Case Report

Defying Sutton's Law: Primary Intrapulmonary Germ Cell Tumor: A Case Report

Ma. Betina Carabuena*, Carlos Joshua Espino, Alvin Camacho, Eileen Grace Tiu
Department of Radiology, The Medical City, Ortigas Avenue, Pasig City
*Contact Details: betina_carabuena@yahoo.com

ABSTRACT: Germ cell tumors are commonly found in the gonads. Intrapulmonary germ cell tumors are extremely rare and diagnosis requires exclusion of gonadal and extra-gonadal primary sites. Common signs and symptoms include chest pain, followed by hemoptysis and cough. Only a total of 67 cases of intrathoracic germ cell tumors have been published in the literature from 1939 to 2007. We report the case of a 23-year old Filipino male who initially presented with sore throat but on further diagnostic evaluation was found to have a pulmonary mass in the right lower lobe. Computed tomography imaging favored an infectious etiology but a more thorough evaluation with immunohistochemistry staining was consistent with a low grade intrapulmonary germ cell tumor. While Sutton's law describes that it is reasonable to approach diseases with the most common conditions in mind, this case report highlights that exceptions do occur.
Keywords: *computed tomography, germ cell tumor, intrapulmonary, Sutton's law*

INTRODUCTION

Sutton's law states that in the practice of medicine, it is most prudent to look for disease conditions that are commonly encountered. A similar idea was coined by Dr. Theodore Woodward who stated that "When you hear hoof beats, think of horses not zebras".

Approach to the diagnosis of a solitary pulmonary nodule or mass requires evaluation of the radiologic features that would facilitate its classification under either a benign or malignant process. Although there may be some overlap in their appearance radiographically, specific morphologic features are assessed to determine if a pulmonary focus has malignant potential. Particularly, features such as size, margins, contour, internal characteristics (i.e. attenuation, calcifications, wall thickness and air bronchogram), satellite nodules, halo sign and growth rate are evaluated.[1]

Discussed below is an unusual presentation of a germ cell tumor found in the intrathoracic area.

CASE REPORT

A 23-year old single male developed sore throat and fever lasting for about two weeks. He was given two different antibiotics with no relief of symptoms. The complete blood count was within normal limits. A chest radiograph was requested, which revealed a lung nodule in the right parahilar region (Figure 1). Our patient denied symptoms such as dyspnea, cough and weight loss. The patient had no co-morbidities or family history of malignancy. He was a non-smoker and an occasional alcoholic beverage drinker.

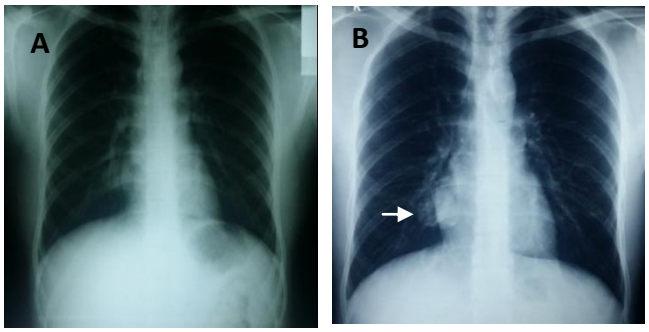

Figure 1. (A) Chest radiograph done in 2015 as part of the patient's annual physical examination signed out as a normal study. (B) Chest radiograph done in 2016 showing a well-circumscribed nodular opacity in the right parahilar region demonstrating the hilum overlay sign.

A contrast-enhanced chest CT scan was requested (Figure 2 and 3) which showed a well-defined soft tissue mass with smooth margins in the medial basal segment of the right lower lobe measuring 3.5 x 3.7 x 3.2 cm. No perilesional alveolo-interstitial opacities were detected. Moreover, the mediastinal compartments were intact with no demonstrable masses or enlarged lymph nodes. The primary consideration at this time was a tuberculous or granulomatous process. However, the possibility of a malignancy was not totally excluded. Tissue diagnosis and follow-up after empiric treatment was suggested.

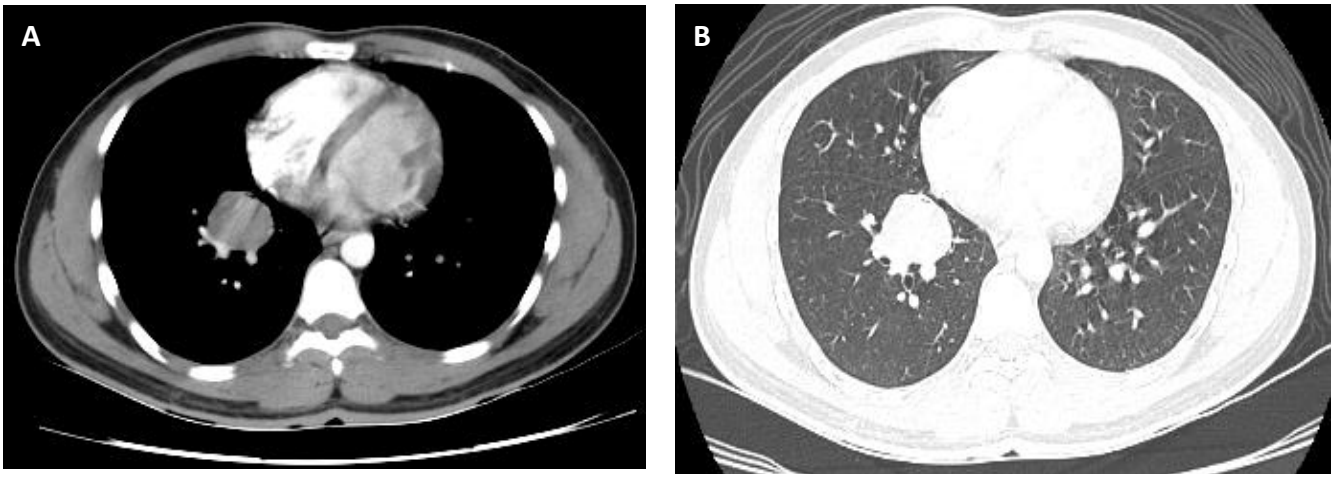

Figure 2. Axial images (A) mediastinal and (B) lung windows showing a pulmonary mass in the medial basal segment of the right lower lobe

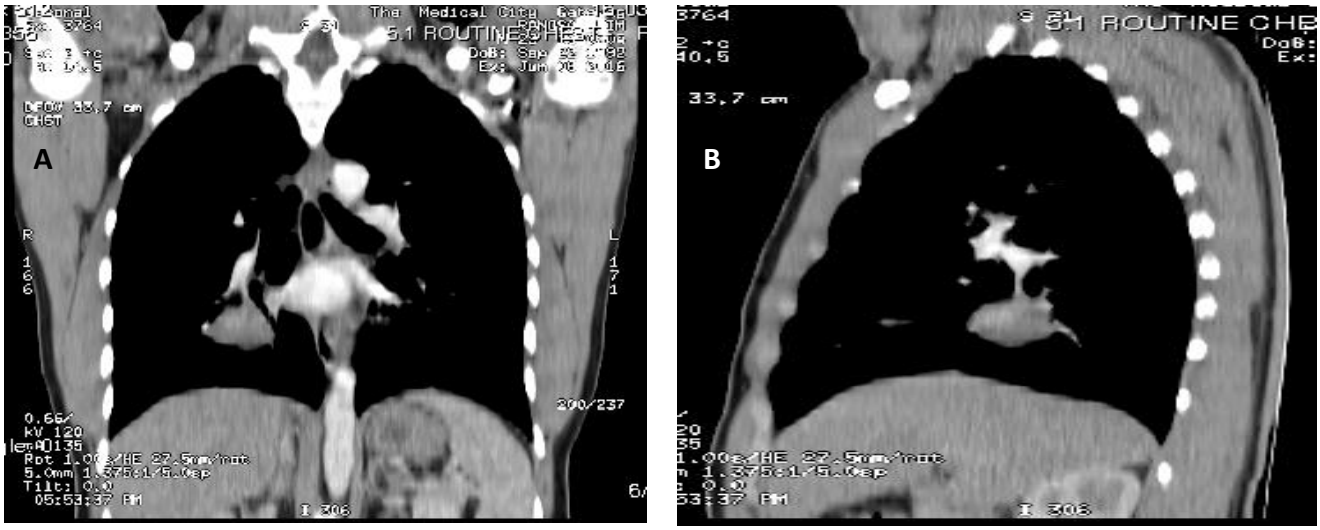

Figure 3. Coronal (A) and sagittal (B) views showing the intrapulmonary location of the non-enhancing lung mass with soft tissue component

The patient underwent CT-guided core needle tissue biopsy. Cytologic evaluation showed neoplastic cells occurring in clusters, some in acinar and rosette-like patterns with fairly uniform small round to ovoid nuclei, finely granular chromatin, inconspicuous nucleoli and ample eosinophilic cytoplasm (Figure 4). Immunohistochemistry was performed showing cells positive for the stains cytokeratin, TTF-1 and SALL 4. This profile was compatible with a germ cell tumor.

Open thoracotomy and right lower lung lobectomy was done yielding a 3.5 x 2 x 2 cm, well-defined encapsulated, cream white, soft and friable mass located in the medial basal segment.

A 0.5 cm hard subpleural nodule was also resected at the lateral aspect of the posterior basal segment. This showed chronic granulomatous inflammation on frozen section. Five resected hilar lymph nodes were negative for tumor infiltration.

Sonographic evaluation of the thyroid gland and testicles was done to search for a possible primary neoplasm, and revealed normal findings and a small left epididymal

head cyst, respectively. Metastatic work-up also included a computed tomography of the head, bone scan and sonographic evaluation of the whole abdomen. Workup only revealed cholelithiasis and bilateral non-obstructing nephrolithiases. No primary neoplastic focus was found elsewhere in the body.

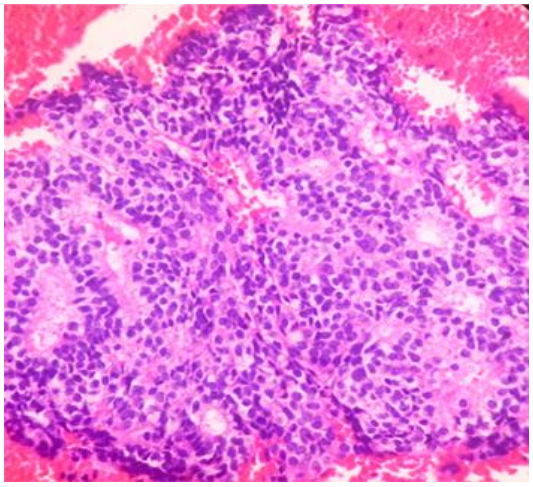

Figure 4. Neoplastic cells occurring in clusters, some in acinar and rosette-like patterns

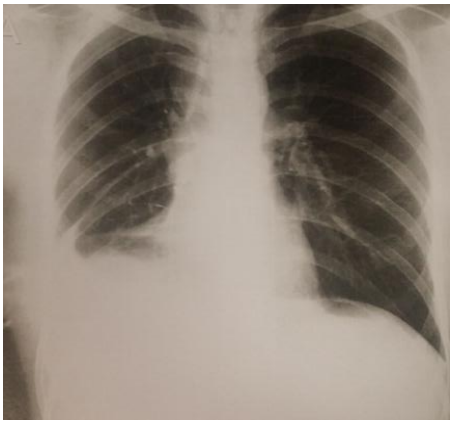

Figure 5. Chest radiograph 2 days post-operatively showing decreased lung volume in the right lower lobe with compensatory hyperaeration of the left lung. Minimal pleural effusion in the right is also noted.

DISCUSSION

Germ cell tumors are commonly found in the gonads, while the most common extra-gonadal site is the mediastinum. Intrapulmonary germ cell tumors are extremely rare, and diagnosis requires exclusion of gonadal and extragonadal primary sites.

Only a total of 67 cases of intrathoracic germ cell tumors, particularly the teratoma type, have been published in the literature from 1939 to 2007.[2] There is no known locally published case to date.

The first case of intrapulmonary teratoma was documented by Mohr in 1939. Several studies postulated that intrathoracic teratomas originate from the thymic tissue of the third pharyngeal pouch.[3] It is theorized that the primordial teratomatous focus in the potential mediastinum is caught up by the respiratory outgrowth; hence, it develops in the lung and not in the mediastinum.[3]

Patients with intrapulmonary germ cell tumors commonly present with chest pain (52%), hemoptysis (42%) or cough (39%).[2] The most specific symptom, if present, is trichoptysis (13%). None of these symptoms were present in our patient. Two-thirds of intrapulmonary germ cell tumors, particularly the teratoma type, occur in the upper lobes, usually in the left. There appears to be no documented case of germ cell tumors occurring in the lower lobes, as in our case.

Radiologically, an intrapulmonary teratoma usually presents as a lobulated mass, and may also show features of cavitation, consolidation or peripheral translucency. Particularly, computed tomography demonstrates discrete areas of different densities due to soft tissue, high focal fat content, punctate calcifications, or a combination of these features.[2]

Intrapulmonary mature teratomas was defined in one study as lung masses with sizes ranging from 2.8 to 3 cm in diameter.[5] They are usually cystic with loculations, while a sparse number of cases appear predominantly solid. Moreover, the cystic foci form connections with the bronchi and have an endobronchial component leading to the classic symptoms of hemoptysis and expectoration of hair or sebum. Interestingly, none of these features were in our patient: his CT imaging only showed a well-circumscribed soft tissue mass with smooth margins without any calcific, cystic or fat components.

Tissue histology is needed for definitive diagnosis. Tumors that may be present similarly include fetal type adenocarcinoma, germ cell tumor (immature teratoma alone or in combination with other germ cell tumors) and pulmonary bastoma. As such, the immunohistochemistry profile done in our patient played a crucial role in arriving at a more definitive diagnosis.

In outpatient, the SALL4 transcription factor was positive. This transcription factor is associated with embryonic pluripotency and is a useful immunohistoechemical marker of germ cell tumors.[6] Another study involved the examination of 3215 tumors for SALL4 expression. Results showed that the transcription factor was consistently expressed in all germ cell tumors, except some trophoblastic tumors and mature components of teratomas.[6]

In our patient, both TTF-1 and SALL4 transcription factors were positive. The TTF-1 strongly suggests the lung mass was a primary pulmonary neoplasm, while the SALL4 transcription factor confirms it as a germ cell tumor.

While the treatment of choice is surgical resection, germ cell tumors are very responsive to chemotherapy. However, since the intra-pulmonary location is extremely rare, no standardized treatment has been established. Published data discuss oncological management of mediastinal germ cell tumors, but no studies have been conducted showing that the same treatment regimen works effectively for the pulmonary intraparenchymal type. These tumors should be managed as a bronchopulmonary carcinoma.[4]

CONCLUSION

Primary germ cell tumors of the lung parenchyma are extremely rare and only a few cases have been reported to date. While common imaging findings have already been established, this case highlights that germ cell tumors can present with atypical radiologic features. This may be attributed to the pluripotency of these types of tumors and as such, utmost care in diagnosis must be exercised when imaging findings do not conform to the typical presentation. Further evaluation with specific immunochemistry tests are often necessary and play a crucial role in correct diagnosis of these tumors.

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