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Case Report

Neurofibromatosis type 1 complicated with malignant transformation and diffuse pulmonary disease

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ABSTRACT

Neurofibromatosis type 1 can be severe and associated with progressive course and death. Although it has been rarely reported, a subset of patients with neurofibromatosis type 1 may develop interstitial lung disease. However, no case of neurofibrosarcoma and lung involvement together has been reported so far. We report a case of a 45-year-old male who was previously diagnosed as having neurofibromatosis type 1, 12 years later after the initial diagnosis he was histologically confirmed to have malignant transformation, and 3 years later he had associated diffuse lung damage.

1. Introduction

Neurofibromatosis, a common neurocutaneous disorder, includes numerous different forms. Neurofibromatosis type 1 (NF1), also known as von Recklinghausen's disease, is the most common type and accounts for at least 85 percent of patients.[1]

Plexiform neurofibromas can undergo malignant transformation to neurofibrosarcomas (also called malignant peripheral nerve sheath tumors, malignant schwannomas or neurogenic sarcomas). The lifetime risk of malignant transformation is estimated to be 5 percent.[1] Neurofibrosarcomas are aggressive and potentially fatal malignancies that most often occur in adolescence and adulthood. The first presentation of malignant transformation often is pain or rapid growth of a nodule within an existing plexiform neurofibroma.[2]

The literature suggests that 10%–20% of adult patients with neurofibromatosis have associated interstitial lung disease. Characteristics of such involvement include bilateral lower lobe fibrosis and may include bullous and cystic changes in advanced cases. However, no case of neurofibrosarcoma complicated with multiple bullae in lungs has been described previously.

2. Case presentation

A 45-year-old male presented with a 12-year history of neurofibromatosis. He had been admitted to a hospital 12 years earlier for a painful cervical mass. An excisional biopsy had been performed that revealed a benign plexiform neurofibroma and he had been followed-up without any treatment.

When he registered in 2002, he complained of a mass over the chest wall, occurring four months before the present hospital admission. He had no constitutional symptoms such as weight loss, fever or night sweats. A complete physical examination was performed which revealed a painful soft tissue mass on the right anterolateral chest wall and multiple, rubbery, well-defined, painless skin nodules over the skull, trunk and extremities, suggestive of neurofibromas. In addition, there were multiple, hyperpigmented, irregularly shaped macules over the back, suggestive of cafe-au-lait spots, eight of which were larger than 15 mm, and both axillary and inguinal freckling were present. Family members were also found to have features of segmental neurofibromatosis. Cafe-au-lait spots were observed in his father, two of his brothers, and his daughter. These findings were consistent with the diagnosis of neurofibromatosis. Thoracic CT scans demonstrated a 10 × 10 cm soft-tissue subcutaneous mass in the right lateral chest wall and a 30 × 15 mm sized solid nodule on the lateral pleural side of the right lung. Subsequent histological examinations of the resected thoracic mass and nodule revealed a malignant mesenchymal tumor and metastatic malignant

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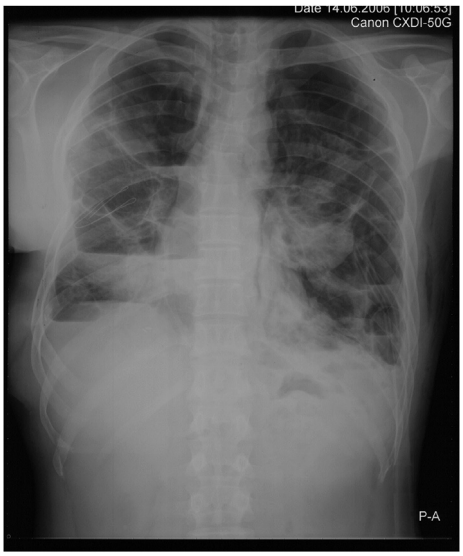

Fig. 1. A chest radiograph showing widespread, thin-walled, bulky bullae with effusion

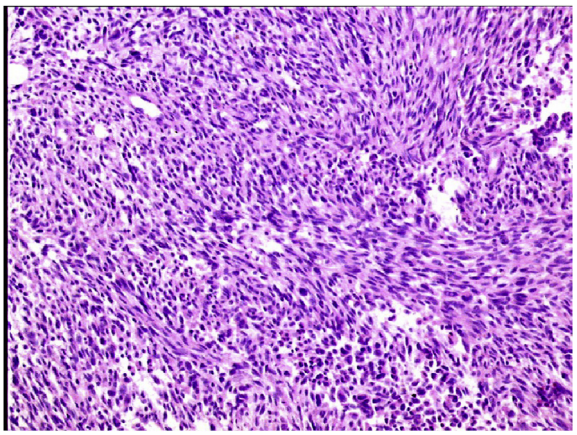

Fig. 3. Cellular fascicles of pleomorphic spindle cells of the malignant peripheral nerve sheath tumor (Hematoxylin & Eosin staining, 100× magnification)

schwannoma, respectively. Adjuvant chemotherapy was proposed but the patient did not accept the treatment and was lost to follow-up for several years.

In February 2005, he returned with a recurrent mass over the chest wall. At the time of presentation, he was restless and experienced progressive weakness and dyspnea. His oxygen saturation, measured by pulse oximetry, was 89% while breathing room air and had severe tachypnea. Chest radiograph (Fig. 1) and computed tomographic scan (Fig. 2) showed widespread, thin-walled, bulky bullae bilaterally placed in lung parenchyma and the presence of a 15 × 15 cm sized, well-demarcated, solid mass on the anterolateral chest wall. Pathologic examination of the resected mass revealed fleshy and opaque soft tissue tumor with white-tan surface and hemorrhagic, necrotic focal areas, macroscopically. Microscopic appearance of the tumor showed highly cellular, pleomorphic Schwann cell-like spindle cells with prominent mitotic activity, consisting of dense fascicles alternating with less cellular areas. Tumor cells revealed focal and strong immunoreactivity for S-100 protein (Figs. 3 and 4). The pathological diagnosis was malignant peripheral nerve sheath tumor. Ophthalmologic examination was found normal and bone abnormalities like pseudarthrosis and dysplasia were not present.

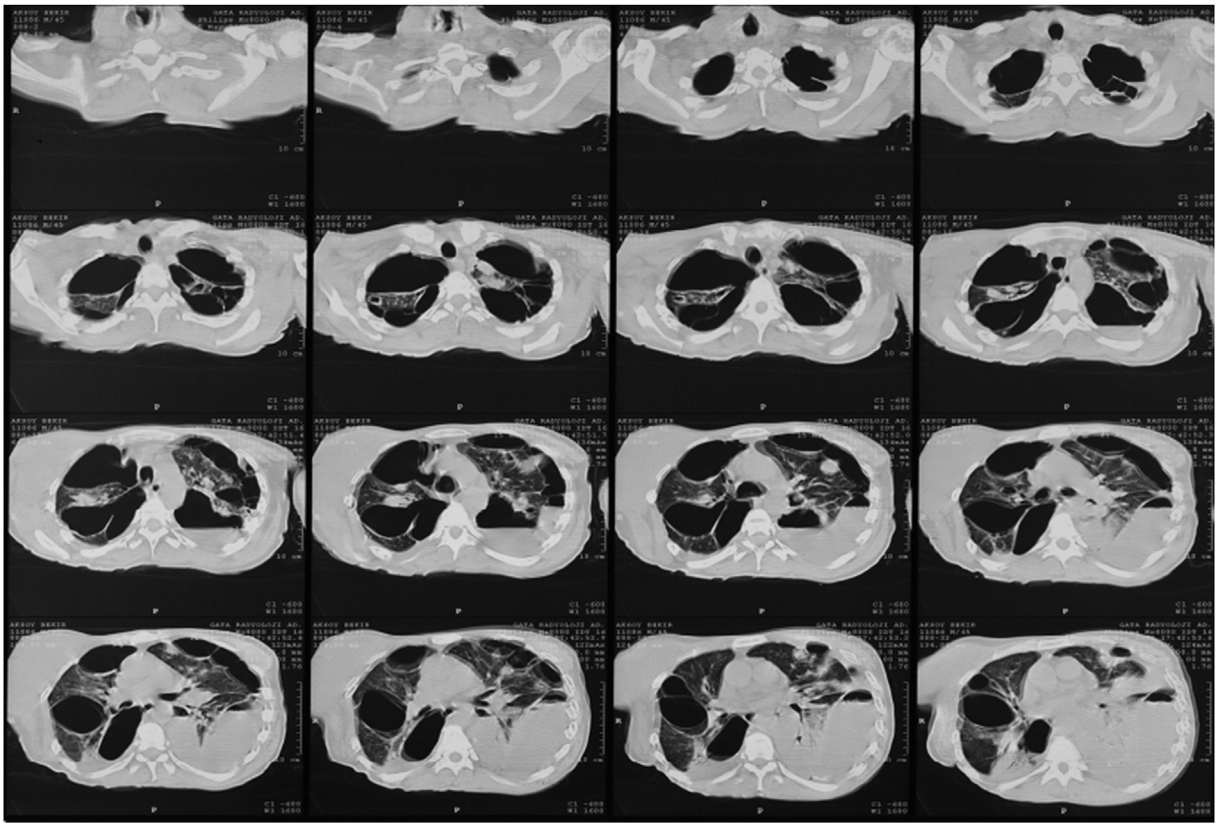

Fig. 2. A computed tomographic scan showing diffuse lung damage and a mass on the anterolateral aspect of the right chest wall

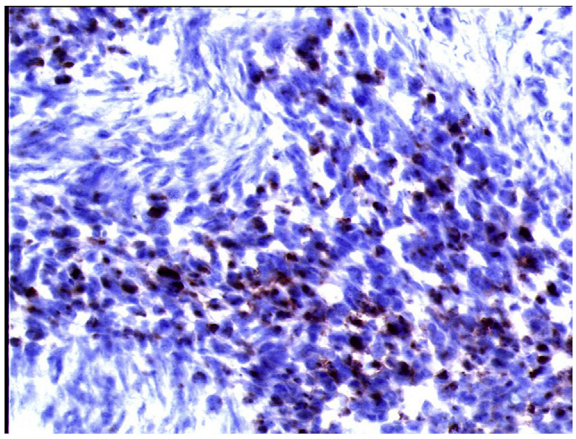

Fig. 4. Focal and strong S-100 protein immunoreactivity of the tumor cells. (Immunohistochemistry, 200× magnification)

He received radiotherapy to chest wall (a total dose of 48 Gy in 16 daily fractions of 300 cGy, administered five days per week), three cycles of chemotherapy and underwent thoracic drainage and pleurodesis for intractable pleural effusion. Unfortunately, he died 3 months later because of the rapidly progressive course of disease.

3. Discussion

The diagnostic criteria for NF1, developed by the National Institutes of Health Consensus Conference in 1987 and updated in 1997, are based upon specific clinical features.[3–5] The diagnostic criteria are met in a patient who has at least two of the followings: 1) Six or more cafe-au-lait macules larger than 5 mm in greatest diameter in prepubertal individuals or larger than 15 mm in greatest diameter in postpubertal individuals, 2) Two or more neurofibromas of any type or one or more plexiform neurofibromas, 3) Freckling in the axillary or inguinal regions, 4) Optic glioma, 5) Two or more Lisch nodules (iris hamartomas), 6) A distinctive osseous lesion, such as sphenoid dysplasia or thinning of the long bone cortex, with or without pseudarthrosis, and 7) A first-degree relative with type 1 neurofibromatosis according to the above criteria. Four of these diagnostic criteria were completely fulfilled in the present patient.

NF patients have an increased potential for malignant transformation. However, a few cases of neurofibrosarcoma associated with NF1 have so far been reported worldwide.[6,7] Additionally, lung involvement in NF1 is very rare and only sporadic cases have been reported in the literature.[8–10] To our knowledge, no case of neurofibrosarcoma and multiple bullae in lungs together, as present in the case reported herein, has been reported till date. Interstitial involvement of the lung, caused by bullae subsequently increasing in size, progressively developed in the present case over the past 3 years. The result was diffuse parenchymal lung damage. It's remarkable that he was a non-smoker and had never lived with smokers.

In conclusion, the presence of NF1 complicated with malignant transformation and bulky parenchymal bullae in lung together is noteworthy. The unpredictable course of NF1 makes prolonged follow-up mandatory.

Conflict of interest

None.

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