Breathlessness With Bumps, Lumps, and Humps*

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A 61-year-old retired bus driver with a 35-pack-year history of cigarette smoking presented with a 15-year history of gradually progressive breathlessness without cough or sputum production. Examination showed kyphoscoliotic deformity of his upper thoracic spine, multiple skin nodules, and bilateral crackles on auscultation of the chest but no digital clubbing.

A chest radiograph showed a well-defined rounded opacity at the left apex, ribbon deformity of the left upper ribs, and predominantly nodular interstitial shadowing most marked in the mid and lower zones. There was a sharp angular kyphoscoliosis with dysplastic upper vertebral bodies (Fig 1). Thoracic computed tomography (CT) showed a 4 × 3 × 3-cm sharply circumscribed soft-tissue mass in the paravertebral region at the left apex. The spinal canal was enlarged and distorted in this region. High-resolution CT images of the lung parenchyma (2-mm sections at 30-mm increments) showed scattered, multiple, thin-walled bullae, which were largest and most numerous in the upper lobes (Fig 2). In addition, there was irregular septal thickening with a peripheral subpleural predominance in the middle and lower lobes, indicative of moderate pulmonary fibrosis.

Pulmonary function testing showed the following values: FEV\textsubscript{1}, 1.53 L (53 percent of predicted); forced vital capacity, 2.63 L (73 percent of predicted); total lung capacity by helium dilution, 4.35 L (71 percent of predicted); residual volume, 1.98 L (88 percent of predicted); diffusing capacity for carbon monoxide by the single-breath method, 4.3 mmol/min/kPa (52 percent of predicted); and diffusion coefficient, 1.08 (76 percent of predicted). While the patient was breathing room air, his arterial PaO\textsubscript{2} was 83 mm Hg and his PaCO\textsubscript{2} was 41 mm Hg.

Bronchoalveolar lavage showed a total white cell count of 1 × 10\textsuperscript{6}/ml, consisting almost entirely of macrophages (macrophages, 99.4 percent; lymphocytes, 0.2 percent; neutrophils, 0.2 percent). Transbronchial biopsy specimens taken from the left lower lobe showed pneumocyte hyperplasia, focal thickening of the interstitial septa, and mild fibrosis and thickening of the media of the blood vessels.

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**Diagnosis: Thoracic neurofibromatosis**

Neurofibromatosis was first described as a discrete entity by von Recklinghausen in 1882. It is one of the most common autosomal-dominant inherited traits, affecting at least 20 per 100,000 of the population. It can be broadly divided into two forms. The classical peripheral form is characterized by cutaneous neurofibromas, café-au-lait spots, and a diverse variety of systemic manifestations, whereas the rarer central form is characterized by the occurrence of bilateral acoustic neuramas.

This patient's chest radiograph demonstrates many of the major thoracic manifestations of this disease, showing a paravertebral neurofibroma, kyphoscoliotic vertebral deformity, cutaneous neurofibroma, and diffuse fibroblastic interstitial disease. Neurofibromas are the most common thoracic manifestation of neurofibromatosis and arise from elements of the nerve sheaths in the sympathetic chain, vagus, intercostal, and intrapulmonary nerves. They particularly occur adjacent to the spinal column, where they may cause scalloping and erosion of vertebral bodies or may extend into the spinal canal as a dumbbell tumor. Although the associated changes are usually benign, malignant change may occur. Neurofibromas may arise at other sites in the respiratory tract, and upper airway obstruction due to neurofibroma has been reported but is rare.

Kyphoscoliosis affects at least 2 percent of patients with neurofibromatosis. The lower cervical and upper thoracic portions of the spine are most commonly affected, with acute anterior angulation and S-shaped rotary scoliosis. Deformity usually becomes manifest in adolescence, and early surgical intervention may be necessary to halt the progression of the curvature. Although kyphoscoliosis is often associated with paravertebral neurofibromas, it is not clear that the tumors are the cause of the spinal deformity.

Interstitial lung disease in association with neurofibromatosis was first reported in 1963. Although neurofibromatosis is hereditary, lung fibrosis does not become evident until the third or fourth decade of life. Pulmonary function studies typically show a combination of a restrictive and an obstructive ventilatory defect with impaired diffusing capacity.

Radiographic appearances vary from a honeycomb pattern of interstitial disease to a more diffuse pattern of fibrosis, which is usually symmetrical and particularly affects the lower lobes. Bullae are a characteristic feature and particularly occur in the upper lobes, where they may be complicated by the occurrence of pneumothorax. Occasionally, pleural shadowing extending into the lung fields may be seen.

The macroscopic findings on direct examination of the lungs are similar to the radiographic features but usually show a more marked fibroblastic pattern. Histologic changes are indistinguishable from those of idiopathic pulmonary fibrosis and are often of a desquamative nature. Bronchiolar obliteration is seen occasionally. An unusual feature in some cases is the occurrence of obliterative arteritis with thrombosis and recanalization. As in interstitial fibrosis due to other causes, the disease may be complicated by the development of a scar carcinoma. Bronchoalveolar lavage has rarely been performed in this disease, but it showed a predominance of macrophages in the reported case of one patient who, like our patient, was a smoker.

The pathogenesis of interstitial lung disease in neurofibromatosis is unknown, but previous authors have speculated that it may be the expression of an inherited mesenchymal defect resulting in abnormal, primary deposition of collagen in the lungs.

**REFERENCES**