Review Article

TANAFFOS

Anthracosis of the Lungs: Etiology, Clinical Manifestations and Diagnosis: A Review

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Anthracosis of the lungs is black discoloration of bronchial mucosa that can occlude bronchial lumen and is associated with bronchial anthracofibrosis (BAF). This disease usually presents with a chronic course of dyspnea and or cough in an elderly non-smoker woman or man. In addition, concomitant exposure to dust and wood smoke is the most postulated etiology for anthracosis. Pulmonary function tests usually show an obstructive pattern with no response to bronchodilators and normal DLCO, but some cases with restrictive pattern have also been seen. Computed tomography (CT) may show more specific findings such as lymph node or bronchial calcification and mass lesions. Final diagnosis can be made by bronchoscopy when obtaining samples for tuberculosis (TB), which is the most common disease associated with BAF. Endobronchial ultrasound shows a hypoechoic scattered nodular pattern in adjacent lymph nodes, which is unique to anthracosis. Treatment is very similar to that of chronic obstructive pulmonary disease (COPD) with a chronic course and low mortality. This review discusses this disease as a separate entity; hence, anthracosis should be added to the list of obstructive lung diseases and benign mass lesions and differentiated from biomass induced COPD.

Key words: Anthracosis, Anthracofibrosis, Anthracostenosis, Anthracotic bronchitis, Coal worker pneumoconiosis, Tuberculosis, Chronic obstructive pulmonary disease

INTRODUCTION

Anthracosis (*anthrac-* meaning coal, carbon + *-osis* meaning condition) is defined in Bioline as, "the asymptomatic, milder type of pneumoconiosis as caused by the accumulation of carbon in the lungs due to repeated exposure to air pollution or inhalation of smoke or coal dust particles" (1). Anthracosis may be seen as a superficial black discoloration (simple anthracosis) (Figure 1A) or scattered foci of black spots, which retract mucosa inward due to the effect of adjacent anthracotic lymphadenopathy (Figure 1B). Anthracosis is an ancient disease discovered in mummies (2-4). The early scientific reports of this disease were mainly from Western countries and the term "anthracosis" was coined by Pearson in 1813

(5). Pearson and others believed that anthracosis was a complication of coal worker pneumoconiosis (6). However, the interest of Western countries in this disease declined as the frequency of anthracosis declined in their countries. The second wave of anthracosis in the literature started in Asia, as it is still a problem in this continent. Most of these studies showed that pneumoconiosis and exposure to coal were not the most frequent risk factors and thus researchers excluded pneumoconiosis patients from the category of anthracosis (7,8). Chung et al. (7) introduced BAF as a unique clinical syndrome. It is the severe form of disease, which distorts and narrows the bronchial lumen (Figure 1C). Later, some new terms were introduced such as anthracostenosis (9) or anthracotic bronchitis (10) used

to describe extensive deposition of carbon in the main bronchial walls; which in the majority of cases is accompanied by severe submucosal edema, bronchial stenosis, protruded mucosal folds and lung collapse (10) (Figure 1C).
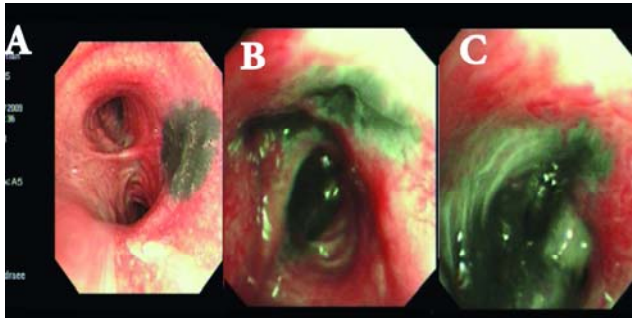

Figure 1. A) Bronchoscopic picture of simple anthracosis; B) Anthracosis with retracted mucosa; C) Bronchial anthracofibrosis

Prevalence

Prevalence of anthracosis in the general population has been roughly estimated because the exact diagnosis of anthracosis requires bronchoscopy, which is impossible for the general population due to ethical considerations. Available data from large series of patients who underwent bronchoscopy for other reasons have shown the frequency of simple anthracosis to be 3.4 - 21% (11, 12). This rate was 0.1-22.5 for BAF (13,14) (cumulated means 5.7%) (Table1). Frequency of BAF is lower in Western countries and Wynn et al. reported seven BAF cases among 7000 bronchoscopies (15). Reports from other continents such as North America or Africa were also scanty (14,16) and reports of anthracosis in children are very rare (17). As mentioned above, anthracosis was previously prevalent in coal workers, but new reports are now mostly reporting this disease in farmers (40%) (11)(Table 1) and rural dwellers (55-66%) (8,10, 18). The number of affected females in some large series has been equal to males (8,10), but accumulation of data show that BAF in females is slightly more prevalent than males (Table 1). Moreover, almost all studies have shown that anthracosis subjects are elderly (Table 1). In a meta-analysis, the mean age of patients affected with anthracosis was 63±3.8 years, which shows that these patients are significantly older than non-anthracosis subjects (52±6.4 years) (t= 3.43, P=0.02) (19).

Proposed etiological factors
Dust

The exact reason of anthracosis and the origin of anthracotic nodule have yet to be discovered. Dust exposure, especially coal dust in anthracosis subjects was reported during 1960-1980 in Europe (5,6). Later on, Wynn et al. (15) reported seven subjects who were exposed to coal and tile dust in their work place. Recent studies in Europe have shown deposition of mica and silica crystals in calcified mediastinal lymph nodes of anthracotic patients using transmission electron microscopy (20,21). Hwang et al. (14) studied 10 BAF subjects from Asia and the Indian subcontinent. They reported that aluminum silicates and quartz were present in 37-70% and 2-7% of subjects, respectively. In a study in Japan, elemental constitution of lobectomized lung tissue obtained by autopsy was analyzed by a wavelength-dispersive X-ray fluorescence spectrometer (22); the most important non-carbonaceous fraction of intrapulmonary particulate pollutant was silicon and aluminum, especially in farmers compared to other occupational categories. Electron microscopic evaluations of the lung tissue from mummies also showed silica, aluminum, and iron deposits (3). Although the effect of coal on BAF subjects was again reported in Eastern countries (23); heavy exposure to dust such as in miners, stone breakers and well diggers` was reported in only 3% of BAF subjects (11). Therefore, the pathogenesis of these crystals causing anthracosis should be different from that of routine air pollution and occupational exposure, and according to a recent widespread investigation (24) and in mummies (4), concurrent exposure to carbon smoke from the combustion of fuels and inorganic compounds that contain limestone and alumina-silicates is the most possible cause for anthracosis.

Table 1. Patient demographics and clinical manifestation of lung anthracosis

Studies	Anthracosis Number	Frequency	Mean age or median (range)	% Non-smokers	Female/male ratio	Biomass exposure	Occupation Female	Occupation Male	Dyspnea	Cough
Chung et al 1998[7]	28	3%	64 (42-86)	86%	2.5/1	0	Not miner	Not miner	60%	71%
Amoli 1998[26]	10	1.1%	62.5 (46-72)	100%	1/0	100%	Housewives	---	90%	70%
Amoli 2009[46]	102	NA	60 (29-77)	73%	1.4/1	Most	Housewives	Workers	Most	Most
Kim et al2009[8]	333	11%	72.3 (47-90)	78.1%	2.1/1	100%	Housewives	Farmers	38.4%	30%
Ghanei et al 2011[35]	71	7.7%	68.2±10.7	NA	1.2/1	27%	Not miner	Not miner	72%	80%
Wynn et al 2008[15]	7	0.1%†	72.7±6.4 (67-82)	42%	2/5	NA	Worker	Miner	100%	85%
Najafizadeh et al 2003[10]	47	16%	70 (51-82)	89.6%	1/1	29.3%	NA	NA	NA	93%
Hwang et al2010[14]	10	16.7%	69±9.8	100%	4/1	0%	NA	NA	NA	NA
Towhidi et al 2003[58]	96	8%	71 (52-90)	72%	2.2/1	0	NA	NA	51%	100%
No et al 2003[75]	166	12%	72.4 (56-91)	77%	6.2/1	25%	NA	NA	50%	48%
Na et al 2002[37]	30	3.4%	71 (53-88)	66%	5/1	NA	Not miner	Not miner	36%	50%
Park et al2008[48]	49	NA	76 (56-90)	76%	3.7/1	NA	Not miner	Not miner	NA	NA
Kim et al 2004[70]	37	3%	67.5±8.2 (21-97)	75%	5.1/1	83%	NA	NA	93%	40%
Kim et al 2000[18]	54	NA	67 (33-78)	85%	2.3/1	NA	Not miner	Two miner	NA	NA
Mirsadraee et al 2005[12]	63	11.7%	60±16	81%	1.1/1	NA	Housewives	Farmers	71%	100%
Jang et al 2007[73]	54	NA	75 (50-99)	80%	1.8/1	NA	NA	NA	57%	44%
Mirsadraee et al [33]	70	NA	69.3 ± 9.4	79%	1.5/1	40%	Housewives	Farmers	81%	68%
Törün et al 2007[27]	27	NA	66.8 (53-77)	100%	12.5/1	100%	Housewives	Farmers	63%	100%
Sigari et al 2009[11]	778	5.4%	63 (25-80)	NA	1/1	NA	Housewives	Farmers	35.7%	83.6%
Hemmati et al 2008[72]	34	16%	61.8	NA	1.2/1	52%	NA	NA	47%	73%
Najafizadeh et al 2008[39]	87	NA	69 ± 13 (36-84)	88.5%	1.9/1	29.9%	NA	NA	NA	NA
Rezaei Talab 2007[13]	225	22.5%	65 ± 12.5	NA	1.3/1	7%	Housewives	Farmers	NA	NA
Mirsadraee et al 2011 [38]	54	NA	70.5 ± 10.4	82%	1/1	39%	housewives	Farmers	66%	74%
Cumulated frequency (Average)	2457	5.7% (0.1-22.5)	67.9 ±10.1 (21-99)	77.6% (42-100%)	1.7/1	61.5% (7-100%)			64.2% (35-93)	98.5% (30-100)

† This frequency was omitted from cumulated frequency because of non-homogeneity with other studies.

Smoke

Biomass smoke has been mostly reported as a risk factor for anthracosis in Asian countries such as Korea (8), India (25), Iran (26) and Turkey (27). Some reports from Africa (28) and Latin America (29,30) have indicated chronic respiratory disease induced by biomass smoke exposure. The hypothesis about biomass as a causative factor for anthracosis is due to the resemblance of anthracotic pigments to carbon particles and the fact that most of the anthracotic subjects (77.6%) are non-smokers (Table 1). Biomass is produced by burning of wood, leaves or dung (manure) of farm animals for heating, cooking or baking (8). Depending on the geographical and socioeconomic status, exposure to biomass was reported in 7-100% of BAF subjects, but the cumulated incidence rate was 61.5% (Table 1). The mean duration of biomass exposure was reported to be 36 years (12-60) (8) and duration (years) of smoke exposure showed significant association with anthracosis (OR: 1.05, 95%CI: 1.01-1.09)

(31). Amoli (26) described using rustic traditional wood ovens requiring the baker to put his/head into the oven to place or remove the bread. In other studies, indoor exposure to wood smoke similar to bread baking in traditional ovens increased the risk of BAF by 4.3 to 4.8 folds especially in women (32, 33). Furthermore, some investigators have attempted to explain the pathophysiology of anthracosis, including bronchial narrowing, lymph node enlargement with or without calcification and susceptibility to TB and malignancy on the basis of biomass smoke inhalation (8). However, there were some anthracotic subjects who had used other fuels such as kerosene or gas; these cases cannot be explained by this hypothesis.

Cigarette smoking is not a risk factor for anthracosis and its frequency was significantly lower in anthracotic subjects compared to COPD subjects who underwent bronchoscopy (Table 1). Moreover, anthracotic plaque and bronchial deformity were not observed in typical COPD subjects (who had a history of cigarette smoking); therefore, in case of detecting anthracosis during bronchoscopy, it should not be considered as a variant of COPD. Increased motility of bronchial cilia was postulated to be the cause of low prevalence of anthracosis in cigarette smokers (24).

Tuberculosis

Three decades ago, presence of TB in BAF was shown by Chung et al (7). Thereafter, several studies have reported the association of anthracosis with TB (Table 2). In a meta-analysis, which reviewed all studies on the association of TB and anthracosis, it was shown that the cumulated incidence of TB in anthracosis and BAF subjects who underwent routine bronchoscopy was 16.6% (95% CI=8.5-31) and 32.3% (95% CI=21-57) respectively (19). The risk of TB increased in anthracosis with a cumulated odds ratio of 3.16 (95% CI= 2.49-6.85), which was significantly higher than that in the control group (Figure 2) (19).

History of close contact with subjects suffering from TB and PPD skin test more than 10 mm was reported to be useful for diagnosing TB in BAF subjects suspicious for TB (34). It is noteworthy that 38% of BAF subjects who suffered from associated TB reported close contact with TB patients (34). PPD reaction more than 10 mm was reported in 63% of TB-proven BAF subjects, while this finding was shown in 34% of BAF non-TB subjects (35). Serological markers for the activity of TB, such as IL-2 sRα, IFN-γ and TBGL antibody, were evaluated in BAF cases, but they were not useful for evaluation of TB activity in patients with anthracofibrosis (36).

Two studies used polymerase chain reaction for evaluation of TB and the frequency of TB superimposed on BAF was reported to be 37% and 34% (37,38), which were slightly higher than the result of traditional methods such as acid fast bacilli testing or culture (31%) (38). Evaluation of space-oligonucleotide (spoligotyping) of *M. tuberculosis* by PCR showed that *M. tuberculosis* in anthracosis is not a special subtype (in comparison to the common subtype of their community) (39). Other non-TB mycobacterial infections such as *Mycobacterium kansasii* were also reported to be associated with BAF (40). The reason for TB susceptibility has with wood smoke on the immune system have been postulated (8,24).

Bronchogenic carcinoma

Malignant lesions associated with anthracosis have been sparsely reported (41-43), but accumulation of data from studies reported the frequency of malignancy revealed lung cancer in 0-7% of subjects (cumulated frequency=3.4%) (Table 2). The reason for the variation in frequency of lung cancer associated with anthracosis has yet to be understood, but in one study by Ohshima (22), subjects with lung cancer had a high level of iron, calcium, copper, lead, chromium and nickel in their lung tissue and lower levels of silicon and aluminum as the main mineral intrapulmonary particulate pollutant of routine anthracosis subjects (22). Therefore, we can conclude than there is no epidemiological or etiological association between anthracosis and lung cancer.
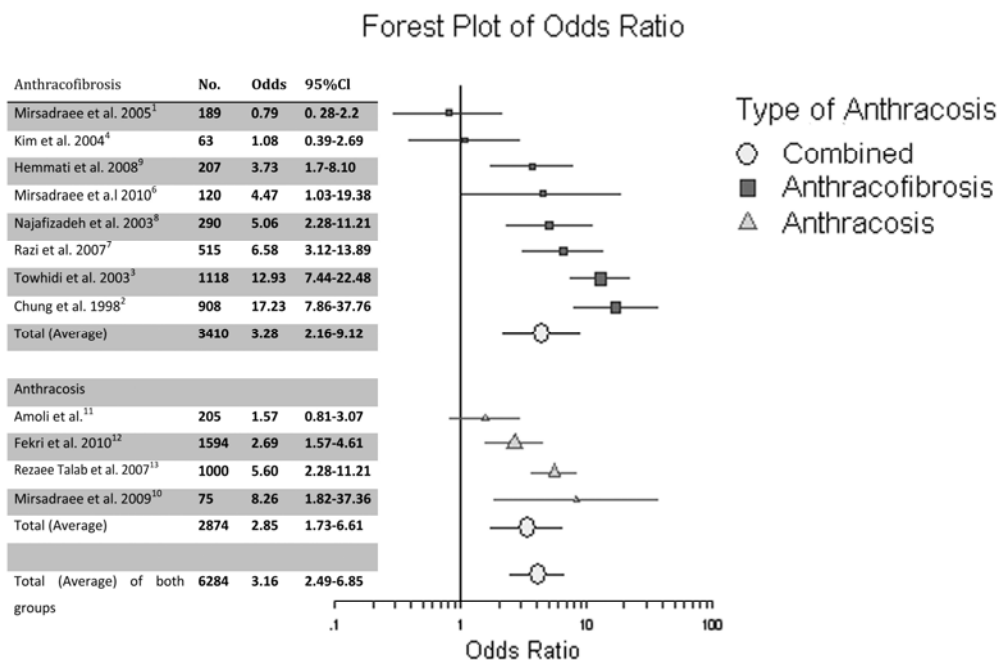
Forest Plot of Odds Ratio

Anthracofibrosis	No.	Odds	95%CI
Mirsadraee et al. 2005[1]	189	0.79	0. 28-2.2
Kim et al. 2004[4]	63	1.08	0.39-2.69
Hemmati et al. 2008[9]	207	3.73	1.7-8.10
Mirsadraee et a.l 2010[6]	120	4.47	1.03-19.38
Najafizadeh et al. 2003[8]	290	5.06	2.28-11.21
Razi et al. 2007[7]	515	6.58	3.12-13.89
Towhidi et al. 2003[3]	1118	12.93	7.44-22.48
Chung et al. 1998[2]	908	17.23	7.86-37.76
Total (Average)	3410	3.28	2.16-9.12
Anthracosis			
Amoli et al.[11]	205	1.57	0.81-3.07
Fekri et al. 2010[12]	1594	2.69	1.57-4.61
Rezaee Talab et al. 2007[13]	1000	5.60	2.28-11.21
Mirsadraee et al. 2009[10]	75	8.26	1.82-37.36
Total (Average)	2874	2.85	1.73-6.61
Total (Average) of both groups	6284	3.16	2.49-6.85

Type of Anthracosis

○ Combined
■ Anthracofibrosis
△ Anthracosis

Odds Ratio

Figure 2. Forest plot for evaluating the association and risk of tuberculosis in anthracosis and BAF subjects (19).

Table 2. Summary of diagnostic procedures in subjects with anthracosis of the lungs

Studies	BAF Number	CT findings			Bronchoscopy				Associated disease	
		Lymph node enlargement (Calcification)	Bronchial wall lesion	Parenchymal lesion†	Upper lobes	RML	Lower lobes	Multi- focal	TB	Malignancy
Chung et al 1998[7]	28	42% (28%)	85%	100%	75%	75%	64%	78%	60%	0
Kim et al 2009[8]	333	66% (44%)	63%	72%	90%	80%	62%	69%	34%	3.6%
Park et al 2008[48]	49	91% (NA)	95%	NA	98%	84%	40%	65%	20%	NA
Wynn 2008[15]	7	28% (28%)	28%	100%	71%	57%	57%	86%	0	0
Kim et al 2000[18]	54	94% (57%)	84%	94%	26%	63%	15%	52%	40%	0
Hwang et al[14*]	10	70% (NA)	60%	90%	10%	80%	40%	30%	100%	0
Najafizadeh et al 2003[10]	47	NA (61%)	74%	62%	80%	NA	63%	NA	27.7%	3%
Lee et al 2002[65]	43	89% (38%)	84%	76%	NA	NA	NA	NA	29%	7%
Towhidi et al 2003[58]	96	NA	NA	68%	82%	41%	31%	79%	30%	0
No et al 2003[75]	166	69% (45%)	55%	59%	90%	75%	60%	70%	21.7%	6.6%
Jang et al 2007[73]	54	65% (53%)	68%	75%	NA	NA	NA	NA	27%	4%
Na et al 2002[37]	30	58% (26%)	67%	96%	70%	76%	NA	50%	37%	0
Razi et al2007[76]	51	5.9% (NA)	NA	47%	47%	33%	23%	60%	25.4.%	0
Törün et al 2007[27]	27	29.6% (22.2%)	NA	74%	92%	81%	74%	100%	25.9%	0
Hemmati et al 2008[72]	34	79% (NA)	NA	64%	91%	52%	NA	NA	44%	0
Najafizadeh et al 2008[39]	87	NA	36%	29.8%	35%	29.8%	34%	48.2%	26%	NA
Mirsadraee et al[38]	70	88% (88%)	48%	97%	80%	35%	43%	60%	33%	0
Cumulated frequency	1186	55% (36%)	56.2%	50%	79.3%	60%	45%	64.7%	32.3%	3.4%

- *BAF was collected from TB proven subjects.
- †Parenchymal lesion included atelectasis, mass or alveolar type infiltration

Pathology

Anthracosis involvement mainly starts from the respiratory bronchioles (44,45). Histopathology of the lung tissue has shown carbon-like particles inside the cytoplasm of the macrophages in the bronchial wall (46) (Figure 3) and free particles in the mediastinal lymph nodes (47). Submucosal fibrosis may also be seen in the bronchial wall (37) and the epithelial lining is usually intact (26). In a study, lobectomy was done on two BAF subjects and fibrosis of the bronchi and reactive hyperplasia with anthracotic pigmentation were the major histopathological findings (48). Perforation of anthracotic lymph nodes into the bronchial lumen may be the mechanism that produces anthracosis with retracted mucosa (Figure 1B) (18). Bronchial cytology showed macrophage-containing anthracotic nodules in 71% of subjects (12). Associated pathology such as TB or cancer is usually distinct from BAF histopathology (37, 49). These findings are completely distinct from the histopathological findings of COPD as the most important clinical differential diagnosis of BAF.

Animal studies

Anthracosis was discovered in the lung tissue of wild and domestic animals (47,50). A study in cattle showed anthracosis in 3.8% of lung and lymph node tissues (47). In some experimental studies, investigators were successful in inducing anthracosis in animal models (51); moreover, the frequency of anthracosis in rats that were exposed to exhaust smoke was evaluated as well (52).
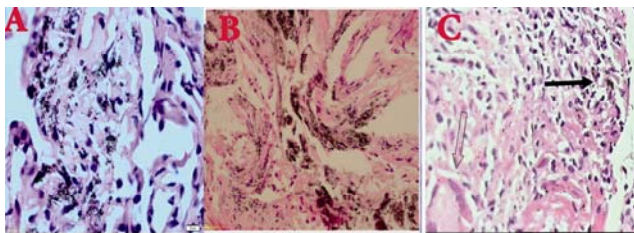

Figure 3. Histopathology of BAF, A) Anthracotic nodule in cytoplasm of macrophages; B) Collagen deposition in bronchial biopsy of a patient who suffered from anthracofibrosis. C) Association of anthracosis (filled black arrow) and granuloma due to tuberculosis (none- filled arrow).

Anthracosis in other organs

Anthracosis has also been reported in the liver, spleen (53) and esophagus (54,55). Anthracosis in the esophagus is important as it mimics the picture of malignant melanoma (56). An interesting case of sinusitis was reported, where the subject suffered from anthracosis of the sinuses (57).

Clinical manifestations

BAF usually presents with pictures very similar to COPD with the exception of a history of cigarette smoking. Cough and dyspnea are the most frequent symptoms of BAF and anthracosis in most reports (Table 1). Association of TB does not change the chronic symptoms, but it may cause new onset weight loss or fever (25%) (58) which should be differentiated from pneumonia, which is reported to be superimposed on 30% of BAF subjects (8).

Physical examination of the lungs usually shows wheezing (7) and less frequently rales or decreased breath sounds (10). Some anthracosis subjects had normal physical examinations, but the frequency has not been mentioned in the literature.

Anthracosis may present with complications of enlarged mediastinal lymph nodes such as vocal cord paralysis (49) or broncholithiasis (59). Many of these cases were also reported in association with tuberculosis (49, 60).

Pulmonary function tests

Preliminary studies on BAF subjects showed a mild obstructive pattern (mean FEV1 83.9%±22.9% predicted) and class I and II GOLD classification (8) (Table 3). Generally, BAF subjects could be classified under obstructive lung disease, but some of them have shown normal or restrictive patterns (Table 3). In a study on BAF subjects, post bronchodilator response was not significant and DLCO and DLCO/VA were mainly within the normal range (61). Another study showed that the resistance of the airways had a significant correlation with the number of bronchial stenoses (62). Therefore, we conclude that obstruction should be fixed in the bronchi and the respiratory unit should be intact. Statistical analysis did not show a correlation between the severity of clinical findings and spirometry (61).

Table 3. Review of results of spirometry in anthracosis subjects

Studies	BAF Number	Classification of spirometry			Mean of predicted value					
		Obstructive	Restrictive*	Normal	FVC	FEV1	FEV1/FVC	FEF$_{25-75}$	RV	TLC
Jung et al 2005[62]	113	49.6%	8.8%	41.5%	94.3±24.7	84.1±25.2	69±13	41.1±21.4	119±39	94±13.3
Mirsadraee et al[59]	40	95%	5%	0	75.8±19.5	57.3±18.4	60.6±13.3	25.7±14	144±80	104±29.1
Jang et al 2007[73]	21	62%	5%	33%	NA	NA	NA	NA	NA	NA
No et al 2003[75]	113	47.8%	12.4%	39.8%	NA					
Lee et al 2002[65]	43	50%	0	50%	NA					
Kim et al 2009[8]	151	NA	NA	NA	90.8±22	83.9±22.2	68.8±11.4	NA	NA	NA
Amoli 2009[46]	39	62%	31%	7%						
Ghanei 2011[35]	71	46%	36.5%	17.5%						
Cumulated frequency (Average)	440	59%	14%	27%						

- Included mixed pattern

These findings were across the findings of Tanaka et al. (63), who evaluated the peripheral bronchi with an ultrafine bronchoscope. They showed that anthracosis started from the small bronchi and then spread to the larger bronchi. For this reason, we conclude that when BAF is found in the proximal bronchi, all other distal bronchi should assume to be occluded by anthracosis. Therefore, anthracosis and BAF should be considered in the list of differential diagnoses of obstructive lung disease.

Radiological findings
Chest X-ray

Chest X-ray (CXR) was reported to be normal in only 7% of subjects (33). The most frequent abnormalities reported in CXR were non-homogeneous pulmonary infiltrate (Figure 4), subsegmental atelectasis and mass lesions (40% and 16%, respectively in BAF subjects) (33). CXR in some cases showed resolution of abnormalities when the anthracosis subjects were proven to suffer from TB and were treated with anti-TB medications (7,37,64).

Computed tomography

Computed tomography (CT) was more sensitive for anthracosis and showed more specific radiological findings (Figure 5). The earliest reports have shown mediastinal or hilar lymphadenopathy in 94% of cases, 57% of them were calcified (high attenuation); followed by bronchial narrowing with or without atelectasis in 94% (18). A study evaluated the most important CT findings, and showed a significantly higher frequency and chance of lymph node

high attenuation (calcification) (80%, odds ratio=22.9, Cl 95%=7.31-75), bronchial wall high attenuation (calcification) (62%, odds ratio=6, Cl 95%=2.07-18.3), bronchial stenosis (48%, odds ratio=2.91, Cl 95%=0.96-8.99), atelectasis (20%, odds ratio=4.75, 95% Cl=0.8-386.8) and mass lesion (14%) in BAF compared to non-anthracotic subjects (33) (Table 2). Bronchial stenosis was usually smooth without endobronchial nodules (80%), and although not frequent, distal atelectasis was not seen in some cases (18). Bronchial wall thickening was also reported in 20% of BAF subjects (18). Involvement might be unilateral or bilateral, but the right middle lobe, followed by the upper lobes were frequently reported as the most commonly involved lobes (7,18,33,65).
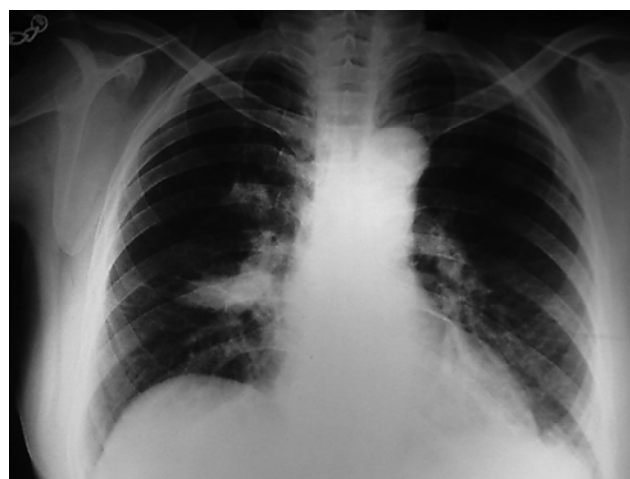

Figure 4. Chest X-ray (posterior anterior view) in a subject suffering from anthracofibrosis. Please note the non-specific infiltration in the left lower zone and the mass lesion in the right lower zone.
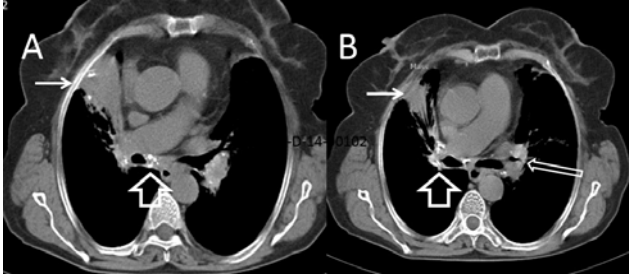
Figure 5. Computed tomography of a subject with diffuse anthracofibrosis; A: Mediastinal calcification (wide non-filled arrow) and mass lesion in parenchyma (narrow filled arrow), B: Bronchial narrowing (narrow non-filled arrow) and mass lesion in parenchyma (narrow filled arrow).

CT images were unremarkable in 17% of simple anthracosis subjects and 6% of anthracofibrosis subjects (33). Pleural disease was observed in a quarter of BAF subjects (8).

As a routine practice, anthracosis may be erroneously diagnosed as TB, lung cancer, atelectasis or pneumonia (16,48). Park et al. used CT scans for differentiating BAF from endobronchial TB (48). The results of their study showed that BAF subjects tend to show bilateral smooth bronchial stenosis and peribronchial lymphadenopathy. This is in contrast to subjects with endobronchial TB who tend to have limited ipsilateral irregular bronchial stenosis, especially in the lobar bronchus and it can extend to contiguous bronchus and trachea. Choe et al, (66) also showed that necrotic lymph nodes, multiple poorly defined small nodules, including branching opacities (including tree in bud) and consolidation with internal low density were in favor of TB.

MRI was used to differentiate BAF from lung cancer in case of a mass lesion (67), which showed that BAF had low density in the T2 weighted image, and differentiated BAF from lung cancer. But some reports showed positive FDG-PET results in BAF, which make the use of FDG-PET scan for differentiating between malignancy and BAF difficult (68,69).

Bronchoscopic findings

Bronchoscopy is the gold standard for diagnosing anthracosis. As mentioned above, anthracosis may be

detected in different images as simple flat anthracosis (Figure 1A), deep seated retracted anthracosis (originating from an anthracotic lymph node besides the bronchus) (Figure 1B), and protruded black discoloration of mucosa with or without narrowing of bronchi (BAF) (Figure 1C). In addition to black lesions, bronchial swelling with infiltration, erythema (Figure 1C) and thickening that may cause obliteration of bronchi may be seen (46). Anthracosis can be localized or disseminated, unilateral or bilateral (18) and the most frequent place of involvement is the right middle lobe (RML), followed by the upper lobe bronchi (Table 2), especially at the bifurcation or inlet of the lobar or segmental bronchi (8,12). Tracheal involvement is rare and was detected in 3.8% of BAF subjects (11). Also, bronchial washing may show free black particles (45) and biopsy is usually difficult as the mucosa has a hard consistency (7). Bleeding during biopsy is frequent (9%) (8, 37), but it usually causes no further complications (7,8,37).

Detecting endobronchial TB associated with BAF with bronchoscopy is difficult; Kim et al. (70) described edematous-hyperemic mucosa and ulceration as a useful picture for diagnosing TB associated with BAF.

Endobronchial ultrasound has not been studied extensively in anthracotic subjects, but Mirsadraee and Farshchi (71) reported a picture from typical anthracosis that showed a scattered nodular hypoechoic pattern in the subepithelial area of the bronchus or lymph node adjacent to the bronchial mucosa (Figure 6).

Diagnosis

Anthracosis should be considered in the list of differential diagnoses of diseases such as COPD, TB (without anthracosis), lung cancer, fungal infection (such as mucormycosis and actinomycosis) and amyloidosis. A history of long-standing dyspnea and/or cough in an elderly non-smoker man or woman exacerbated in winter is suggestive for anthracosis. Wheezing during lung auscultation is in favor of BAF. Obstructive lung disease in spirometry with lymph node or bronchial calcification

(high attenuation), especially in subjects who also show mass lesion (or atelectasis) strongly makes the diagnosis of anthracosis more likely. Kim et al, (18) also described smooth bronchial narrowing with enlarged calcified lymph nodes as a useful marker for differentiating BAF from lung cancer. However, in all suggested cases, bronchoscopy as the gold standard of diagnosis should be performed and bronchoscopy specimens should be sent for TB evaluation. In case of a mass lesion in radiological findings, open lung biopsy, transthoracic lung biopsy or advanced bronchoscopic techniques may be necessary to rule out TB (72) or malignancy (43,44).

The most important differential diagnosis of anthracosis (BAF) is COPD. Table 4 shows the most important differences between anthracosis (BAF) and COPD. According to this evidence, anthracosis should not be considered as a variant of COPD (with exposure to biomass instead of cigarette smoke). Progressive massive fibrosis should also be considered as a differential diagnosis, but history of work related exposure to dust and more diffuse involvement of the lung could differentiate it from pneumoconiosis.
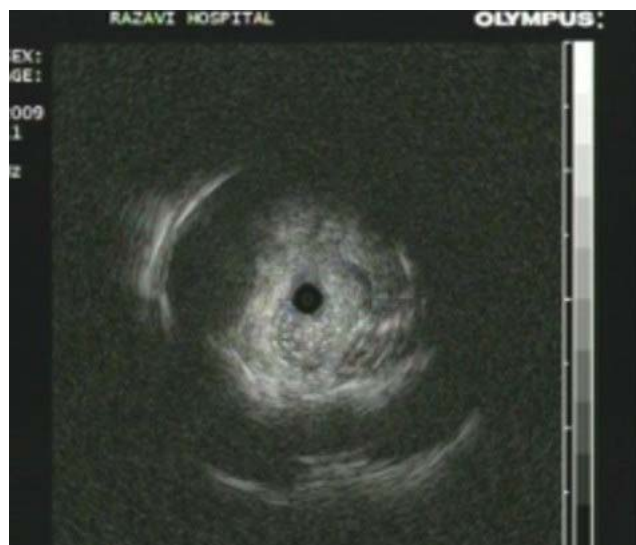

Figure 6. Endobronchial ultrasonography of an anthracofibrosis that protruded to the bronchial lumen. Note the hyperechoic nodule inside the lesion.

Table 4. Important differences between bronchial anthracofibrosis and COPD

	Bronchial anthracofibrosis	COPD[77]
Age	Over 67 years	Over 55 years
Smoking	22.4%	80%
Female/ Male ratio	1.7/1	1/1
Biomass exposure	61.5%	3.7%[78]
Histopathological findings	Macrophage containing black pigments	Submucosal gland hypertrophy, smooth muscle hyperplasia and alveolar destruction
Clinical findings	Cough, dyspnea and wheeze	Cough, dyspnea and wheeze
PFT	Obstructive and restrictive and Normal DLCO	Obstructive, Low DLCO in emphysema
Radiological findings	Infiltration	Normal or hyper-inflation, low attenuation with no visible wall
Mass lesion	Yes	No
Lymphadenopathy	Yes	No
Bronchoscopy	Black discoloration+ obstruction	Normal

Treatment

No established treatment for anthracosis has been reported thus far. Empirical treatment including bronchodilators (short or long acting), corticosteroids (inhalation or systemic) (73) and antibiotics have been used. Systemic corticosteroids showed temporary relief in 60% (9/15) of non-TB BAF subjects (73). In case of confirmed TB associated with anthracosis, anti-TB medications can improve the general condition and sometimes, the radiological manifestations of patients (7,33,64). However, anthracosis alone can usually be controlled with conservative management, although in some cases of severe localized bronchial obstruction of large airways, bronchial stents were successfully used (74).

Clinical course, quality of life and follow up

Follow up of radiographic mass lesions has shown a slow progress of the lesion not similar to the spread

pattern of malignant lesions. In these subjects, open lung biopsy may be indicated.

Kim et al. (8) described the clinical course of 280 BAF subjects and showed that subjects who suffered only from BAF or a combination of BAF and malignancy had significantly lower survival rates than subjects with BAF and TB, acute exacerbation of airway disease or pneumonia. Causes of death in this study (18/288) were malignancy (6), acute infection (5), cardiac disease (3), trauma (2), acute exacerbation (1) and hemoptysis (1). Na et al. (37) treated BAF subjects with anti-TB treatment and showed improvement and resolution of lesions in 66.6% (10/15) of subjects.

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