Intrathoracic peripheral nerve sheath tumors in patients with neurofibromatosis type 1 (von Recklinghausen disease)

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Inrathoracic neurogenic tumors comprise 15% to 25% of all primary mediastinal tumors in adults, and 95% originate within the posterior mediastinum.¹ In most, these are benign slow-growing schwannomas and neurofibromas of peripheral nerve origin. However, patients with neurofibromatosis type 1 (NF1) are particularly at risk for malignant transformation of these tumors and have a poor long-term prognosis.²

Clinical Summaries

We present 3 cases of intrathoracic peripheral nerve sheath tumors in patients with NF1 disease.

PATIENT 1. A 55-year-old man presented with a recent onset of dyspnea and a known posterior mediastinal mass diagnosed 20 years earlier. The mass had increased in size over the past 5 years. Chest radiography revealed a smooth shadow adjacent to the right upper thoracic spine, and computed tomographic (CT) scan confirmed a 4.3×3.4 -cm low-attenuation mass occupying the right posterior mediastinum. Intraoperative bronchoscopy results were negative. He underwent a posterolateral thoracotomy with resection of a well-circumscribed $5 \times 4 \times 3$ -cm mass. The histopathologic diagnosis was neurofibroma. His postoperative course was uneventful, and he is doing well 15 months after resection.

PATIENT 2. A 35-year-old woman with prior resection of a brachial plexus neurofibroma presented with recent onset of dyspnea. The chest radiograph showed a left perihilar mass. CT scan confirmed a mediastinal mass abutting the major vessels. A magnetic resonance imaging (MRI) scan demonstrated no signs of invasion (**Figure 1**). Intraoperative bronchoscopy was unremarkable. Exploratory video-assisted thoracic surgery and biopsy revealed that histologic characteristics were consistent with neurofibroma, and a $12 \times 6 \times 3$ -cm well-circumscribed mass was readily resected via a posterolateral thoracotomy. The final histopathologic analysis confirmed a neurofibroma. She made an uneventful recovery and remains free of disease 16 months later.

PATIENT 3. A 27-year-old man with prior excision of a right thigh neurofibroma 10 years earlier presented with a several-month history of progressive dyspnea and weight loss. A chest radiograph film showed inhomogeneous opacification of the left hemithorax.

Figure 1. An MRI scan of the chest demonstrates a 4.3×7.7 -cm anterosuperior mediastinal mass abutting the aortic arch, its branches, and the left main pulmonary artery without signs of invasion.

CT scan revealed a large heterogenous mass occupying the entire left hemithorax with marked mediastinal shift (**Figure 2**). An MRI scan demonstrated tumor encasement of the left hilar vessels, indistinct lung, and the heart displaced into the right hemithorax. An intraoperative bronchoscopy showed complete extrinsic compression of the upper and lower lobe bronchi. Given the anticipated technical challenges, resection was approached through a bilateral transsternal anterolateral thoracotomy (clamshell) incision that allowed for exposure and cardiopulmonary bypass if necessary. The mass and the completely collapsed and firmly adherent entire left lung were resected en bloc. The histopathologic characteristics were pleomorphic sarcoma consistent with a malignant peripheral nerve sheath tumor. The patient made a satisfactory recovery and was discharged 10 days later. He died 4 months later of an inoperable subdiaphragmatic tumor.

Discussion

NF1 is an autosomal dominant neurocutaneous disorder. The NF1 gene mutation is on chromosome 17, and its product, neurofibromin, normally functions as a tumor suppressor to reduce cell proliferation by inactivating the proto-oncogene p21-ras.³ NF1 patients, therefore, have an increased predilection for the development of both benign and malignant nerve sheath tumors. Mediastinal tumors in NF1 patients are typically neurofibromas that originate in the posterior mediastinum and have a particular pre-

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Figure 2. A CT scan of the chest demonstrates a large heterogeneous enhancing mass occupying the entire left hemithorax with mediastinal shift to the right. At resection, the tumor was multi-lobulated and well circumscribed with a pseudocapsule. It weighed 13 pounds and measured 40 × 25 × 12 cm.

disposition for malignant transformation.² These tumors can remain clinically silent and are discovered as incidental findings on imaging studies or grow to large sizes before causing symptoms or invasion into adjacent vital structures. CT scan usually provides sufficient information to assess the mediastinal mass; however, the radiologic features of benign and malignant peripheral nerve sheath tumors are nonspecific. MRI scan may further delineate intraspinal involvement or relationships to critical structures. Currently, the role for positron emission tomographic imaging remains undefined. The coexistence of retroperitoneal neurogenic tumors, although rare, should be recognized during the evaluation and

management of NF1 patients with suspected mediastinal neurogenic tumors.

Traditionally, extirpation of mediastinal neurogenic tumors is approached through a posterolateral thoracotomy. Thoracoscopic resection of neurogenic tumors continues to mature, with recognized limitations in patients with large (>6 cm) tumors, suspected malignancy, intervertebral extension, and involvement of adjacent structures.⁴

Patients with benign tumors and complete resection have excellent outcomes. Despite delayed referral in our first case and a location central to vital structures in the second case, both patients are doing well, having undergone early and complete resection soon after presentation. The third patient had a poor long-term outcome despite an aggressive intrathoracic resection and uncomplicated postoperative course. Significant prognostic factors in patients with malignant tumors include size, low histopathologic grade, and completeness of resection.⁵ As demonstrated by the 3 cases presented, complete resection is possible in most patients regardless of the tumor size and location. An aggressive surgical approach is warranted because of the risk of malignant transformation and the chemoresistance of these tumors.

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