



Case Report

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Pleural Malignant Solitary Fibrous Tumor Mimicking a Nerve Sheath Tumor in a Patient with Neurofibromatosis Type 1

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Abstract

Neurofibromatosis type 1 (NF1), formerly known as von Recklinghausen's disease is a nervous system tumor disorder of variable expressivity. Malignant solitary fibrous tumors (SFT) are rare spindle cell soft tissue tumors. We report a case of a 35-year-old male who presented clinically with NF1 and a mass that mimicked a nerve sheath tumor radiologically, but pathologically was, in fact, a malignant solitary fibrous tumor. Based on a literature review, the association between NF1 and malignant SFT has never been published.

Keywords: Neurofibromatosis type 1; Malignant solitary fibrous tumor

Abbreviations: SFT: Solitary Fibrous Tumors; NF1: Neurofibromatosis type 1

Mini Review

Neurofibromatosis type 1 (NF1) is a multisystem disease characterized by cutaneous findings, as well as benign and malignant tumors of the nervous system. NF1 occurs in about 1 in 3,000 individuals, and about half of the affected individuals are first cases in their family [1].

A solitary fibrous tumor (SFT) is a rare spindle cell tumor that most commonly arises in the pleura. These tumors comprise only 1-2% of all soft tissue tumors, and of those, between 12 to 22% are malignant [2-3].

No link has ever been made between NF1 and a malignant SFT Conzo et al. [4-5] first described SFT in an NF1 patient, and Yamamoto, et al later reported another case, but neither case dealt with malignant SFT.

Here, we describe a patient with clinical NF1, who presented with a mass that mimicked a nerve sheath tumor, but biopsy and immunohistochemical assays showed that the correct diagnosis was of a malignant solitary fibrous tumor.

Case Presentation

In August 2015, a 35-year-old man presented from an outside hospital with chest pain, recurrent left lower lobe pneumonia

and a pleural mass seen on chest radiograph. Physical exam revealed multiple café-au-lait spots on his face, back, chest, abdomen, and legs that ranged from 5mm to 15mm, as well as nodules present on the patient's right flank, as seen in (Figure 1), and lateral to his left eyebrow. Ophthalmologic exam revealed bilateral Lisch nodules. Due to the array of clinical findings, a biopsy of the right flank nodule was performed and revealed a neurofibroma with plexiform features (Figure 2).



Figure 1: Photograph depicting patient's neurofibroma and café-au-lait spot on his right flank.

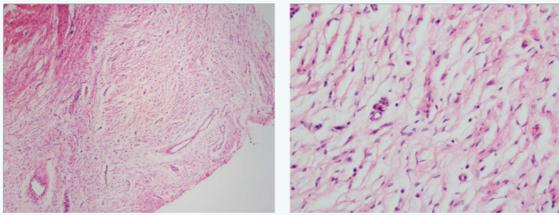


Figure 2: Punch biopsy of the right flank mass (a and b) shows a spindle cell tumor with loose/edematous stroma and prominent thin-walled blood vessels. The tumor cellularity shows thin spindle cells with wavy nuclei, wispy cytoplasmic extensions and bland cytologic features without atypia, necrosis or mitoses. The findings are diagnostic of neurofibroma with plexiform features. (Original magnification: 3a 40 xs, b 100 xs)

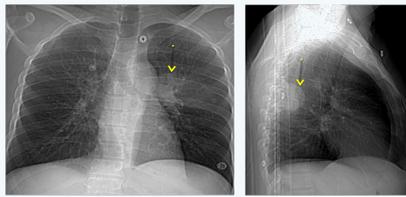


Figure 3: Computed Tomography (CT) frontal scout view

(a) Of the thorax depicting a left perihilar mass that is silhouetted by anterior structures, as well as a lateral scout view
(b) Of the thorax depicting a posterior mass projecting over the thoracic spine.

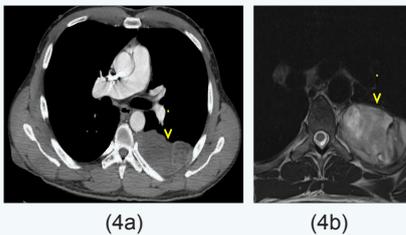


Figure 4: Axial image of chest CT with intravenous contrast in soft tissue window

(a) Depicting a large left pleural based mass with a small cutaneous mass of the right flank. An axial T1-weighted post-contrast MRI
(b) Shows the large heterogeneous enhancing left pleural mass.

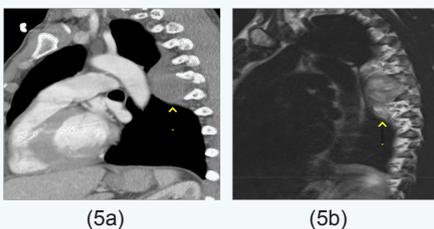


Figure 5: Sagittal image of chest CT with intravenous contrast in soft tissue window (a) depicting a large left pleural based mass with extension into the neural foramina. A sagittal T2-weighted MRI (b) shows the heterogeneous paraspinal mass with extension to neural foramina at multiple levels.

The chest x-ray from the outside hospital was not available at the time of writing, but, as a surrogate, scout images from

the initial CT scan performed in our institution may be seen in (Figure 3), displaying the thoracic mass initially appreciated at the outside hospital. A CT scan of the thorax with contrast was performed in our institution, which showed a left posterior intrathoracic soft tissue mass with areas of enhancement, neural foraminal widening and rib splaying (Figures 4a & 5a). An MRI of the same area was performed (Figure 4b & 5b) to better show the mass in question, and a biopsy was recommended as the mass was more suggestive of a nerve sheath tumor, or, less likely, a pleural fibroma.

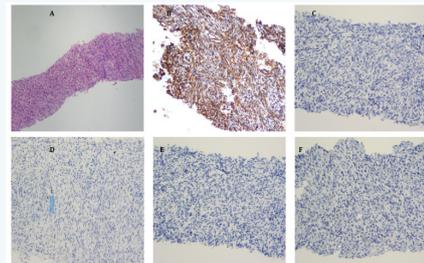


Figure 6: Fine needle aspiration and biopsy of the pleural mass showed acellular aspirate smears and cell block. H&E stain (a) of the biopsy shows bland spindle cells with a patternless growth pattern in a collagenous background without atypia, hypercellularity or mitotic activity. Immunohistochemical stains show the tumor cells to be positive for CD34 (b) supporting the diagnosis. The tumor is negative for cytokeratin AE1-3 (c), S-100 (d), desmin (e), and calretinin (f) ruling out spindle cell carcinoma, neurofibromatosis and schwannoma, myogenic tumors, and mesothelioma, respectively. (Original magnification: H&E 40x, Immunohistochemical stains 100x).

Ultrasound-guided fine needle aspiration and biopsy of the left pleural mass showed bland spindle cells without defined architectural pattern within a collagenous background without necrosis or mitotic activity. Immunohistochemical staining was positive for CD34, supporting a diagnosis of solitary fibrous tumor (Figure 6)

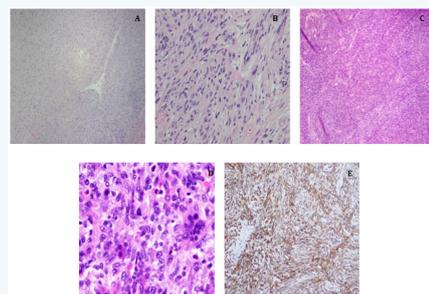


Figure 7: Surgical resection of the pleural mass shows a spindle cell lesion with variable cellularity ranging from moderate (a-b) to densely cellular (c-d). Histologic analysis of the moderately cellular areas (a-b) shows bland spindle cells with staghorn-like vessels, patternless growth and lack of atypia, necrosis or mitotic activity. The densely cellular areas (c-d) show fascicular growth of enlarged spindle cells with cytologic atypia, mitotic activity and areas of necrosis (not shown). Immunohistochemical stain for CD34 (e) shows positive staining in the tumor cells confirming the diagnosis of solitary fibrous tumor. The atypical findings in the dense areas (c-d) are diagnostic of malignant transformation.

Subsequently, the pleural mass was resected and histologic evaluation showed a spindle cell lesion with biphasic morphology. The majority of the tumor showed classic solitary fibrous tumor with benign features (Figures 7a & b) with a portion of the tumor showing markedly increased cellularity, cytologic atypia and increased mitotic activity (>4/10 high power fields) diagnostic of malignant transformation (Figures 7c & d). Immunohistochemical stain for CD34 (Figure 7e) was positive, confirming the findings.

Discussion

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen's disease, is caused by an alteration of the NF1 gene, which is a tumor suppressor gene located on the long arm of chromosome 17 (17q11.2). While genetic testing is not required, it is helpful in confirming the diagnosis. The NF1 gene encodes a protein called neurofibromin, which is a member of the GTPase activating protein family. A loss of function mutation to the NF1 gene results in increased cellular proliferation that manifests as multisystemic tumorous growth. Neurofibromatosis can be diagnosed clinically if at least 2 of the 7 following criteria are fulfilled: 6 or more hyperpigmented macules, axillary or inguinal freckles, two or more neurofibromas or one plexiform neurofibroma, optic nerve glioma, two or more iris hamartomas, body dysplasia, or a first degree relative with NF1 [6].

On the other hand, SFT classically presents as a pleural mass. Klemperer and Rabin first described the tumor in the pleura in 1931 [7]. Most of the tumors are benign neoplasms that are diagnosed in adults with an age range between 50-70 years-old and a male/female ratio of approximately 1 [8-10]. Of the pleural-based SFTs, most arise from visceral pleura (80%) with the remainder arising from parietal pleura [9]. Gross examination of an SFT typically shows a smooth glistening capsule surface [9]. Histologically, most tumors are composed of collagen-forming spindle-cells, arranged in interlacing fascicles with a classic "patternless" pattern [2]. The morphologic findings are typical, though not always demonstrable in small biopsy sections; therefore the characteristic immunohistochemical positivity for CD34 is significantly helpful in separating SFT from other spindle cell neoplasms [11]. Criteria for malignancy include the presence of necrosis, increased mitotic activity, greater cellularity, and cellular polymorphism [10]. Malignant SFT is diagnosed with presence of at least one of these criteria [10]. Approximately 15-35% of SFT are malignant at the time of diagnosis with clinical characteristics of higher recurrences and lower overall survival [2]. Nonetheless, regardless of benign

Or malignant presentation of SFT, the hallmark of treatment is large en-bloc resection of the primary tumor with close clinical surveillance for recurrences. Mediastinal lymph node dissection and adjuvant treatments such as radiotherapy and chemotherapy are not usually employed for treatment purposes, but rather as palliative options for cases of distant metastasis and locally advanced recurrence that are not amenable to

surgery [2].

Historically, NF1 has been associated with various tumors, most notable of which are malignant peripheral nerve sheath tumor, rhabdomyosarcoma, and gastrointestinal stromal tumor (GIST), with an overall occurrence rate that reaches up to 5-13%, 0.5%, and 6% respectively [12-14]. However, there are no systematic reviews that link NF1 with development of SFT. Only two case reports have been published with anecdotal evidences where SFT were found concurrently in NF1 patients. Of these two reports, both patients had pathologic diagnoses of benign SFTs. Specifically, Conzo et al described a patient who had an encapsulated tumor arising from the upper pole of the right kidney that mimicked an adrenal gland or renal tumor, but later proved to be a SFT [4]. Yamamoto et al described a patient who underwent Tc-99m MIBI parathyroid scintigraphy, which showed uptake highly suggestive of an ectopic parathyroid adenoma, but also later proved to be a SFT [5]. Our case appears to be the first documented case of malignant pleural SFT in an NF1 patient, which also showed signs of mimicry, as seen in the first two cases. Initial radiologic evaluation of the pleural mass suggested nerve sheath tumor, especially in the setting of other clinical findings of neurofibromatosis such as plexiform neurofibroma, as well as presence of a para-orbital mass. Nonetheless, other neoplastic causes such as pleural lipoma, pleural fibrosarcoma, mesothelioma, and metastatic pleural disease could not be ruled out by imaging alone without a definitive biopsy of the mass. Therefore, fine needle aspiration of the mass was performed and showed diagnostic features of SFT and subsequent excision showed areas of malignant transformation.

While NF1 patients have an increased risk of developing various tumors and malignancies, there is no definitive link between NF1 and SFT due to lack of published data [15]. Hence, it is difficult to comment on the exact relationship between these two disease processes. Whether or not NF1 is associated with the development of SFT and the relationship between such, as well as possible malignant transformation of SFT would need to be investigated further.

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