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Bronchiectasis and homozygous (P_1ZZ) α_1-antitrypsin deficiency in a young man

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Abstract

Pulmonary complications of α_1-antitrypsin deficiency are most commonly manifested by panlobular emphysema. This report describes histologically proven bronchiectasis in a 21 year old man with massive haemoptysis and homozygous deficiency of α_1-antitrypsin. Neither panlobular emphysema nor cirrhosis of the liver were present. Bronchiectasis must be considered part of the spectrum of the pulmonary pathology that may be encountered in individuals with α_1-antitrypsin deficiency.

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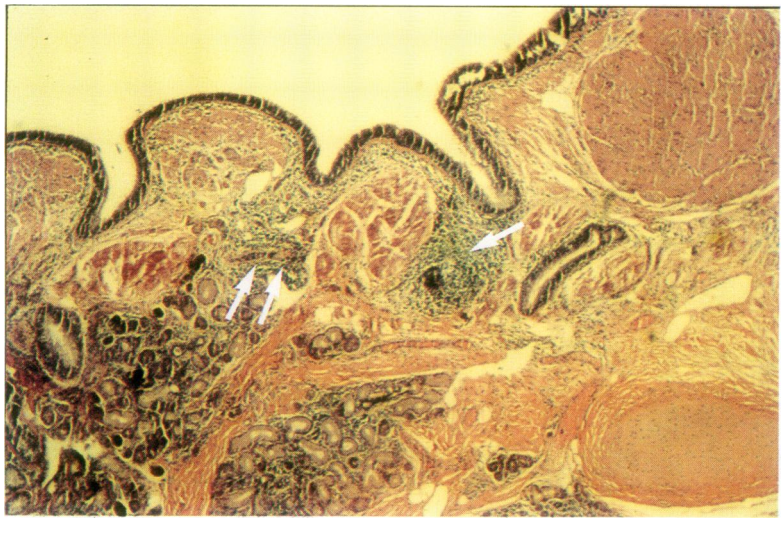
The occurrence of α_1-antitrypsin deficiency in association with cirrhosis of the liver and pan acinar pulmonary emphysema has been well documented. However, the association of α_1-antitrypsin deficiency with bronchiectasis or repeated bronchopulmonary infections, although reported, is not well documented. Various reports have provided clinical and bronchographic documentation of α_1-antitrypsin deficiency in association with bronchiectasis, but only two cases to our knowledge have provided histopathological verification of the bronchiectasis. The purpose of this report is (1) to present the clinical and radiographic features of this uncommon association in a young man with massive haemoptysis, a P_1ZZ homozygous phenotype, and histopathologically proven bronchiectasis; and (2) to review the cumulative experience reported thus far in the medical literature.



Chronic inflammation (arrow) extending deep into mucous glands and focal destruction with interruption of the muscle layer in the bronchial wall (double arrow). Stain: haematoxylin and eosin, original magnification ×240 reduced to 58% in origination.

Case report

In August 1987 a 21 year old non-smoking white man presented to Ben Taub General Hospital in Houston, Texas after coughing two cups of blood. His past medical history included a laparotomy at the age of two for suspected hepatosplenomegaly. However, the results of this exploration were unknown to the patient and his family. He remained well until the age of 16 when he developed frequent episodes of cough, excessive sputum production, and occasional bouts of blood-tinged sputum. At the age of 18 he underwent a thoracotomy for removal of his left lower lobe following an episode of massive haemoptysis. Histopathological examination of the resected left lower lobe showed grossly dilated bronchi. Microscopic evaluation showed several abnormally dilated large bronchi near the pleural surface with chronic inflammation of the bronchial wall. There was also focal destruction and interruption of the bronchial wall musculature and multiple aggregated lymphoid cells, a finding which corresponded microscopically to bronchiectasis with follicular bronchitis (figure).

Physical examination revealed a young man in no acute distress. The pulse was 120/min, respiration rate 20/min, and blood pressure was 130/80 mm Hg. There was no clubbing, cyanosis, or orthostatic hypotension, breath sounds were vesicular, and the heart rhythm was normal. A spleen tip was palpable in the left upper abdominal quadrant, and the liver was non-palpable. There was no peripheral lymphadenopathy. A chest radiograph was unremarkable except for postoperative changes at the left lung base. A fibreoptic bronchoscopy performed two days later showed a moderate amount of dark blood oozing from the bronchial orifice corresponding to the left upper lobe which did not clear after saline lavage. Similar oozing of dark blood was noted in the right upper lobe but cleared readily after saline lavage. The haemoptysis ceased spontaneously. Pulmonary function testing two weeks later showed an FEV_1 of 3·71 (79% predicted), an FVC of 4·69 (80% predicted), and a TLC of 6·95 (90% predicted). The transfer factor for carbon monoxide (T_{LCO}) and liver function tests were normal. A bronchogram with radiopaque contrast material showed saccular bronchiectasis in the lingula and upper lobe, which now occupied the left hemithorax, and mild bronchiectasis of the right upper lobe. Chest computed tomographic scanning confirmed the bronchographic findings and identified a small cirrhotic liver, gastric varices, and

Reports in the medical literature of α_1-antitrypsin deficiency in association with bronchiectasis

Reference	*No. of cases*	*Total P_1ZZ*	*HPVB*
Ericksson (1965)[6]	35	35	Yes (2)
Orell (1971)[7]	8	6	Yes (4)
Longstreth (1975)[1]	1	1	No
Kagan (1975)[11]	1	1	No
Larsson (1978)[8]	28	246	No
Scott (1977)[2]	1	1	No
Jones (1985)[3]	3	3	No
Current case (1994)	1	1	Yes (1)

HPVB = histopathological verification of bronchiectasis.

splenomegaly. However, a percutaneous needle biopsy of the liver showed no microscopic evidence of cirrhosis. Periodic acid Schiff positive granules were not identified within hepatocytes. Serum protein electrophoresis showed the absence of the usual spike seen in the α_1-globulin region. The serum level of α_1-antitrypsin was 18 mg/dl (8% of normal). The α_1-antitrypsin phenotype of the patient's parents and one sibling were all P_1ZZ. Sweat levels of chloride and immunoelectrophoresis were both normal.

Discussion

Although no clear risk for the development of bronchiectasis in homozygous α_1-antitrypsin deficient individuals has ever been established, a few reports have helped to confirm an association between this deficiency and bronchiectasis and pulmonary infections.[1–3] It has been suggested that the absence of this protease inhibitor accentuates the damage due to the unopposed protease activity which occurs in bronchitis and its accompanying neutrophilic infiltration of the bronchial wall.[3 4] Repeated bronchopulmonary infection with severe PI_1ZZ have been reported.[5] It has been postulated that in the α_1-antitrypsin-deficient individual repeated episodes of ordinary bronchitis, of whatever cause, may lead to the development of bronchiectasis.[4] This suggestion seems to be supported by the study by Ericksson[6] in which most of the 35 cases who underwent necropsy had bronchitis, although only two of the 35 had bronchiectasis.

Orell and Mazodier reviewed the pulmonary histopathology of 38 cases of α_1-antitrypsin deficiency collected from the literature and added eight cases of their own.[7] These authors noted that "chronic bronchiectasis was a common but not a constant finding" in the 38 patients in the literature, but they did not mention bronchiectasis specifically in their review of the 38 cases. Of their own eight cases they chose to report their findings in only six, but did not state why two cases were excluded. Interestingly, one of these six cases was contributed by Ericksson, which is acknowledged in the table.[7] Four of the six cases had bronchiectasis, of whom three had peripheral cylindrical bronchiectasis and one had minor bronchiectasis. These cases differ considerably from the one reported here in that they had severe panlobular emphysema, often with features of vanishing lung and bronchiectasis as a secondary feature.[7] In contrast, our case had bronchiectasis but no histopathological evidence of panlobular emphysema.

Our review of the literature suggests that the association of α_1-antitrypsin deficiency and bronchiectasis may not be as uncommon as is usually believed. Most reported patients with this association have been in middle to late life, usually smokers, and only six appear to have been documented with histopathological evaluation of the bronchiectasis. Thus, our patient may represent only the seventh case reported with histopathological verification of the bronchiectasis, and the first to be diagnosed during life. In agreement with most previous study reports, our patient proved to have a P_1ZZ phenotype.

Studies from Sweden indicate that the frequency of the association of α_1-antitrypsin deficiency and bronchiectasis may be as high as 10%.[6–8] However, the true frequency of bronchiectasis in α_1-antitrypsin-deficient individuals remains to be determined. Conversely, the frequency of α_1-antitrypsin deficiency in series of bronchiectasis (from all causes) is also unknown.[4] Although α_1-antitrypsin is the major anti-elastase of the normal lower respiratory tract, other anti-elastases also exist.[9 10] Because of the possible protection by anti-elastases other than α_1-antitrypsin that are not measured, the association between bronchiectasis and anti-elastase deficiency may not be well established.

The ease with which α_1-antitrypsin can be aerosolised into the tracheobronchial tree with return of anti-elastase defences may make this a therapeutic option in patients with bronchiectasis attributed to α_1-antitrypsin deficiency.[5]

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