Mediastinal Rhabdomyoma Diagnosed by Fine Needle Aspiration Cytology
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Citation

Abstract
Extracardiac rhabdomyoma is a rare benign tumor of striated muscle origin which is mostly located in head and neck areas. Only four cases of adult rhabdomyomas in the mediastinum have been reported and these cases were diagnosed on surgical excision or autopsy. We report the clinical and cytological findings of a mediastinal rhabdomyoma which has been diagnosed by transesophageal endoscopic ultrasound-guided fine needle aspiration (FNA). FNA showed loose aggregates and isolated large round to polygonal tumor cells with abundant granular cytoplasm. Immunostains on the cell block showed strong positivity of tumor cells for myoglobin and desmin. This report highlights the cytologic diagnosis of this rare entity and its potential differential diagnosis.

INTRODUCTION
Rhabdomyoma is a rare benign tumor of striated muscle origin.1 Unlike other benign soft tissue neoplasms which are generally more prevalent than their malignant counterparts, adult rhabdomyomas are less frequent than rhabdomyosarcomas.1

Topographically, rhabdomyomas are classified into cardiac and extracardiac types based on their site of origin.2 The cardiac rhabdomyoma almost exclusively occurs in the heart of young children and is often associated with congenital abnormalities like tuberous sclerosis (50% of the cases in clinical series)3, phacomatosis or disorders of glycogen metabolism.5

Extracardiac rhabdomyomas are rare, representing only 2% of muscular tumors.3 Extracardiac rhabdomyomas are distinguished into four clinically and morphologically different types: adult (50% of extracardiac rhabdomyomas), fetal (40%), genital (10%)8, and the rare rhabdomyomatous mesenchymal hamartoma types.9 Seventy percent of extracardiac rhabdomyomas occur in the head and neck region: the most common sites are the larynx, pharynx, and the floor of the mouth.8 They may also occur in some unusual sites, such as the orbit, vagina, bladder, esophagus, trunk, and extremities.7

Although there are more than 160 cases of adult extracardiac rhabdomyomas reported in the literature9, we are aware of only four reported cases of mediastinal rhabdomyomas and these cases were diagnosed after surgical excision or at the time of autopsy.8,10,11,12 We present an incidentally identified mediastinal rhabdomyoma which was diagnosed by transesophageal endoscopic ultrasound-guided fine needle aspiration (FNA) procedure. In addition, we review the role of FNA in the diagnosis of rhabdomyomas and the main morphologic differential diagnosis in the mediastinum.

CASE REPORT
The patient was 76 year old male who presented for evaluation of chronic obstructive pulmonary disease (COPD). His past medical history was significant for tobacco smoking for 25 years, hypertension, urinary tract infection, and diabetes mellitus type II. His surgical history was significant for spina bifida, hiatal hernia repair, abdominal hernia repair, and cholecystectomy. The patient denied dysphagia, dyspnea, chest pain, weight loss, or abdominal pain. On physical examination no palpable mass or lymphadenopathy was detected.

A thoracic computed tomography (CT) scan was performed to evaluate his COPD and showed an incidental 5.6 x 4.2 x 2.6 cm lobulated soft tissue mass in the superior mediastinum abutting the esophagus and right thyroid lobe. The tumor did not show surrounding lymphadenopathy.

An endoscopic ultrasound (EUS) was performed. Esophagoscopy was normal without evidence of an intrinsic
or extrinsic mass. EUS showed a 5.0 cm x 3.2 cm hypoechoic homogenous mass extrinsic to the esophagus, without surrounding lymphadenopathy. EUS-guided fine-needle aspiration (FNA) of the mass was performed with a 22-gauge needle, totaling 6 passes.

The patient has not been scheduled for surgery yet, but a followup CT scan after 12 months showed no increase in the size of this tumor. The patient has remained asymptomatic.

MATERIALS AND METHODS

The FNA sample was evaluated at the University of California, San Diego Department of Pathology. On each pass, a drop of aspirated material was transferred into a glass slide and was smeared with another slide. The air dried slides were stained with Diff-Quick stain, and the alcohol-fixed slides were stained with Papanicolaou stain. Needle rinses in RPMI solution were made into a formalin-fixed, paraffin-embedded cell-block and stained with hematoxylin and eosin (H&E).

CYTOLOGIC FINDINGS

Cellular aspirates of the mediastinal mass showed loose aggregates, syncytial groups, and a few isolated large round to polygonal cells with abundant finely granular cytoplasm (Figs.1 and 2). The nuclei were bland, round to oval with smooth borders, and they were located both centrally and peripherally with distinct conspicuous nucleoli (Fig. 3). No cytoplasmic cross striations, crystalloids or intranuclear cytoplasmic invaginations were noted. A component of small spindle cells was noted within the large groups of polygonal cells (Fig. 4).
Figure 3
Bland round to oval nuclei with smooth borders (1000X OIL Diff- Quick)

Figure 5
Cells arranged in a lobulated pattern (100X Cell block H&E stain)

Figure 4
Spindle cells associated with polygonal cells (200X PAP stain)

Figure 6
Cells with eosinophilic fine granular cytoplasm with occasional peripheral cytoplasmic clearing (400X Cell block H&E stain)

Histological examination of the cell block (H&E stain) showed sheets of tightly packed large polyhedral cells. The cells were arranged in a somewhat lobulated pattern and separated from one another by scant thin fibrous septa and narrow vascular channels (Fig. 5). Individual tumor cells had eosinophilic fine granular cytoplasm with occasional peripheral cytoplasmic clearing (Fig. 6). Cross-striations were not detected even at higher magnification. Tumor cells showed well-defined cell borders with bland-looking, round to eccentric nuclei and occasional inconspicuous nucleoli. No mitotic figures or nuclear atypia were identified.

Immunohistochemical stains were performed on the corresponding cell block. Tumor cells showed strong and diffuse positivity for myoglobin and desmin (Figs. 7 and 8). Pancytokeratin was also weakly positive. S100 and EMA were negative. Overall, the morphologic and immunophenotypic features confirmed the diagnosis of rhabdomyoma.
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Figure 7
Myoglobin immunostain- Strongly positive neoplastic cells (400X Cell block)

Figure 8
Desmin immunostain- Strongly/diffusely positive neoplastic cells (400X Cell block)

DISCUSSION

Extracardiac rhabdomyomas are considered to be true neoplasms in contrast to the cardiac ones which are regarded as hamartomatous processes. Extracardiac rhabdomyomas are distinguished into four clinically and morphologically different types: fetal, genital type, adult, and the rare rhabdomyomatous mesenchymal hamartoma. Fetal rhabdomyoma occurs primarily in the subcutaneous tissues of the head and neck of male infants, usually less than 3 years of age. Genital rhabdomyomas are slow-growing polypoid lesions in the vagina or vulva of young or middle aged women.

Rhabdomyomatous mesenchymal hamartoma of skin is an unusual lesion which occurs principally on the face and neck of male newborns. It typically presents as a small dome-shaped papule or a polypoid pedunculated lesion. Histologically, single or small groups of mature-appearing skeletal muscle fibers are found within the subcutaneous tissue and dermis.

Adult rhabdomyomas occur in patients with a mean age of approximately 51 years, although there is a wide age range (2-80). The tumor is more common in men with 6:1 male to female ratio and no documented racial predilection. Adult rhabdomyomas usually present as a single slow-growing, painless mass, although multifocal cases have been reported. They have a predilection for the head and neck region (90%), particularly in the vicinity of the mouth, but they have been reported in various other sites, including orbit, vagina, bladder, esophagus, trunk and extremities, trigeminal nerve, stomach, psoas muscle, stenohyoid, and prostate.

Four previous adult rhabdomyomas in the mediastinum have been reported in the English literature. Two of these cases were found incidentally at the time of autopsy. One was an 80-year-old African American male with gastric adenocarcinoma metastatic to liver. A pre-mortem chest x-ray had shown tracheal deviation adjacent to an area of increased density; however, mediastinal tomography had failed to reveal any mass lesions. The other case was a 68-year-old male who died as a result of a motor vehicle accident. The other two reported cases were diagnosed based on the surgically excised specimens after they were incidentally detected on chest x-rays. One was a 75-year-old female with unexplained fever for three months and the other was a 52-year-old male with bronchitis and pneumonia. Both of these two patients did not have recurrence during a follow-up period of eight and ten months respectively. (TRIM)

We present the fifth mediastinal adult-type rhabdomyoma, which unlike the previous cases, has been diagnosed by EUS-guided FNA biopsy. FNA has been reported before as a useful method to diagnose extracardiac rhabdomyomas of the head and neck region, but has not yet been described for rare mediastinal location of this tumor.

The classic cytological features of rhabdomyoma include single and syncytial clusters of large round to polygonal cells with abundant eosinophilic finely granular cytoplasm with distinct cell borders similar to the cytoplasm of normal
striated muscle cells. Cytoplasmic cross-striations and crystalloids can be seen especially on the H&E stained cell block. Peripherally located cytoplasmic clearing are due to vacuolization. These vacuoles are caused by removal of glycogen by the fixative and therefore, more commonly seen on the cell block. The vacuoles give the appearance of a spider web to the cells. Most nuclei are single, round and uniform and they are located either centrally or eccentrically. Rare multinucleated cells can be seen. A small number of spindle cells can be found in the background.

As in our case, a limited immunohistochemical panel is usually useful for definitive diagnosis. Rhabdomyomas are strongly positive for skeletal muscle markers including desmin, muscle specific actin (MSA), and myoglobin. Tumor cells also can show focal weak pancytokeratin positivity, which is not an uncommon feature in all the muscle origin tumors. Rhabdomyomas are negative for S100 excluding the possibility of granular cell tumor. The main cytological differential diagnosis of mediastinal rhabdomyoma is from some other tumors in this location, especially the ones with granular cytoplasm, such as granular cell tumor, leiomyoma, paraganglioma, rhabdomyosarcoma, hibernoma, rhabdomyomatous thymoma and thymic carcinoma, as well as aspiration of non-neoplastic skeletal muscle.

Granular cell tumors can occur in the same location with similar histology to adult rhabdomyoma. The tumor cells in both of these entities can arrange singly or in clusters and they are both PAS positive. However, granular cell tumor lacks cross striations, intracellular vacuolization and crystals. The cells of the granular cell tumor also tend to form syncytia with indistinct cell borders and they usually have more metachromatic cytoplasm than rhabdomyoma. Granular cell tumor is strongly positive for S-100 and negative for desmin and myoglobin.

Leiomyoma, the most common benign tumor of the esophagus, can be distinguished from rhabdomyoma by the interlacing fascicles of spindle shaped cells. The large ovoid cells with granular cytoplasm are also absent in leiomyoma.

Due to the neuroendocrine nature of tumor cells in paragangliomas, they can show abundant granular cytoplasm but the tumor cells usually have more nuclear atypia (endocrine atypia). In addition, the tumor cells are positive for the neuroendocrine markers like neuron-specific enolase, synaptophysin, and chromogranin.

Rhabdomyosarcomas display spindle or round cells with very occasional cross-striations, significant cytologic atypia, pleomorphism, and mitosis.

Rhabdomyomatous thymoma and thymic carcinoma exhibit two distinct cell populations, a myoid and an epithelial population. Yet even the rhabdomyomatous cells of these neoplasms are different from rhabdomyoma cells, having eccentrically placed nuclei and a lesser amount of eosinophilic cytoplasm. These tumors are negative for muscle markers and positive for pan-cytokerain.

Hibernoma cells have intracytoplasmic lipid droplets that may be confused with the glycogen in the cytoplasm of rhabdomyoma cells, but the vacuoles and cells are smaller, never have cross-striations and contain lipofuscin pigment. These tumors usually occur in the scapular region of a younger population, and do not express skeletal muscle markers.

Adult rhabdomyomas are benign lesions, and the recommended treatment is complete excision. Local recurrence of the tumor occurs in 10-42% cases and is thought to be due to incomplete resection of the mass. Recurrent lesions due to slow growth may become evident many years after the original resection, even after 30 years. No metastatic spread of any type of rhabdomyoma or malignant transformation has been reported. Preoperative diagnosis is essential for planning a complete curative resection of rhabdomyomas and avoiding unnecessary radical surgery (if mistaken for a malignancy).

Due to low occurrence, the radiologic appearance has not been very well delineated. The absence of invasion into surrounding soft tissues may help to distinguish them from malignant lesions; nevertheless, imaging alone may not clearly differentiate rhabdomyomas from other neoplasms. FNA biopsy is a much less invasive method of diagnosis as compared to incisional biopsy. This case showed that EUS-guided FNA is a reliable tool for definitive diagnosis, especially in the mediastinum in which a more invasive procedure may result in complications like infection or hemorrhage. That is the reason why, although rare, it is important to consider this benign tumor in the differential diagnosis of superior mediastinal masses.

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