An elderly woman with a mediastinal granulosa cell tumour: a rare presentation

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Abstract
Mediastinal lesions occur in a wide variety of clinical conditions. Metastatic granulosa cell tumour (GCT) in the mediastinum is a rare occurrence. We report a case of a woman who had a metastatic (GCT) in her mediastinum 40 years after treatment of the initial neoplasm. Surgical resection of the mediastinal mass revealed a low-grade epithelioid neoplasm with coffee bean-shaped nuclei and immunohistochemical stains that were consistent with metastatic GCT.

Introduction
Mediastinal granulosa cell tumour (GCT) is an unusual diagnosis, with very few cases reported in the literature. The purpose of this article was to report the case of an elderly female who was diagnosed with mediastinal GCT 40 years after resection of the original ovarian tumour and to review the literature.

Case Report
An 81-year-old Caucasian woman with asthma presented to the pulmonary medicine clinic for routine evaluation. Her surgical history was significant for resection of a benign ovarian mass 40 years ago. She was a non-smoker and lived at home with her husband. Review of systems was negative. Vital signs and physical examination were normal. Computed tomography (CT) scan of the chest was obtained to evaluate a known mediastinal lesion that had been identified on a prior CT scan that was ordered for surveillance of aneurysmal dilatation of her ascending thoracic aorta. A repeat CT scan of the chest at the time of our evaluation showed a 2.6 × 2.0 × 4.0 cm mediastinal lesion, which was an increase in size (Fig. 1A–C). The lesion demonstrated interval development of regions of hypoattenuation and peripheral calcification. A positron emission tomography-computed tomography (PET-CT) scan was obtained for further evaluation. The lesion was characterized as a right paratracheal nodal conglomerate. The lesion did not demonstrate hypermetabolic activity (Fig. 1D). There was otherwise normal physiological whole-body 18-fluorodeoxyglucose (18-FDG) avidity. Given the interval enlargement of the mass, she underwent an endobronchial ultrasound (EBUS) with transbronchial needle aspiration (TBNA) of the lesion. The EBUS revealed a well-circumscribed mass in the 4R lymph node region. The TBNA samples demonstrated an epithelioid neoplasm without evidence of lymphoid tissue. She was subsequently referred to cardiothoracic surgery for median sternotomy with mediastinal mass excision. Total thymectomy was performed during the mass excision as thymoma was initially included in her differential diagnosis. Microscopic examination of the mass showed a well-circumscribed neoplasm that
had a trabecular, solid, and focal papillary architecture (Fig. 2A). Cytologically, the neoplasm was composed of epithelioid cells with abundant cytoplasm and oval to reniform nuclei with longitudinal grooves (Fig. 2B). Immunohistochemical stains were positive for pan-cytokeratin, CD99, CD56, estrogen receptor (ER), S100, inhibin, and calretinin. These findings were consistent with metastatic GCT.

The patient revealed that the “benign” pelvic tumour previously resected in 1976 (about 40 years prior to resection of the mediastinal lesion) was indeed a GCT. Prior surgical history was significant for a total abdominal hysterectomy in 1967 and an exploratory laparotomy with bilateral salpingo-oophorectomy in 1976 for stage IA GCT. She received pelvic radiation in 1976 but declined chemotherapy. After removal of the mediastinal mass, she was referred to gynaecological oncology.

Discussion

Differential diagnosis for a mediastinal mass is broad and includes thymoma, lymphoma, germ cell tumour, intrathoracic thyroid, parathyroid adenoma, and metastatic neoplasm. Imaging findings in primary GCTs vary widely and range from solid masses to cystic tumours [1]. In one series, the categorization of radiographic patterns was divided into two common forms: multi-septated cystic masses and lobulated solid masses with internal cystic portions [2]. Imaging findings in metastatic lesions are nonspecific, consisting of predominantly solid components or a mixture of cystic and solid areas.

Mediastinal recurrences of GCT are quite rare. Only two prior cases of mediastinal recurrence of GCT have been reported in the literature [3,4]. The most recent case recurred as a solid, hypovascular tumour in the posterior mediastinum [3]. The other case was 1 out of a series of 110 patients during post-mortem examination; this case predated modern CT imaging [4]. Our case is the first documented case in the medical literature of a mediastinal recurrence of GCT in the superior mediastinum.

Adult-type GCTs account for 1–2% of all ovarian neoplasms and approximately 5–8% of primary ovarian malignancies [5]. One of the common features of an adult GCT is

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Figure 1. Computed tomography (CT) scan of the chest with contrast with axial, coronal, and sagittal views depicted in (A), (B), and (C), respectively. These images depict the mass that was found to be mediastinal granulosa cell tumour. (D) The mass did not demonstrate hypermetabolic activity on positron emission tomography-computed tomography (PET-CT) scan.

Figure 2. Pathology of the tumour. (A) Haematoxylin and eosin stain (H&E stain) of the tumour shows elongated plates/bands of tumour cells with trabecular architecture (10x). (B) Tumour cells demonstrate the characteristic longitudinal nuclear grooves on reniform, coffee bean-shaped nuclei (H&E stain, 100x).
the presence of nuclear grooves [5]. Immunohistochemistry is useful in differentiating GCTs from other neoplasms as GCTs are reactive for inhibin and CD99 [6]. GCT may demonstrate macrofollicular, trabecular, solid, and insular patterns with Call-Exner bodies, which are small follicle-like structures filled with acidophilic material [6]. These tumours occur predominantly in perimenopausal women. Concurrent hyperoestrogenaemia may produce endometrial hyperplasia, polyps, or carcinoma [7]. Endometrial carcinoma is associated with these neoplasms in 3–25% of cases [7]. Patients with GCT require long-term surveillance because of the known, yet unpredictable, recurring behaviour many years after a disease-free interval, even in those with stage I or stage II tumour at diagnosis [8].

Available case series show that time to recurrence averages between 5 and 10 years [9]. However, it is well known that GCT can recur after 10 years [10]. There was one prior case of recurrence at 40 years [11]. In our case report, the mediastinal lesion was resected 40 years after the initial diagnosis, and to our knowledge, it matches the time interval for the latest GCT recurrence reported in the literature [11]. Additionally, it is only the third case of mediastinal recurrence of GCT in the literature and the only case noted to be in the superior mediastinum. This case highlights the critical importance of considering a GCT in the differential diagnosis of mediastinal masses. For GCT metastases, treatment consists of surgical resection with hormonal treatment and, in some cases, post-operative radiation with or without chemotherapy [12]. Tumour markers are available for surveillance, which were normal in our patient. For post-treatment surveillance, this patient will return for a review of systems, physical examination, and serum tumour markers every 2–4 months for the first 2 years after treatment and then every 6 months indefinitely [13]. There is insufficient data to support routine use of radiographic imaging for surveillance of these tumours [13]. This case demonstrates that recurrent GCT should be on the differential for patients with mediastinal masses and a history of GCT.

**Disclosure Statement**

Appropriate written informed consent was obtained for publication of this case report and accompanying images. The views expressed in this case report are those of the authors and do not necessarily reflect the official policy or position of the United States (U.S.) Department of the Navy, U.S. Department of Defense or the U.S. Government.

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