

Retrospective Analysis of the Clinical and Image Presentation of Eight Primary Benign Mediastinal Schwannomas

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Research note

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Abstract

Objective: Mediastinal schwannomas sometimes can be confused with other neoplasms in the initial radiological studies, especially when there is a history of cancer in another site and that require a more accurate analysis by computed tomography (CT) or even magnetic resonance (MRI). Our study was aimed to perform a retrospective analysis of the clinical and imaging features in a series of patients with mediastinal schwannomas that were confirmed by histology and immunohistochemistry.

Results: We found eight patients, five man and three women with an average age of 51 years. The main signs and symptoms at time of diagnosis were chest pain, dyspnea, cough and dysphagia. CT showed that the tumor was located in the posterior compartment of the chest in 7/8 cases. Tumors >10 cm were more heterogeneous and showed cystic changes. All cases underwent posterolateral thoracotomy and radiological follow-up showed no evidence of recurrence. Histological analysis was the gold standard to confirm diagnosis in addition to at least one neurogenic IHC marker. In conclusion, mediastinal schwannomas are benign encapsulated tumors. By CT, schwannomas >10 cm showed cystic degeneration more frequently. Posterolateral thoracotomy allows complete resection and is considered the surgical approach of choice.

Introduction

Schwannomas are benign neoplasms that arise from Schwann cells that surround peripheral nerve fibers. [1,2] Less than 9% of schwannomas occur in the mediastinum. [3] They often originate at the root of a spinal nerve and may involve the thoracic nerve. More than 90% of these lesions are unique and sporadic. [3] They have a peak incidence between fourth to sixth decades of life. [3] Even though there are case reports of giant mediastinal schwannomas, [4-6] they generally measure less than 5 cm at the time of diagnosis, they are characterized by its slow growing, and lack of specific symptoms; therefore, a common presentation occurs as a well-defined lesion without a mass effect while performing a radiographic study aimed to various other complaints. However, when schwannomas are large, it is possible for them to present by localized pain; histologically, common features are cystic degeneration, low cellularity, hemorrhage and small calcifications. [3] There are few studies in the Mexican population that analyze the characteristics of mediastinal schwannomas. [7,8] Our objective was to perform a retrospective analysis of the clinical and tomographic features of patients with primary benign mediastinal schwannoma.

Main Text

Material and methods

Study design and population characteristics

A retrospective study was performed that included patients with a diagnosis of mediastinal schwannoma. All cases were obtained from the surgical pathology archives of UMAE Hospital de Oncología Centro Medico Nacional Siglo XXI. IMSS, from January 2011 to January 2018. Permission was requested in the clinical file to review patient records. Clinical features such as age, gender, time of evolution, type of treatment and follow-up data obtained from medical records. Its association with neurofibromatosis type 2, schwannomatosis and Gorlin-Koutlas syndrome was also investigated. From the radiology file, chest CT scans from each patient was obtained and submitted for re-assessment by two experienced radiologists who investigated the location, shape, size and features of each lesion (ALRC and LMH). All cases were reevaluated by three experienced pathologists (CCU, AMM and FCG) using the WHO criteria.^[9]

Immunohistochemistry

All tissues were fixed in formaldehyde buffered at 10% and paraffin embedded. Histological sections were stained with hematoxylin and eosin. For immunohistochemistry (IHC) analysis, 5- μ m sections of a representative block in each case were obtained. The following antibodies were used: S100 protein (Biosb), glial fibrillar acid protein (GFAP; Invitrogen), CD34 (Biocare), and Ki-67 (Biosb), which were performed on an automated immunostainer (Ventana, Biotek System Tucson, Ariz) with an appropriate positive and negative control run simultaneously. Briefly, paraffin sections mounted on charged glass slides, air -dried over-night, and then de-paraffinized. To enhance immunostaining, a heat-induced epitope-retrieval procedure was performed. After incubation with blocking serum, sections were incubated with primary antibodies, followed by a biotinylated polyvalent secondary antibody solution. All sections were then incubated with horseradish peroxidase-conjugated avidin-biotin complex, followed by 3,3-diaminobenzidine and hydrogen peroxidase.

Results

Clinical features

During the period analyzed, 163 primary soft tissue tumors of the mediastinum were resected, of which only eight patients corresponded to mediastinal schwannomas (5%). Five men (63%) and three women (37%). The average age was 51 years (range, 32-78 years). The average age of the women was 43 years versus 56 years for men. Seventy-five percent of the patients had symptoms. The main clinical manifestations were chest pain in four patients (64%), dyspnea in one patient (17%), cough in one patient (17%), dysphagia in one patient (17%) and two patients were asymptomatic (25%). No weight loss found in any patient. The average time of clinical evolution was 4 months (range, 1 to 6 months). In none of our cases was found an association with neurofibromatosis type 2, schwannomatosis or Gorlin-Koutlas syndrome.

Tomographic features

All patients had a chest X-ray and a chest CT, which allowed identifying the lesion. Chest X-ray films showed a well-defined round radiopaque mass in all cases. Only in three cases, a diagnosis of schwannoma was suspected at the time of CT. In one patient, the mediastinal tumor was identified as an asymptomatic finding secondary to a kidney transplant check-up. Other of our patients had a history of clinical stage IIB breast cancer, which in follow-up with chest X-ray revealed a mediastinal mass in the left hemithorax. Initially it was thought that it could correspond to recurrence of the disease. This was ruled out by performing a CT scan in which the diagnosis of schwannoma was proposed, leading the patient to a surgical approach.

In seven patients, the tumor was located in the posterior mediastinum (88%) by CT; in one of them, the mass was located in the posterior upper para-esophageal compartment. No patient had evidence of tumoral activity was observed elsewhere. In all cases, the mass was ovoid and well defined. In four cases, the lesion was homogeneous and in four cases it showed heterogeneous reinforcement with hypo and hyperintense areas after the application of contrast material (Fig. 1a and b).

Pathologic findings

Macroscopically, all cases were solitary tumors, with ovoid growth, encapsulated, with gray-yellow outer surface. The average size of the tumors was 8 cm (range, 3.5-14.0 cm). The average size of the tumors in the group of women was 8.6 cm (range, 4.0-14.0 cm) versus 7.16 cm in the male gender (range, 3.5-11.0 cm). Fifty percent of the tumors showed cystic degeneration. These tumors had an average size of 10.0 cm (range, 7.0-14.0 cm) compared to tumors without cystic changes which had an average size of 5.4 cm (range, 3.5-8, 0 cm) (Fig. 1c and d). All cases were completely resected and in none was necrosis.

Histopathological features

Histologically, only in three cases (38%), a small nerve fragment was identified in the extracapsular portion (Fig. 2a). Four cases showed cystic changes (50%; Fig. 2b). Six cases presented myxoid areas (75%) and in five cases there was hemorrhage (Fig. 2c). All cases showed hypercellular areas forming short bundles (Antoni A) alternating with scarce formation of palisades (bodies of Verocay) with hypocellular component (Antoni B) (Fig. 2d). The neoplastic cells were spindle-shaped, with twisted nuclei and indistinct cytoplasmic borders, immersed in a collagenized stroma. (Figure 2e). One case (case # two) showed senescent changes with greater nuclear atypia and hyalinized stroma (Fig. 2f).

Immunohistochemistry findings

By IHC, all cases were intensely positive for S100 protein in nucleus and cytoplasm, and showed focal expression of GFAP, mainly in Antonia A areas. Neither case showed expression for CD34. The proliferation index with Ki-67 was less than 1% in all cases. One cases (case # five) showed hypercellularity with a storiform pattern in approximately 50% of the tumor mimicking solitary fibrous tumor. However, the neoplastic cells were positive for two neurogenic markers (S100 protein and GFAP) and negative for CD34 (Fig. 3).

Treatment and follow-up of patients

All the patients underwent surgery through posterolateral thoracotomy and radiological follow-up. In four cases, the thoracotomy was on the left-sided versus three right-sided cases. In all patients the tumor resected completely. The mean follow-up of the patients was 27 months (range 0-48 months). All patients were found alive without clinical or radiological recurrence of the disease at their last visit. In none of the patients a malignant transformation of the disease was diagnosed.

Discussion

It is estimated that 9% of all schwannomas occur in the mediastinum.^[10] Fifty percent of neurogenic tumors of the mediastinum are schwannomas.^[3] In our series, schwannomas represented 5% of all soft tissue tumors of the mediastinum. More than 90% of schwannomas are solitary, sporadic, and slow-growing neoplasms. These lesions affect both genders equally, all age groups reached a higher incidence between the fourth and sixth decades of life.^[1-3] In our series, the average age was 51 years while women were found to be a decade younger than men.

The clinical history, physical examination and image evaluation must be considered. Mediastinal schwannomas can originate from spinal, paravertebral sympathetic branches, vagus, phrenic and intercostal nerves, respectively.^[1-3,11] In our study, about half of cases originated in the paravertebral region. The classic presentation is an incidental asymptomatic mass found on routine investigations as simple as a chest X-ray.^[12] Interestingly, some patients experience paresthesia or chest pain from compression of adjacent structures or extensions of the tumor in the thoracic spine. Other clinical manifestations are dry cough, dyspnea, and dysphagia. In our study and in contrast to other international publications, 57% of the patients had symptoms attributable to a mediastinal schwannoma. The ideal treatment consists of video-assisted thoracic surgery with complete resection of the mass because of its subsequent growth and mass-effect.^[1-3] In our study, all patients underwent open posterolateral thoracotomy as standard.

CT and MRI can help accurately to determine the exact location of the mediastinal tumor and also defines its relationship to adjacent structures. On CT scanning, schwannomas appears as well-defined rounded mass with smooth margins, they are isodense or hypodense in the paravertebral region or long the courses of intercostal nerves.^[13] They have a variable enhancement pattern after administration of the intravenous contrast material including multiple hypodense or cystic areas with central hypodensity and central enhancement, as well as peripheral hypodensity.^[13,14] Calcifications are occasionally detected, and low attenuation correlates with areas of hypocellularity, cystic change, hemorrhage, and lipidisation.^[3,15]

While there are few cases reports of giant mediastinal schwannomas, these are often identified incidentally by chest X-ray, followed by CT scans that show a clearly defined mass with low densities and mild enhancement.^[4-6] Giant schwannomas are more heterogeneous with cystic degeneration.^[3] In our

series, cystic degeneration was observed more frequently in tumors larger than 10 cm. Tumors smaller than 10 cm were more frequently homogeneous with solid areas in the absence of cystic degeneration. This supports the idea that degenerate changes directly related to the size of the tumor. Heterogeneous changes observed by CT have a histological translation. In our study, the schwannomas that were homogenous by CT more frequently identified in the histological analysis of classical areas Antoni A and Antoni B. While in tumors that were heterogeneous by CT scan, they presented microscopically extensive hypocellular areas with marked cystic degeneration, reticular pattern, edema, hemorrhage and sometimes calcifications. However, by IHC positivity for S100 protein confirms the diagnosis in all cases.

Mediastinal schwannomas can be misdiagnosed as lymph node metastasis from locally advanced breast cancer.^[16] The clinical distinction between mediastinal schwannoma and metastasis in cases that have a history of cancer, can be difficult and requires its surgical removal and histopathological analysis. The location and composition through imaging studies are critical to make a differential diagnosis. Even through sophisticated studies such as ¹⁸F-fluorodeoxyglucose positron emission tomography and computed tomography (¹⁸F-FDG PET/CT), mediastinal schwannoma can simulate metastases to breast cancer lymph nodes, as shown by Martinez-Esteve et al.^[16] Similarly, we found a patient with a clinical history of stage IIB breast cancer during follow-up showed a mediastinal mass on a chest X-ray that was initially thought to be a recurrence of the disease. However, when a CT scan was performed, the site of origin of the tumor was defined precisely and it proposed that it could correspond to schwannoma. Finally, it was resected and the histopathological analysis showed a schwannoma with diffuse expression of S100 protein and GFAP.

Cellular schwannoma are an infrequent variant with a predominantly cellular growth pattern, in the absence of Verocay bodies. Usually seen at paravertebral, pelvic, retroperitoneal, or mediastinal location.^[17] This variant can be confused with a malignant peripheral nerve sheath tumor or with a solitary fibrous tumor.^[18,19] In our study, we found only one case of a cellular schwannoma (13%) with storiform pattern mimicking a solitary fibrous tumor. The diagnosis of schwannoma was supported by light microscopy and corroborated by S100 protein and GFAP expression and negative for CD34.

Conclusion

Mediastinal schwannomas are benign encapsulated tumors, which on CT are more frequently located in the posterior compartment. Tumors >10 cm are usually heterogeneous with cystic degeneration. Posterolateral thoracotomy allows complete resection and is the surgical approach of choice. Histological analysis remains the gold standard to confirm the diagnosis along with IHC markers that include at least one neurogenic marker.

Limitations

It is a retrospective study with a small sample. Therefore, a large-scale study that includes a larger number of patients is necessary.

Abbreviations

AFINES: Program to support and promote student research; CT: Computed tomography; ¹⁸F-FDG PET/CT: ¹⁸F-fluorodeoxyglucose positron emission tomography and computed tomography; GFAP: Glial fibrillary acid protein; IHC: Immunohistochemistry; MRI: Magnetic resonance imaging; UMAE: Unidad Medica de Alta Especialidad; UNAM: Universidad Nacional Autonoma de Mexico; X-ray: radiograph.

Declarations

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Author's contribution

RSM, IDOS, ALRC, LMH, CCU, AMM, AGD, and FCG have substantial contributions to conception and design of the study; RSM, IDOS and FCG collected the sample and analyzed the data, also made contributions to acquisition of clinical data; ALRC and LMH analyzed and describe the characteristics of the tumor by CT and MRI; CCU, AMM, AGD, and FCG evaluated the histological findings and the results of the IHC; AMM, AGD and FCG draft the paper. All authors have given approval the final version of manuscript to be published.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The study was approved by the ethics committee of the UMAE Hospital de Oncologia Centro Médico Nacional Siglo XXI (R-2019-3001-013). In addition, informed consent was obtained from each of the patients.

Consent to publish

Not applicable.

Competing of interest

The authors declare that they no competing interest.

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Figures

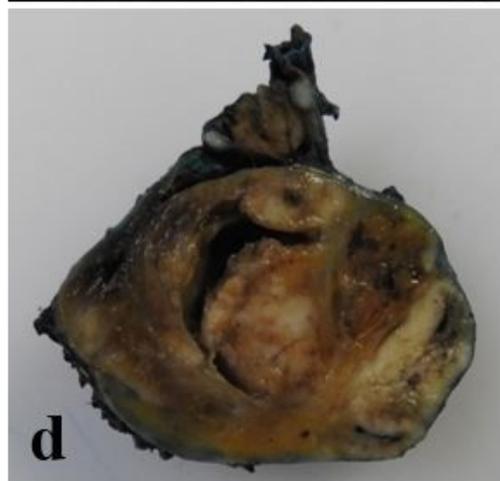


Figure 1

Benign mediastinal schwannoma. a-b) CT images the tumor was located in the posterior mediastinum. Tumor showed heterogeneous reinforcement with hypo and hyperintense areas after the application of contrast material; c) Macroscopic images of the well-encapsulated ovoid tumor with smooth surface, gray-yellow color; d) Cross section of the tumor shows solid areas with cystic degeneration.

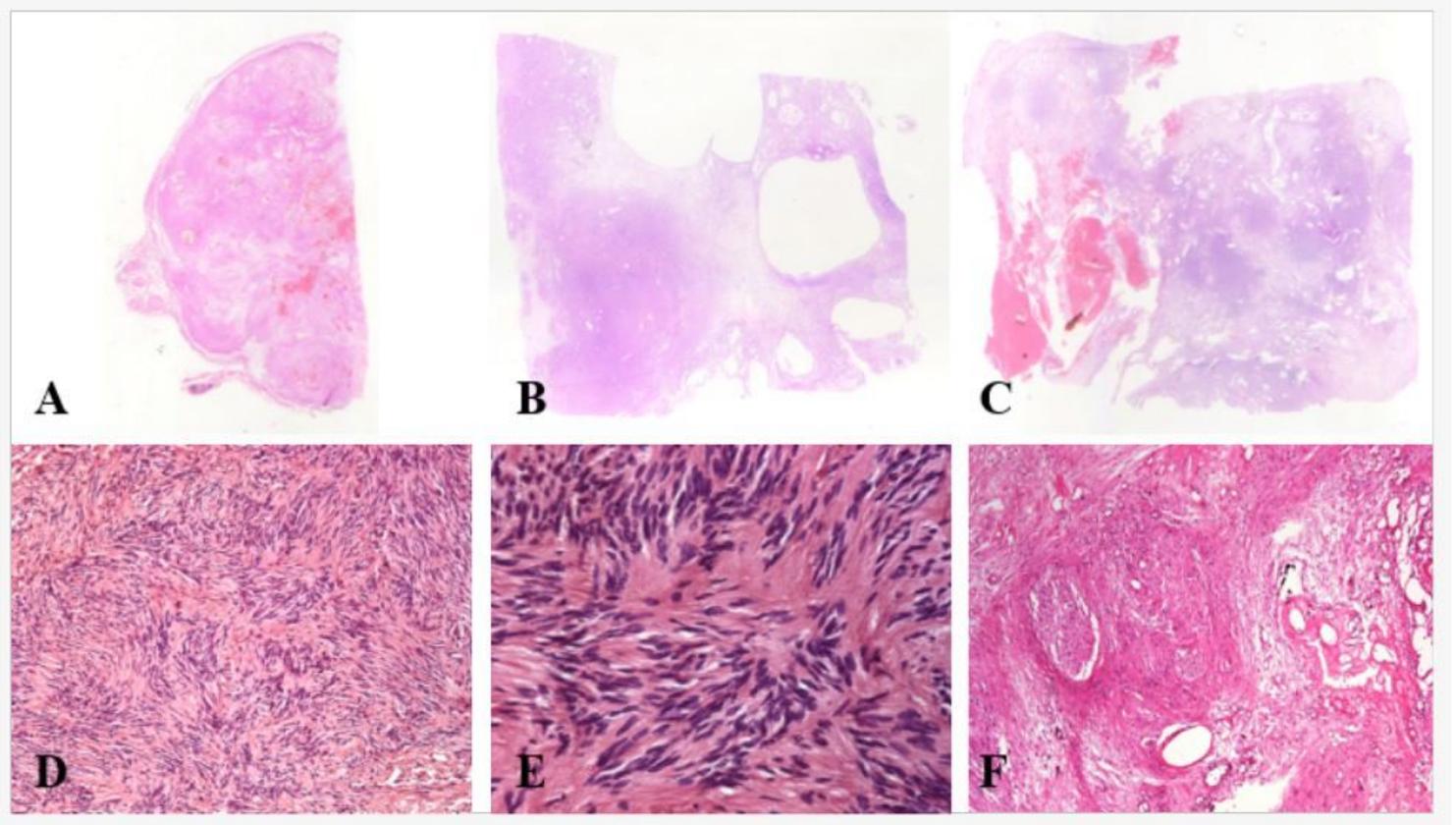


Figure 2

Microscopic images of the conventional mediastinal schwannoma. a) Encapsulated tumor with presence of nerves on the external surface; b) Solid areas with cystic degeneration; c) Areas of hemorrhage and vascular congestion; d) Antoni A and Antoni B areas with biphasic patterns; e) Verocay body, formed palisaded Schwann cells; f) Hyalinized thick-walled vessels.

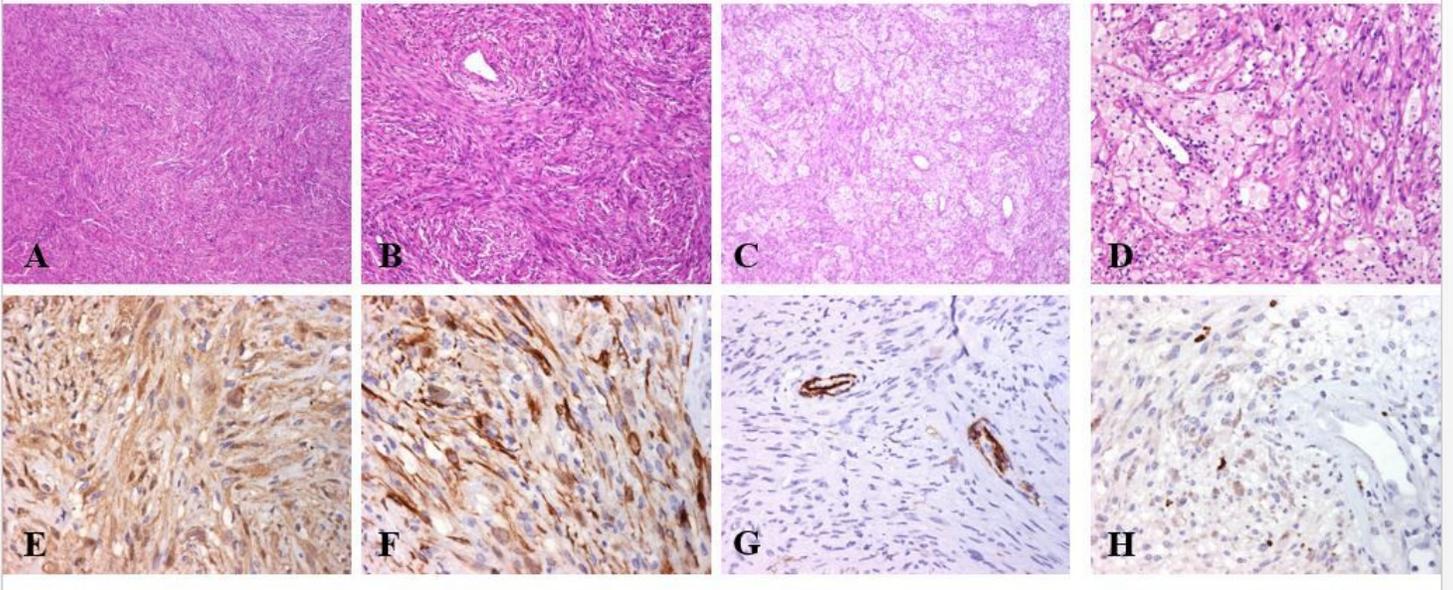


Figure 3

Microscopic images of the cellular mediastinal schwannoma. a) Tumor shows hypercellular areas; b) Cellular schwannoma with storiform growth pattern mimicking solitary fibrous tumor; c-d) Groups of numerous histiocytes; e) Diffuse expression by IHC for S100 protein in neoplastic cells; f) Intense expression by IHC for GFAP in neoplastic cells; g) Neoplastic cells were negative for CD34; h) The neoplastic cells show a proliferation index of 1% (Ki-67).

Supplementary Files

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