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JUXTAPLEURAL SCHWANNOMAS: A CASE SERIES

Pulmonary Medicine

Dr Muniza Bai	DM Senior Resident, Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS New Delhi, India
Dr Vidushi Rathi	Senior Medical Officer, Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS New Delhi, India
Dr Deepali Jain	Professor, Department of Pathology, AIIMS New Delhi, India.
Dr Priyanka Naranje	Assistant Professor, Department of Radiodiagnosis and Interventional Radiology, AIIMS New Delhi, India.
Dr Ashu Seith Bhalla	Professor, Department of Radiodiagnosis and Interventional Radiology, AIIMS New Delhi, India.
Dr Anant Mohan*	Professor and Head, Department of Pulmonary, Critical Care and Sleep Medicine, AIIMS New Delhi, India. *Corresponding Author

ABSTRACT

Most thoracic schwannomas are located in the paravertebral space. Juxtapleural schwannomas originate close to the pleura and chest wall from soft tissue, bone, cartilage, nerves, muscles of fat. They may be an incidental finding as a lung mass or nodule in chest radiograph or patients may have mild symptoms. We herein describe three cases of juxtapleural schwannomas and discuss their varied clinical presentations, radiology, histopathology and the line of management.

KEYWORDS

Schwannoma, Nerve Sheath Tumor, Juxtapleural, Thoracic

INTRODUCTION

Schwannomas are among the few truly encapsulated tumors of the human body and originate from the Schwann cells of the nerve sheath. They are mostly solitary in nature. Most thoracic schwannomas are located in the paravertebral space. We report 3 cases of juxtapleural benign schwannomas in adults and briefly review the literature.

Case Details

Case 1

Case Presentation

A 55-year male presented with persistent cough, intermittent hemoptysis, loss of appetite and unintentional subjective weight loss for 3 years. He had never smoked and was a welder by occupation. His medical history comprised of medications for known hypothyroidism, and a past history of antitubercular therapy (ATT) for 6 months for microbiologically confirmed pulmonary tuberculosis, 3 years back. Despite treatment he had persistent cough with intermittent hemoptysis associated with loss of appetite and unintentional subjective weight loss. He denied fever or shortness of breath.

Investigations

Chest radiograph showed bilateral bronchiectatic changes with non-homogenous opacities and an oval mass in right lower lobe(Figure 1a). Contrast enhanced computed tomogram (CECT) chest showed bilateral bronchiectasis with diffuse centrilobular and tree-in-bud nodules. A well-defined lobulated juxtapleural soft tissue lesion of size 6.4*4*3.7cm with smooth margins was noted posteriorly (Figures 1b and 1c). An ultrasound guided biopsy of the mass revealed a showed a soft tissue spindle cell lesion, with cellular fibrillary areas (Antoni A type) and hypocellular loose areas (Antoni B type). Areas of nuclear palisading Verocay bodies were seen. The tumor cells had spindled nucleus with tapered ends and scant cytoplasm without areas of necrosis or nuclear atypia (Figure 2a and b). On immuno-histochemistry, tumor cells showed S-100 positivity (Figure 2c). The histomorphological and immunohistochemistry findings were consistent with benign schwannoma.

Treatment and Follow up

Flexible bronchoscopy and bronchoalveolar lavage ruled out pulmonary tuberculosis and yielded Pseudomonas in bacterial culture, for which he received a course of oral antibiotics. He is currently on bronchodilators for post- tubercular obstructive airway disease. He is clinically better and kept on close observation for the schwannoma.

Case 2

Case Presentation

A 53-year-old male patient with no known co-morbidities, presented with intermittent left sided pleuritic chest pain of about 1 year duration. He had no cough, hemoptysis, dyspnea or fever and denied any history of trauma. His personal history was significant for smoking with 20 cigarettes a day over the last two decades. His past history revealed treatment for tuberculosis on clinicoradiological basis 15 years back, the records of which were unavailable. Clinical examination was unremarkable and no local tenderness was elicited.

Investigations

Chest radiograph revealed a well-defined opacity in left lower zone and few fibrotic lesions in right lung upper zone (Figure 1d). A positron emission computed tomogram was ordered for detailed assessment. CECT chest revealed a juxtapleural nodular lesion in lingula measuring 17x13mm (Figure 1e). Bilateral emphysematous changes were also visualized along with right apical pleural thickening. FDG-PET imaging showed avidity (SUVmax 1.5) in the lingular lesion and no other metabolically active lesion was identified elsewhere. On comparing with a CT done a year back there was no significant interval change. Ultrasound guided biopsy from the lesion was carried out and revealed features of benign nerve sheath tumor which was SOX10 and S100 positive, identifying it as Schwannoma.

Treatment and Follow up

In view of mild symptoms and non-progressive nature of lesion, it was decided to keep the patient under close observation after consultation with the oncologist.

Case 3

Case Presentation

A 32-year female, homemaker with no comorbidities presented with history of right sided chest pain radiating to back and shoulders, fever on and off, loss of appetite and weight for 6 months.

Investigations

Chest radiography showed right upper zone homogenous opacity (Figure 1f). A CECT chest which showed well defined juxtapleural heterogeneously enhancing lesion in right upper lobe and multiple heterogeneously enhancing mediastinal nodes were also seen (Figures 1g and h). Positron emission computed tomogram (PET-CT) revealed a low- grade FDG avid (SUVmax 2.55) soft tissue juxtapleural mass of size 6.7cms in right upper lobe (Figure 1i). The lesion was abutting the right 2nd to 4th ribs without any obvious erosion or destruction. FDG

avid mediastinal adenopathy were noted. There was no metabolically active lesion elsewhere in the body. An ultrasound guided biopsy of the mass yielded tumour fragments with spindle cells and buckled nuclei with minimal pleomorphism favouring a benign nerve sheath tumour. On immunohistochemistry, SOX 10 was positive favouring a diagnosis of benign schwannoma. An endobronchial ultrasound guided fine needle aspiration was done from the paratracheal and subcarinal nodal stations which revealed necrotising granulomas consistent with tuberculosis.

Treatment and Follow up

She is currently on antitubercular treatment for mediastinal tuberculosis. She is planned for definitive surgical resection of the schwannoma after completion of at least 2 months of antitubercular treatment.

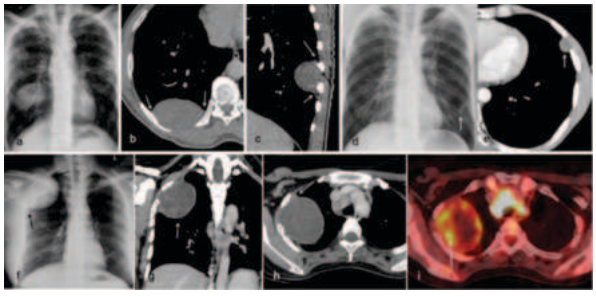

Figure 1. Juxta-pleural Schwannomas In Three Patients.

Case 1 [a-c]: a. Chest radiograph reveals an oval mass in right lower zone with well defined margins and normal overlying ribs.b (axial) and c (sagittal) mediastinal window images shows the homogenous oblong, juxtapleural mass forming obtuse angle contact with adjacent pleural margins (white arrows). The mass is seen in close relation to inferior margin of rib (black arrow), causing mild scalloping. There was no calcification within the mass or any adjacent rib destruction.

Case 2 [d,e]: d.Chest radiograph reveals small mass lesion in left lower zone showing incomplete border sign (arrow). e.CT shows well defined homogenous oblong mass in juxtapleural location in intercostal space (arrow).

Case 3. [f,g,h,i]: f. Chest radiograph shows large pleural based mass in right upper zone with sharp interface with underlying lung and obtuse margins of contact with adjacent pleural margins (arrow) suggesting an extrapulmonary location. g,h. Mediastinal window images in coronal(g) and axial (h) views shows solid-cystic juxtapleural mass (arrows) along right upper/lateral costal pleural region,with no overlying rib destruction or calcification. Few enlarged station 2R nodes were also noted. i. FDG PET-CT shows mild FDG avidity in peripheral solid areas of the mass (arrow) and within nodes.

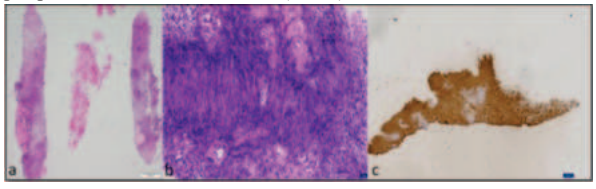

Figure 2. a. Photomicrograph of CT guided biopsy shows cores of tumor tissue with hypo and hypercellular areas. H&Ex40
b. Higher magnification shows palisades of spindle shaped tumor cells with hyalinized blood vessels. H&Ex400
c. S-100 immunostain is diffusely and strongly positive in tumor cell cytoplasm and nuclei. Hyalinized blood vessels stand out due to negative immunoreactivity.

DISCUSSION

Most thoracic schwannomas are located in the paravertebral space. Juxtrapleural, primary pulmonary and endobronchial schwannomas are rare. Juxtapleural tumors are closely located related to the pleura and chest wall. They may originate from osseous structures, soft tissue, muscles, nerves or fat.(1) Neurogenic tumors with juxtapleural location arise from spinal nerve roots or intercostal nerves. Benign neurogenic tumors include schwannomas and neurofibromas. Juxtapleural schwannomas are usually peripherally located, appear as a round mass with well-defined margins. They are usually asymptomatic, most often incidentally detected during routine radiography. They may have mild cough or pleuritic chest pain.

Schwannomas are often located in the juxtapleural region and the costovertebral angle of the posterior mediastinum.(2) Ohtsuka et al reported 62 patients comprising of 28 males and 34 females, aged 5-83 years with intrapulmonary or intrabronchial schwannomas. In nearly 34 patients, tumor originated in close proximity to terminal segmental bronchus.(3)

Intrapulmonary schwannomas are either centrally or peripherally located.(4) Centrally located tumors are either intraluminal or extraluminal. Intrabronchial tumors present as distal atelectasis or post obstructive pneumonia. They may present with symptoms mimicking asthma, bronchitis, post obstructive pneumonia secondary to intraluminal tumor. (5)Malignant lesions have been associated with constitutional symptoms such as anorexia, malaise and weight loss. There have been few case reports of metastasis of pulmonary schwannomas to the heart, local recurrence from the remnant capsule of a resected tumor, and malignant transformation of schwannomas. (6–8)

Juxtapleural schwannomas are usually peripherally located, however they may appear like a lung mass or nodule in chest radiograph. Computed tomography usually reveals a peripherally located round, ovoid or lobulated well demarcated homogenous mass with soft tissue density. Multiplanar reconstruction may be needed in some cases to identify the location of tumor as juxtapleural or intrapulmonary.

The step forward to differentiate pulmonary from pleural or juxtapleural neoplasms is as follows. Pulmonary neoplasms usually create acute angles with chest wall. They are centered in the lung and engulf the pulmonary vasculature. A pleural neoplasm shows obtuse angles with the chest wall and has tapered margins. They displace the pulmonary vasculature, may change location on respiration and show incomplete border sign (only a portion of the margin of the mass is visible). The next step would be differentiating pleural from extrapleural origin of a mass. Typically, pleural lesions do not erode ribs and displace the extrapleural fat outward whereas the extrapleural neoplasms displace the extrapleural fat inward.(9)

Schwannomas may be partly solid due to hemorrhage or cystic and may contain punctate calcifications. The presence of well-defined margins or split fat sign suggest a benign tumor. They may bulge into the bronchial lumen or ulcerate into the bronchial mucosa. Malignant tumors are larger in size with infiltrative margins. (10,11)

Schwannomas may show some specific signs on imaging as ennumerated in table1.

Table1. Radiological Signs of Schwannoma

Chest radiograph	Pressure erosion and splaying of ribs seen in long standing tumors, called ancient schwannomas (may be seen in neurofibromas)
CECT chest	Split fat sign: Presence of fat around the tumor due to the displaced but intact surrounding fat Cystic schwannomas: large areas of necrosis simulating cysts
T2 weighted MRI	Target sign: Central low signal intensity and peripheral high signal intensity Fascicular sign: On T2W imaging, ring like appearance is seen and signal intensity is heterogenous

There have been case reports of primary neurogenic pulmonary tumors co-existing with Von Recklinghausen's disease. The basic pathophysiology of this disease is the defect in the development of Schwann cells. It is characterised by the presence of multiple neurofibromas in the skin and internal organs. It may be associated with malignant neurofibromas and malignant Schwannomas. FDG PET doesn't have a diagnostic value to differentiate between benign and malignant Schwannomas. Beaulieu et al, reported the SUV uptake of 10 schwannomas ranging from 1.9 to 7.2.(12) This wide variation in the SUV uptakes could be due to the difference in cellularity, microvascular density and vascular permeability. Areas of necrosis or cystic degeneration can also cause heterogenous uptake.

On gross examination, benign neurilemmomas are lobulated masses of

varying dimensions, well demarcated from the surrounding tissue. On cut section, they are firm, solid and yellow owing to the mucin and lipid content. Malignant tumors are usually large. Though distinct from the surrounding parenchyma, they are not encapsulated. Malignant schwannomas should be carefully differentiated from mesenchymal tumors, such as fibrosarcoma and spindle cell anaplastic carcinoma. (13)

On microscopic examination, benign schwannomas neoplasms are sharply surrounded by a fibrous capsule. It is associated with 2 microscopic patterns – the Antoni A (cellular) and the Antoni B (less cellular type).(13) The Antoni A type has highly cellular areas of spindle shaped cells interspersed with irregular wavy nuclei and palisade like arrangement. The Antoni B type are relatively hypocellular with elongated cells. The matrix separating these cells are poorly stained for hematoxylin, eosin and alcian blue stains. Diffuse staining for S-100 protein is a typical feature of these cells. Absence of myogenic markers SMA and desmin rules out a myogenic tumor. Histological presence of spindle cells can be seen in leiomyomas, fibroma, angiofibroma and sclerosing hemangioma.

Signs of malignant transformation include absence of capsule, unclear cellular borders, perineural invasion, increased and atypical mitotic figures, pleomorphic fusiform cells, areas of hemorrhage, cystic degeneration and metastasis. The utility of Ki67, a tumor cell proliferative markers has been reported in determining malignant potential. Kindblom et al. studied Ki67 expression in 26 cases of malignant peripheral nerve sheath tumors (MPNSTs) and 24 benign nerve sheath tumors. 23 out of the 26 MPNSTs showed Ki67 immunoreactivity in 5-65% of the tumor cell nuclei whereas none of the 24 schwannomas had nuclear staining exceeding 5%. (14)

Benign nerve sheath tumors include benign schwannoma and neurofibroma, with schwannomas being more frequent in incidence compared to neurofibromas. The key differences between schwannoma, neurofibroma and malignant peripheral nerve sheath tumors are summarised in table2.

Table 2. Differences Between Schwannoma, Neurofibroma And Malignant Peripheral Nerve Sheath Tumors

	Schwannoma	Neurofibroma	Malignant peripheral nerve sheath tumor
ORIGIN	Spinal nerve roots	Cutaneous nerves in chest wall	Major nerve trunks
RADIOLOGY			
Mass-nerve relationship	Mass eccentric related to tumor	Mass central relative to nerve	Mass central relative to nerve
Capsule	70% of cases True capsule	30% of cases No true capsule. Pseudocapsule or no capsule present	Rare No capsule
Appearance	Smooth well defined homogenous Heterogenous in case of cystic degeneration	Smooth well defined homogenous	Larger, heterogenous with areas of necrosis
Margins	Well circumscribed	Well circumscribed	Infiltrative
Split fat sign	Present	Absent	Absent
Target sign	50% of cases	50-70% of cases	Absent
Fascicular sign	Present	Present	Absent
Intratumoral cysts	Common	Rare	Absent
Calcification	Present (10%)	More frequent	Less common
Bony destruction	Absent	Absent	Present
PET CT	Low SUVs	Low to intermediate SUVs	High SUVs
Histopathology			
Microscopy	Antoni A cells, Antoni B cells or both	Nerve sheath cells, collagen bundles, myxoid degeneration areas	Features of cytological atypia, hypercellularity, loss of neurofibroma architecture, mytotic figures, necrosis
IHC markers	S-100 strong and diffuse positivity, SOX 10 +, CD 34 +	CD 34+, S 100 variable	Focal and patchy positivity for S100 and SOX 10, Loss of SMARCB1 differentiation

The mainstay of treatment of neurilemmomas is surgical resection. The extent of surgery may range from enucleation, segmentectomy, lobectomy to rarely pneumonectomy in case of large proximal lesions.(15) Bronchoscopic management for intraluminal tumors by resection using forceps, laser, cryotherapy, electrosurgical snaring or ethanol injection have been reported.(14) YAG (yttrium aluminium garnet) laser resection for schwannomas have also been reported.(16) Situations where schwannomas are incidentally found and subjects are asymptomatic or mildly symptomatic with no progression in the lesion, they can be considered for watchful wait or observation. Prognosis of schwannomas is good as they are usually benign with low rates of recurrence and malignant transformation. However, malignant schwannomas have high invasive tendency, tend to recur and are associated with low survival rates. They rarely show distant metastases.

Learning Points

1. Juxtapleural tumors originate close to the pleura and chest wall from soft tissue, bone, cartilage, nerves, muscles of fat. It may be an incidental finding in radiology or patients may have mild symptoms. They may simulate lung mass or nodule in chest radiography. Multiplanar reconstruction may be required in computed tomography to identify tumor location.
2. Histopathological examination is important to differentiate it from other benign as well as malignant nerve sheath tumors. PET CT may not help differentiate a benign from a malignant schwannoma.
3. Surgical resection is the mainstay of treatment, however close observation without surgical intervention can be instituted in patients who are asymptomatic for the schwannomas, with no progression of the lesion.

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