Lung cancer and parenchymal lung disease in a patient with neurofibromatosis type 1

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TO THE EDITOR:

A 63-year-old nonsmoking female patient with neurofibromatosis type 1 (NF1) was referred to our hospital with a 2-month history of cough and a chest X-ray finding of an opacity in the right lung (Figure 1A). Physical examination revealed multiple cutaneous neurofibromas and *café-au-lait* spots primarily on the trunk. A CT scan of the chest showed a spiculated nodule in the right upper lobe (Figure 1B), as well as mediastinal and right hilar lymph node enlargement, together with cystic and emphysematous changes in the lung parenchyma and skin nodules (neurofibromas) on the chest wall (Figures 1B, 1C, and 1D). Hypodense nodular lesions (metastases) were observed in the liver. Alpha-1 antitrypsin levels were normal. A transbronchial lung biopsy was performed, with histopathological findings of adenocarcinoma. A diagnosis of pulmonary adenocarcinoma with neurofibromatosis-associated diffuse lung disease was established, and the patient underwent chemotherapy. Her condition worsened, and she died 5 months later.

The most common pulmonary manifestations of NF1 are diffuse interstitial lung disease and emphysematous, cystic, and bullous changes in the lung, with a prevalence rate of 10-20%. In addition, NF1 can increase lung sensitivity to cigarette smoke, leading to early emphysema-like changes. Therefore, in addition to being a risk factor for lung cancer, smoking is a potential risk factor for interstitial lung disease in NF1 patients.[1,2] Although NF1 is the most common inherited syndrome predisposing to neoplasia, particularly neural crest-derived tumors, it is not commonly reported in association with lung cancer.[3]

Two major hypotheses have been proposed to explain the association between NF1 and lung cancer.[1] One hypothesis is related to the development of tumors from previous scar tissue or bullae secondary to interstitial fibrosis.[1] The other hypothesis is related to chromosome 17p deletions, the prevalence of which is increased in certain NF1 patients.[1,4] It should be noted that the p53 tumor suppressor gene is located on the short arm of chromosome 17.[1,4] Inactivation of p53 has been implicated in the development of small cell lung cancer in patients with NF1, and p53 mutations have been found in approximately 50% of patients with non-small cell lung cancer.[1,4] This increased risk of lung cancer in never smokers with NF1, as was the case with our

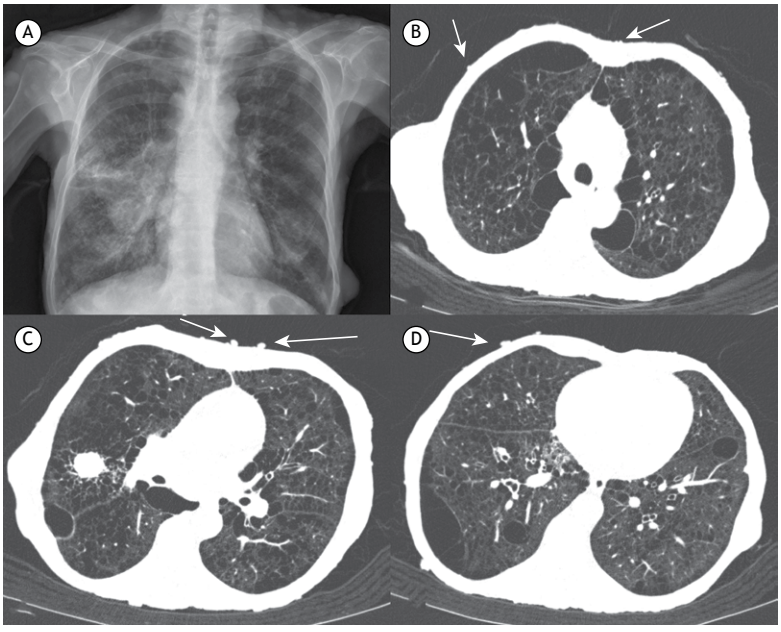

Figure 1. In A, chest X-ray showing an ill-defined opacity in the right lung and mediastinal enlargement, suggestive of lymph node enlargement. Note soft-tissue nodules on the chest wall and shoulders. In B, C, and D, axial CT images of the chest (lung window settings) showing cystic and emphysematous changes predominantly in the upper lobes, as well as a solid nodule with spiculated margins in the right upper lobe. Note nodules (neurofibromas) on the chest wall (arrows).

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patient, can be further compounded by tobacco use; studies have demonstrated a higher frequency of p53 mutations in smokers than in never smokers.[1] Because our patient was a never smoker, her case highlights the role of NF1 as a risk factor for the development of lung cancer and the need for assessing pulmonary involvement in patients with NF1, especially those with known interstitial lung disease, by means of low-dose chest CT performed at long intervals for early detection of lung cancer.

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