Amiodarone pulmonary toxicity presenting as a solitary lung mass.

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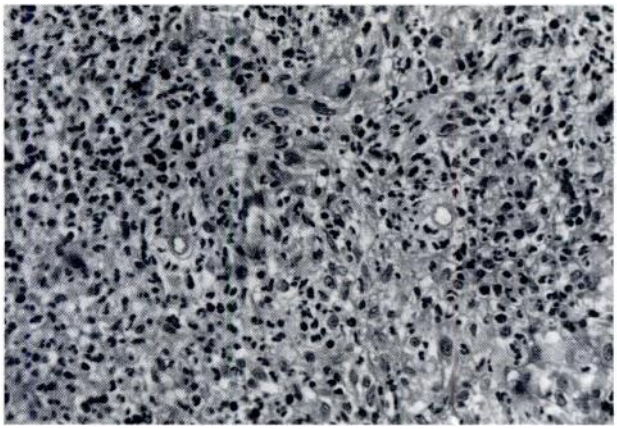

FIGURE 3. Hematoxylin and eosin stain of the tracheal lesions. *Blastomycosis dermatitidis* is distinguished by the double-contoured appearance (original magnification, ×400).

vesicular lesions in the trachea extending from 3 cm below the larynx to the bifurcation (Fig 2). In addition, there was near closure of the orifice to the lingular segment by similar lesions. A biopsy of the lesions in the trachea revealed blastomycosis (Fig 3).

The patient was started on intravenous amphotericin B given through a Hickman catheter. She received a total of 2 g/day of amphotericin B over a period of approximately 2½ months and tolerated the drug well. Repeat chest x-ray films showed gradual resolution, and six months after the infusion of amphotericin B was completed, the patient's chest x-ray film findings were entirely normal and she felt well (Fig 4). She was offered but has refused a repeat bronchoscopic examination. The heart murmur disappeared as the fever and anemia resolved during the initial two weeks of amphotericin B therapy.

DISCUSSION

To our knowledge, this is the first reported case demonstrating tracheal infection in pulmonary blastomycosis. The trachea is not mentioned as a site of infection in Sarosi's extensive review.[2] However, blastomycosis has been described in the mouth, oropharynx and larynx. The Mayo Clinic report described six patients with laryngeal blastomycosis of a total of 107 patients observed over a period of 30 years.[1] Their cases showed both gross and microscopic findings suggestive of well-differentiated squamous cell carcinoma leading to misdiagnosis and inappropriate surgical and irradiation therapies. The lesions in our patient, although not consistent grossly with either blastomycosis or carcinoma, were very diagnostic histologically of blastomycosis. The larynx was spared in our patient, as the lesions began in the proximal trachea and extended to the bifurcation. Payne and Koopmann[3] described a patient with persistent hoarseness where the diagnosis was felt to be carcinoma until the tissues were studied more extensively. The mode of spread to the larynx has been felt to be hematogenous or by direct exposure from infected sputum. Our patient most likely experienced direct extension from the lingula and the orifice of the lingula into the distal trachea rather than hematogenous spread. Further reports of laryngeal and esophageal blastomycosis are documented by other authors, but none has mentioned the trachea.[4-6]

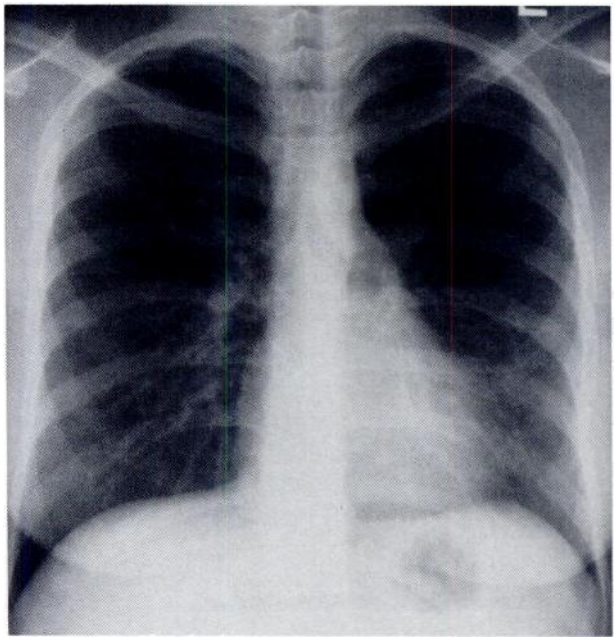

FIGURE 4. Roentgenogram of the chest showing near total resolution of the lingular infiltrate.

Finally, the diagnosis was initially made on hematoxylin and eosin staining demonstrating the organism. One can speculate how often tracheal blastomycosis is missed, especially if bronchoscopic examination is not employed in the diagnosis of a pulmonary lesion. The major method of diagnosis of blastomycosis is by KOH preparation or culture of coughed sputum. Bronchoscopy is employed in more chronic cases where carcinoma is in the differential diagnosis. When blastomycosis is discovered, the trachea has been spared. Since this is the first reported case of tracheal blastomycosis, this manifestation of the disease must be rare.

REFERENCES

1 Dumich PS, Neel HB. Blastomycosis of the larynx. Laryngoscope 1983; 93:1266-70

2 Sarosi GA, Davies SF. State of the art. Blastomycosis. Am Rev Respir Dis 1979; 120:911-38

3 Payne J, Koopmann CF. Laryngeal carcinoma—or is it laryngeal blastomycosis? Laryngoscope 1984; 94:608-11

4 McKenzie R, Khakoo R. Blastomycosis of the esophagus presenting with gastrointestinal bleeding. Gastroenterology 1985; 88:1271-73

5 Bennett M. Laryngeal blastomycosis. Laryngoscope 1964; 73:498-512

6 Suen JY, Wetmore SJ, Wetzel WJ. Blastomycosis of the larynx. Ann Otol 1980; 89:563-66

Amiodarone Pulmonary Toxicity Presenting as a Solitary Lung Mass*

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Following treatment with amiodarone, a patient developed weight loss, fatigue and severe myopathy, without respiratory symptoms. A solitary lung infiltrate, impaired thyroid and liver function tests, and leukocytosis were evident. Biopsies from the lung lesion, liver, and bone marrow re-

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vealed foam cells. All these signs and symptoms subsided following cessation of amiodarone therapy. It is demonstrated that amiodarone may induce a localized lung lesion rather than diffuse pulmonary disease.

Amiodarone has been widely used in the last 15 years for the treatment of cardiac arrhythmias.[1] One of its most serious side effects is pulmonary toxicity.[2] Early symptoms in most patients include exertional dyspnea and non-productive cough. The characteristic x-ray film findings are diffuse bilateral alveolar and interstitial infiltrates.[3] We report a case of amiodarone pulmonary toxicity presenting as a solitary lung lesion.

Case Report

A 65-year-old man with ischemic heart disease, left ventricular aneurysm and congestive heart failure, underwent cardiac aneurysmectomy in 1968. In September 1983 he began to suffer from recurrent attacks of ventricular tachycardia and was treated with quinidine sulfate 1200 mg/day. In September 1984 recurrent bouts of ventricular tachycardia occurred and the quinidine was replaced by procainamide 1 g/day and amiodarone hydrochloride 400 mg/day.

Two years later he was hospitalized due to severe fatigue, dysphagia and an 11 kg weight loss. On admission, he appeared cachectic. A grade 3/6 systolic murmur was heard over the apex. The lungs were clear. The liver was palpated 2 cm below the costal margin. Laboratory results revealed ESR of 110 mm in the first hour. The haemoglobin was 14.5 g/dl, white blood cell count 26×10^9/liter and platelet count 700×10^9/liter. The globulin was 4.5 g/dl and the albumin 3.4 g/dl. Protein electrophoresis revealed polyclonal elevation of gamma globulin. Thyroid function tests revealed T_4 of 25 μg/dl, T_3 of 146 ng/dl, T_3 resin uptake of 60 percent and FTI of 20. TRH test results were compatible with thyrotoxicosis. The ANF was +2. Chest x-ray film (Fig 1) showed an infiltrative lesion in the right upper lobe. On chest CT scan (Fig 2) a round mass with irregular borders was seen. Bronchoscopy did not demonstrate any airway obstruction. Eight biopsies taken from the mass showed a mononuclear infiltration with scattered foam cells in the alveolar walls.

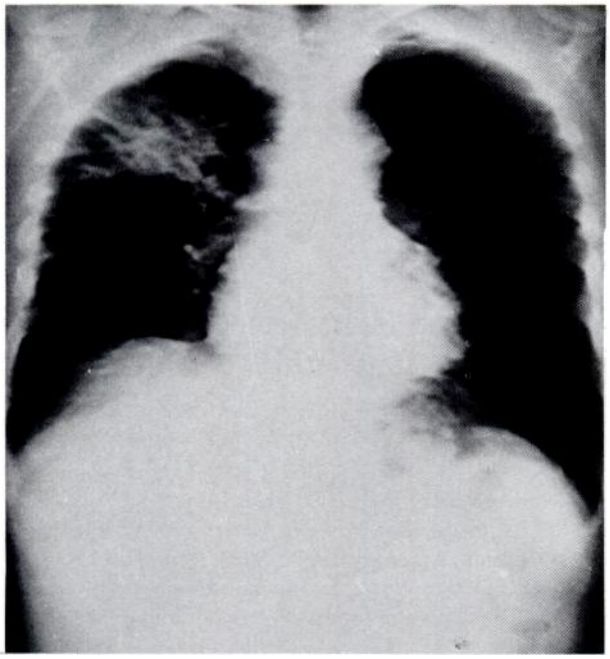

Figure 1. Roentgenogram of the chest on admission showing an infiltrative lesion in the right upper lobe.

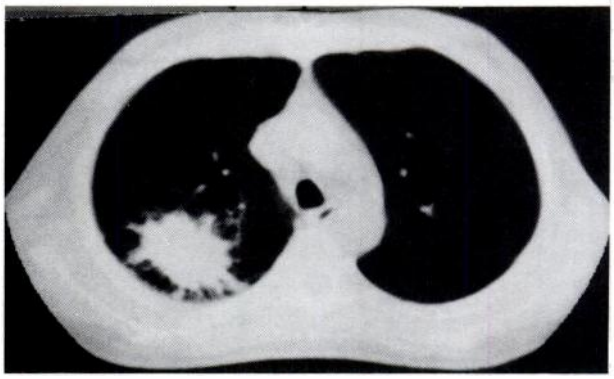

Figure 2. Chest CT scan on admission showing a round mass with irregular borders in the right upper lobe.

Liver biopsy revealed chronic active hepatitis with fibrosis, and foam cells were found in the sinusoids. Bone marrow was hypercellular and contained some foam cells.

During the following month the patient lost another 12 kg and became bedridden due to severe proximal myopathy. The treatment with procainamide was stopped without any improvement. Two weeks later, the treatment with amiodarone was replaced by mexiletene. Within several weeks, the patient improved tremendously. The dysphagia disappeared and he gained weight. The chest x-ray film showed clearing and the CT scan revealed nearly complete disappearance of the lung infiltrate (Fig 3). The white blood cell count decreased to 14×10^9/L. The platelet count decreased to 445×10^9/L. Liver function test results were all normal except for alkaline phosphatase of 155 IU and results of thyroid function tests were normal.

Discussion

Administration of amiodarone is associated with toxic effects in various organs, mainly lung, liver, thyroid, nerves, heart and skin. The side effects are mediated via inhibition of lysosomal enzymes resulting in the accumulation of phospholipids in foam cells.[4]

The main clinical manifestations of amiodarone-induced pulmonary disease include exertional dyspnea, non-productive cough and weight loss. The white blood count is often normal to moderately elevated, but may be markedly elevated.[5] The erythrocyte sedimentation rate is elevated and there may be mild disturbance in liver function tests.[5]

Radiographic findings characteristically consist of diffuse or patchy bilateral alveolar infiltrates. Chest x-ray film find-

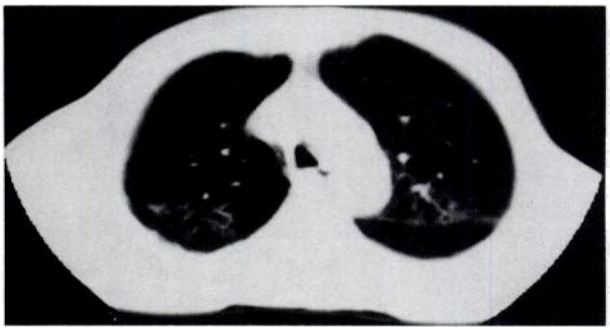

Figure 3. Chest CT scan two months after cessation of amiodarone therapy, showing nearly complete resolution of right upper lobe infiltrate.

ings suggest pulmonary edema, pneumonitis, or tuberculosis; rarely, pleural effusion or areas of pleural thickening may be found.[2,6]

Amiodarone-induced pulmonary toxicity may be at least in part dose-related and most of the patients developed the infiltrates with a dose greater than 600 mg/day, usually after treatment with more than 130 g of the drug. The histologic finding is compatible with nonspecific pneumonitis with intra-alveolar accumulation of foamy macrophages and hyperplasia of type 2 pneumocytes.

Our case represented a unique, outstanding clinical laboratory and roentgenographic finding. There was no symptom related to the lung disease. Instead, dysphagia, severe myopathy and severe weight loss were the prominent signs. Moreover, leukocytosis and thrombocytosis, together with normal bone marrow, protean clinical and laboratory manifestations compatible with the so-called paraneoplastic syndrome, were evident. The finding of a solitary lung lesion without any other lung involvement, to the best of our knowledge, has never been reported with amiodarone lung disease. Yet, the impaired thyroid function, liver disease, leukocytosis and lung infiltrate were suggestive of amiodarone toxicity, especially in view of the foam cells found in bone marrow, lung, and liver biopsy, and the relatively high dose of amiodarone used by the patient. Indeed, discontinuation of amiodarone resulted in clinical improvement with resolution of the lung mass. We have no explanation for the solitary, localized lung lesion. It is possible that a very early diagnosis of the lung involvement due to severe extrapulmonary symptoms resulted in a solitary finding in the lung. Alternatively, some prior localized vascular or inflammatory pulmonary process could have resulted in increased localized accumulation of the drug.

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References

1 Rosenbaum MB, Chiale PA, Halpern MS, Nau GS, Przybylski J, Levi RJ, et al. Clinical efficacy of amiodarone as an antiarrhythmic agent. Am J Cardiol 1976; 38:934-44
2 Rakita L, Sobol SM, Mostow ND, Vrobel T. Amiodarone pulmonary toxicity. Am Heart J 1983; 106:906-16
3 Lok-wan Liu F, Cohen RD, Downar E, Butarry JW, Edelson JD, Rebuck AS. Amiodarone pulmonary toxicity: functional and ultrastructural evaluation. Thorax 1986; 41:100-05
4 Hostetler KY, Reasor MH, Walker ER, Yazaki PJ, Frazee BW. Role of phospholipase A inhibition in amiodarone pulmonary toxicity in rats. Biochim et Biophys Acta 1986; 400-05
5 Marchlinski FE, Gansler TS, Waxman HL, Josephson ME. Amiodarone pulmonary toxicity. Ann Intern Med 1982; 97:839-45
6 Lubbe WF, Mercer CJ. Amiodarone: its side effects, adverse reactions and dosage schedules. N Zealand Med J 1982; 95:502

Diffuse Alveolar Hemorrhage Temporally Related to Cocaine Smoking*

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Previous reports of respiratory complications from cocaine abuse have focused on pulmonary barotrauma or a reduction in carbon monoxide diffusing capacity. We report a patient who developed life-threatening alveolar hemorrhage following repeated inhalation of alkaloid cocaine.

Recreational abuse of cocaine has reached epidemic proportions in this country.[1] Novel methods are being used to enhance delivery and absorption of this drug. The most popular is freebasing, a method of inhalation which rapidly produces high plasma levels of cocaine.[2] To date, published respiratory complications of cocaine inhalation include pulmonary barotrauma[3,4] or a reduction in carbon monoxide diffusing capacity.[5,6] We report diffuse alveolar hemorrhage in a smoker of alkaloid cocaine, a potentially life-threatening complication of cocaine inhalation.

Case Report

A healthy 36-year-old black woman presented to another hospital complaining of dyspnea for two weeks and blood-streaked sputum. Tracheobronchitis was diagnosed and she was instructed to take oral ampicillin. Nine days later, she presented to us with greater dyspnea and hemoptysis.

Her past medical history was unremarkable. She smoked one pack of cigarettes daily for ten years and she denied IV drug abuse. On examination, the patient was breathing 30 times per minute with a pulse rate of 110/min, blood pressure of 102/68 mm Hg and a temperature of 37.6°C. Chest auscultation was significant for bibasilar rales. She had no skin lesion.

The white blood cell count was 13,900/cu mm, with 36 percent neutrophils, 28 percent lymphocytes and 26 percent eosinophils. The hematocrit was 19 percent. The erythrocyte sedimentation rate was 34 mm per hour, serum creatinine was 0.7 mg/dl, blood urea nitrogen was 10 mg/dl and the urinalysis was normal. The antinuclear antibody titer was undetectable. Arterial blood drawn while inspiring room air showed PaO_2, 64 mm Hg; $PaCO_2$, 31 mm Hg; pH, 7.41. A chest radiograph showed diffuse alveolar infiltrates with a normal cardiac silhouette (Fig 1).

Fiberoptic bronchoscopy demonstrated fresh blood coming from the lower lobe bronchi. Analysis of the bronchial lavage fluid revealed only hemosiderin-laden macrophages. The patient was transfused to a hematocrit of 33 percent and methylprednisolone (1 g intravenously every six hours) was started.

During the next 24 hours, the patient reported improvement in her dyspnea. However, on the following day, her dyspnea worsened and she expectorated ½ cup of blood. The hematocrit fell to 21 percent and the arterial PaO_2 was 72 mm Hg while breathing 70 percent oxygen by face mask. An open lung biopsy was performed

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