

A Giant Atypical Neurofibroma in the Right Thoracic Cavity of a 57-Year-Old Man: A Case Report with Review of the Literature

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Abstract

Intrathoracic neurogenic tumors are not uncommon, but presentation as a giant mass in the thoracic cavity is rare. Although several cases of intrathoracic giant malignant peripheral nerve sheath tumor have been reported, only one case of intrathoracic giant benign neurofibroma appears in the literature. In this report, we describe a very rare case of atypical giant neurofibroma in the right thoracic cavity. The patient was a 57 year old African American man, who developed sudden cardiac arrest and passed away in the emergency room. At autopsy, a huge encapsulated firm tumor was found in the right thoracic cavity, attached to the vertebral bodies and superficially adherent to the upper and middle lobes of the right lung. This giant mass weighed 2140 grams and measured 31 x 30 x 5.5 cm. Microscopically, the tumor consisted of interweaving fascicles of spindle cells with scattered atypical nuclei. Immunohistochemical studies showed that tumor cells were focally positive for S100, and negative for SMA, desmin, calretinin, Pan CK, CK5/6, EMA, CD99, CD34 and p53. The overall morphological and immunohistochemical features were diagnostic of an atypical neurofibroma. [NA J Med Sci. 2009;2(4):135-138.]

Key Words:

Neurofibroma, intrathoracic neurogenic tumor, calretinin

Introduction

Intrathoracic neurogenic tumors are not uncommon, accounting for 20% - 30% of all mediastinal tumors.¹ In infants and children, 84.8% of intrathoracic neurogenic tumors are nerve cell tumors and most are malignant

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(67.2%).^{4,5} On the other hand, 73.5% of intrathoracic neurogenic tumors in the adult are nerve sheath tumors and most are benign, including ganglioneuroma, schwannoma, and neurofibroma.^{1,3,4} In most cases, they are clinically asymptomatic and surgically removable. Although several cases of intrathoracic giant malignant peripheral nerve sheath tumor have been reported, only one case of a benign giant intrathoracic neurofibroma is published in the literature.² Here, we describe a rare case of atypical giant neurofibroma in the right thoracic cavity with a review of the related literature.

Case Report

The patient was a 57 year-old African American male who came to the Buffalo General Hospital on October 21, 2008 because of cough. A chest X-ray showed a large right thoracic mass-like opacity replacing the upper and mid right thorax. This lesion extended to the right hilum with displacement of the trachea to the left. On the same day, a chest CTA procedure (**Figure 1**) was performed, revealing a moderate right pleural effusion. Severe consolidation was seen throughout the right upper lobe, suspicious for an underlying mass. The area of consolidation measured at least 10.7 cm transversely x 10.1 cm in the AP view. Two additional masses were seen that were suspicious for associated adenopathy, measuring 6.1 x 4.3 cm and 8.4 x 5.6 cm, respectively. A bronchoscopic examination was done on October 27, 2008, and no endobronchial lesion was seen. The results of bronchial brushing and transbronchial biopsies were both negative for tumor cells. A CT-guided right chest biopsy was then performed on November 10, 2008 which showed loose fibroconnective and vascular tissue. The patient was discharged. On December 22, 2008, when the patient was shoveling snow, he developed sudden chest pain and was sent to the emergency room. Resuscitation was unsuccessful and preliminary cause of death was cardiac arrest.

During autopsy, a huge tumor mass was found in the right pleural cavity (**Figure 2**). The tumor was firmly attached to the superior chest wall and the vertebral bodies (cervical 6 to thoracic 2). It was superficially adherent to the surface of the upper and middle lobes of the right lung. Grossly, the tumor was encapsulated and lobulated, weighing 2140 grams and measuring 31 x 30 x 5.5 cm. Cut surface showed a white gray trabecular appearance with very firm consistency. Focal

hemorrhage was noted without obvious necrosis. In addition, the right and left pleural cavities contained 2400 ml and 50 ml of serous fluid, respectively. The right lung weighed only 300 grams and was atelectatic due to compression by the tumor mass and the pleural effusion. The left lung weighed 580 grams. The lung parenchyma appeared congested with edema. The mediastinal structures were markedly shifted to the left. The heart was grossly unremarkable. All other gross autopsy findings were minor and presumed to be secondary. Although the cause of death is not clear, we speculate that the mediastinal shift resulted in the cardiac arrest and sudden death.

Microscopically (**Figure 3**), interweaving fascicles of tightly-packed elongated cells coexisted with (**Figure 3A**) with hypo- and hypercellular areas that were separated by fibrous stroma. Foci of branched vessels and dense hyaline fibrosis were noted. Scattered large hyperchromatic nuclei were seen. The majority of the tumor cells did not exhibit wavy pointed nuclei. Mitotic figures numbered 1-2/ per 10 high power fields. Mast cells were frequently identified. Based on the location and the gross and microscopic appearance, the differential diagnoses included neurofibroma/neurofibrosarcoma, solitary fibrous tumor, monophasic synovial sarcoma, leiomyoma, mesothelioma and fibrosarcoma.

Immunochemically, the tumor cells were positive for S100 (**Figure 3F**), and negative for CD34, EMA, CD99, calretinin, pancytokeratin, CK5/6, smooth muscle antigen, desmin, and P53. Ki67 showed very few positive cells (Picture not shown). Among the differential diagnoses, only neurofibroma/neurofibrosarcoma and synovial sarcoma are usually positive for S100. In addition, the negative staining results for EMA and CD99 did not support the diagnosis of synovial sarcoma. Considering the presence of focal atypical cells, areas of hypercellularity, the low mitosis rate and negative staining for P53, this lesion was diagnosed as an atypical neurofibroma.

Discussion

Giant intrathoracic neurofibromas are very rare tumors. Only one similar report can be found in the literature.² That article reported a giant neurofibroma of the diaphragm, but it is published in a non-English journal and we are unable to obtain a detailed description for comparison. The rare occurrence of this tumor may partially explain why neurofibroma was not on the list of differential diagnoses until the autopsy was performed. The lesion originated from the nerve roots, grew into the thoracic cavity and compressed the lung parenchyma. Radiologically, it mimicked a lung mass with associated adenopathy, which prompted the clinicians to perform a bronchoscopy, subsequent bronchial

brushings and transbronchial biopsies, all of which were pathologically negative for tumor cells. Even when a CT-guided right chest biopsy was performed, neurofibroma was not considered.

Histologically, this was a spindle cell neoplasm. Given its location and its gross and microscopic appearance, it was very difficult to distinguish between neurofibroma, solitary fibrous tumor, synovial sarcoma, leiomyoma and mesothelioma. Based solely on the location and H&E appearance with the coexistence of hypo- and hypercellular areas separated by fibrous stroma, and branched vessels, solitary fibrous tumor was the initial diagnosis. As a result of the immunohistochemical work-up, the tumor was found to be a neurofibroma.

Although most cases of intrathoracic neurogenic tumors in adults are reported to be benign, malignant transformation does occur, especially in a patient with neurofibromatosis type I.⁶ Therefore when a giant intrathoracic neurogenic tumor is identified, its malignant potential should be evaluated, based on its hypercellularity, the presence of necrosis, its cytological atypia, the mitotic index, the proliferation index (Ki-67 expression) and its P53 positivity in immunohistochemical stains.

In summary, we report a rare case of giant atypical neurofibroma of the right thoracic cavity. To our knowledge, this is only the second such case reported to date.

Disclosure/conflict of interest

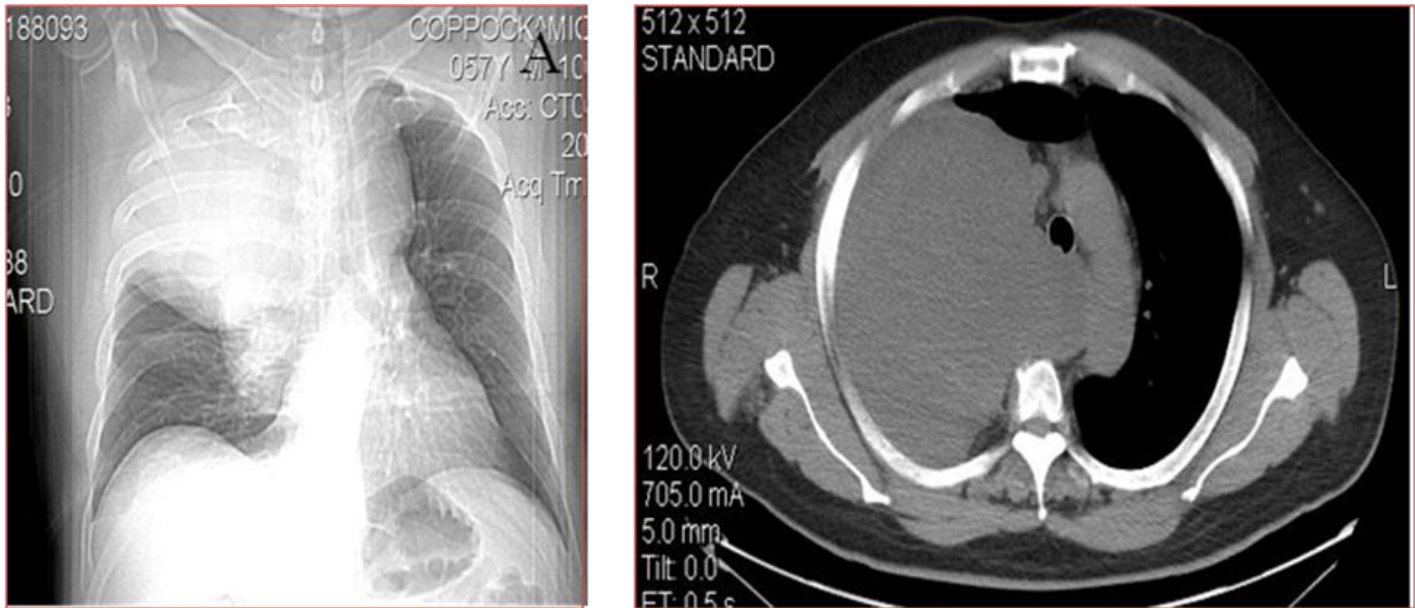
The Authors have no competing financial or conflicts of interest to disclose.

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References

1. Ribet ME, Cardot GR. Neurogenic tumors of the thorax. *Ann Thorac Surg.* 1994;58(4):1091-1095.
2. Korolev AA, Golubev OA. A giant neurofibroma of the diaphragm. *Arkh Patol.* 2002;64(2):49-50.
3. Saito H, Minamiya Y, Tozawa K, et al. Mediastinal neurofibroma originating from the left Intrathoracic phrenic nerve: report of a case. *Surg Today.* 2004;34(11):950-953.
4. Takeda S, Miyoshi S, Minami M, Matsuda H. Intrathoracic neurogenic tumors—50 years' experience in a Japanese institution. *Eur J Cardiothoracic Surg.* 2004;26(4):807-812.
5. Imazu M, Nakamura Y, Nakatani H, et al. Cervicothoracic malignant peripheral nerve sheath tumor in a 12-year-old girl with neurofibromatosis type I. *Eur J Pediatr Surg.* 2006;16(4):285-287.
6. Shimizu J, Arano Y, Murata T, et al. A case of intrathoracic giant malignant peripheral nerve sheath tumor in neurofibromatosis type I (von Recklinghausen's Disease). *Ann Thorac Cardiovasc Surg.* 2008;14(1):42-47.

**Figure 1.**

- A.** Chest X-ray (left). A chest X-ray showed a large right thoracic mass-like opacity replacing the upper and mid right thorax. This lesion extended to the right hilum with displacement of the trachea to the left.
- B.** Chest CT (right). CT scan of the intrathoracic tumor mass. Severe consolidation was seen throughout the right upper lobe, initially suspicious for an underlying lung mass measuring at least 10.7 cm transversely x 10.1 cm anterior-posteriorly. Two additional masses were seen measuring 6.1 x 4.3 cm and 8.4 x 5.6 cm respectively, suggesting associated adenopathy. At autopsy these masses were actually the different portions of the same tumor.

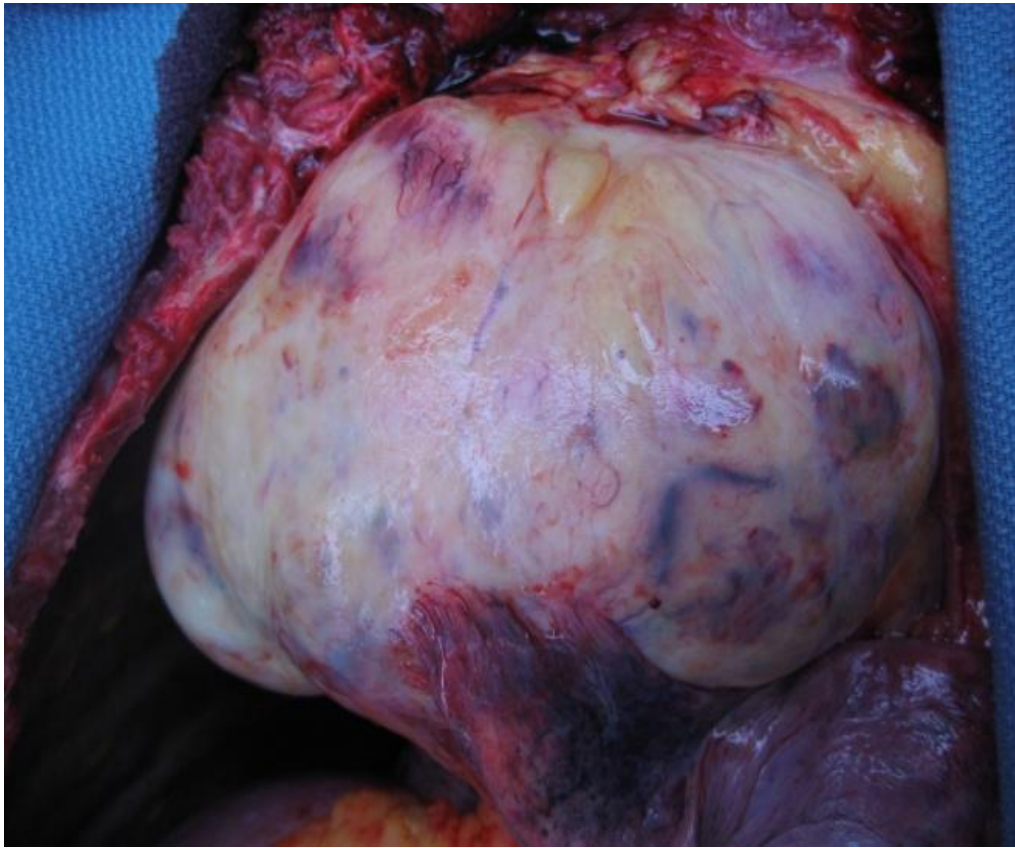


Figure 2. Gross appearance of the intrathoracic tumor mass. The tumor was firmly attached to the superior chest wall and the vertebral bodies (cervical 6 to thoracic 2). It was superficially adherent to the surface of the upper and middle lobes of the right lung. Grossly, the tumor was encapsulated and lobulated, weighing 2140 grams and measuring 31 x 30 x 5.5 cm. Cut surface showed a white gray trabecular appearance with very firm consistency. Focal hemorrhage was noted without obvious necrosis.

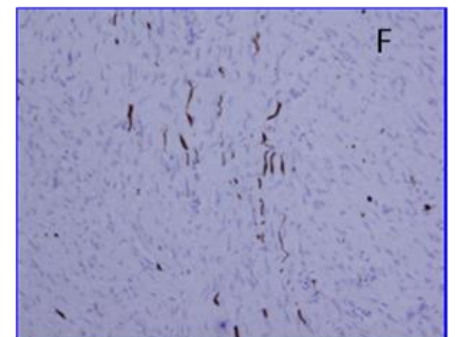
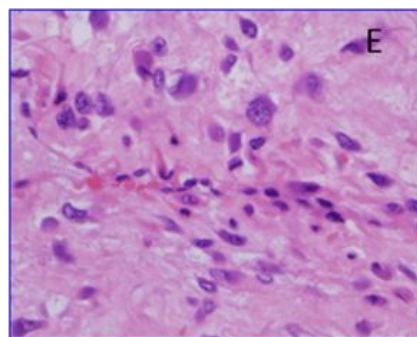
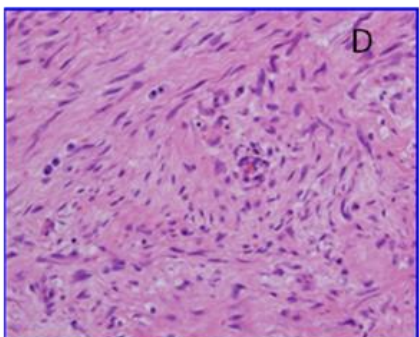
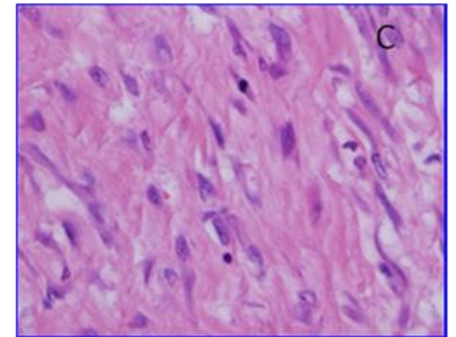
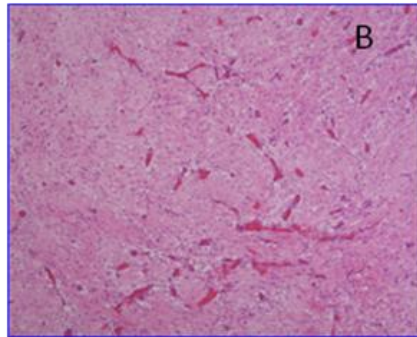
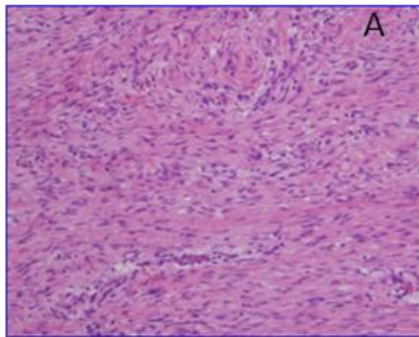


Figure 3.

Microscopic appearance and immunohistochemical staining of the intrathoracic tumor mass. Interweaving fascicles of closely-packed elongated cells was the essential feature (3A 10X). Foci of branched vessels and areas of dense hyaline fibrosis were noted (3B 10X). The majority of tumor cells did not exhibit wavy pointed nuclei. Mitotic figures were 1-2/ Per 10 high power fields (3C 40X). Mast cells were frequently identified (3D 20X). Scattered large hyperchromatic nuclei were seen (3E 40X). Immunohistochemically, tumor cells were positive for S100 (3F 10X).