:YAG laser vaporization of suture and itraconazole	2	Recurred after 6 months Cured [8]
14	39	Male	-	<i>A. fumigatus</i>	Nonspecific inflammatory infiltration and fungal invasion of mucosa	Itraconazole 100 mg t.i.d.	20	Cured [8]
15	47	Male	-	<i>A. fumigatus</i>	Fungal hyphae and spores	First time: removal of granulation tissueInhaled amphotericin (3 mg/day) Second time: Nd:YAG removal of suture and necrotic tissue	1	Relapsed at 5 months Cured [4]
16	56	Female	-	<i>A. fumigatus</i>	Fungal ball	Inhaled amphotericinRemoval of mass and Nd:YAG vaporization of suture	1.5	Relapsed twice then cured [4] Cured [5]
17	44	Male	-	-	Mucus plug with fibrin, leukocytes, charcot leyden crystal with proliferating aspergillus fumigatus	APC and removal of mass	-	-
18	58	Female	-	<i>A. fumigatus</i>	-	Itraconazole	3	Cured [9] (Continued)

Table 3 (Continued)

Case no.	Fungal characteristics		Histopathology	Treatment		Outcome		
	Age (years)	Sex		Method	Duration (months)			
19	70	Female	-	A. niger	Granulation tissue with fungal hyphae	Intravenous micafungin Oral itraconazole Voriconazole Inhaled amphotericin	12 6 1	Recurrence after 3 months Cured [10]
20	64	Female	-	A. niger/A. fumigatus	Fungal hyphae and spores with calcium oxalate crystals	Removal of necrotic tissue Oral voriconazole	3	Cured [10]
21	59	Female	-	-	Multiple fragments of suture material, necrotic tissue with fungal hyphae (Aspergillus spp.)	Itraconazole	4	Cured

A. cheval, Aspergillus cheval; A. fumigatus, Aspergillus fumigatus; A. niger, Aspergillus niger; A. oryzae, Aspergillus oryzae; A. tamarii, Aspergillus tamarii; A. versicolor, Aspergillus versicolor; APC, argon plasma coagulation; RUL, right upper lobe.

surrounding inflamed tissue or granulation tissue covered in purulent material or fungal mass. Histopathological examination of the bronchial biopsies from the stump reveals inflammatory cells and necrotic areas infiltrated by hyphae with morphological feature suggestive of *Aspergillus* spp. In addition, suture material may be seen as in our case. Culture of the tissue can be positive for *Aspergillus* spp.

No concomitant presence of other forms of aspergillosis has been published to date except for the presence of a mycetoma [7] and empyema [6] in two of the cases. However, clinical overlap and progression to other forms of aspergillosis is well known [1,2]. There is no clear recommendation for the treatment of BSA. However, removal of the suture and granulation tissue if possible remains the most effective therapy and prevents relapse. Endobronchial sutures can be removed by means of bronchoscope using forceps, endoscopic suture scissor, or laser therapy. In one of the reported cases in which polypoidal growth was present with airway narrowing, argon plasma coagulation was used to coagulate the lesion with subsequent forceps debridement [5]. In most of the cases, local instillation of antifungal agents (tincture iodine and phenylacetic quicksilver) and or inhalation of antifungal agent (amphotericin and mycostatin) had been used [3,4]. In one of the reported cases, only removal of suture led to cure, whereas in other two cases patients developed relapse until the thread was removed [4,7]. In cases in which suture thread cannot be removed, oral itraconazole and voriconazole had been used with success [8-10], but the exact dosage and duration of treatment cannot be specified due to case reports and patient had received therapy as long as 20 months depending upon the clinical response [8].

In conclusion, BSA should be considered as a possible differential diagnosis in patients who undergo lung surgery and present with symptoms of cough, purulent sputum, or hemoptysis and early bronchoscopy and biopsy must be performed. Removal of the suture thread is the most effective therapy and oral itraconazole or voriconazole can be used adjunctively or if the relapse occurs.

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Conflicts of interest

There are no conflicts of interest.

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