

Primary Pulmonary Germ Cell Tumor with Bone Metastasis

Tong-Tong Li¹, Xu Yan², Tong Zhou³, Ying Liu¹, Zhen-Xiang Yu¹

¹Department of Respiration, The First Hospital of Jilin University, Changchun, Jilin 130021, China

²Department of Pathology, The First Hospital of Jilin University, Changchun, Jilin 130021, China

³Department of Endocrinology, The First Hospital of Jilin University, Changchun, Jilin 130021, China

Male germ cell tumors (GCTs) are predominantly derived from testis, while about 2–5% of which arise at extragonadal sites. Extragonadal GCTs (EGCTs) have similar histological components as gonadal GCTs and often occur in the midline of the body, making diagnosis difficult.

A 17-year-old boy presented to the pulmonary department with a history of persistent/continuous/chronic cough for the past 15 days following a cold; he had no sputum, fever, or chest pain, occasionally accompanied by shortness of breath. Three days ago, the patient developed unexplained left side chest pain and fever up to 38.5°C.

The patient's routine laboratory tests were normal. An elevated serum alpha-fetoprotein (AFP) (41.39 ng/ml, reference range <20 ng/ml) and C-reactive protein (77.10 ng/ml, reference range <3.4 ng/ml) were detected. Carcinoembryonic antigen and neuron-specific enolase levels were normal. Tuberculosis T-sport test was negative.

Computed tomography (CT) of the lung revealed a lesion with obstructive pneumonia in the left inferior lobe accompanied by mediastinal and left pulmonary hilar lymphadenopathies [Figure 1a]. Central type lung cancer with obstructive atelectasis and obstructive inflammation accompanied with metastases in the left pulmonary portal and mediastinal lymph nodes as well as multiple bone metastases were evidenced by positron emission tomography-CT (PET-CT) scan [Figure 1b].

On bronchoscopic examination, the left lower lobe bronchial openings were found to be nearly occluded and inflamed showing by rough, hyperemic, and swollen mucous membrane [Figure 1c]. Biopsy examination and the alveolar lavage were performed through the bronchoscope. Microscopically, beneath the bronchial mucosa, the tumor was composed of sheet-like pattern of noncohesive tumor cells with a fibrous stromal network. The fibrous septa almost always contained focal lymphocytic infiltrate. The tumor cells typically had abundant clear to pale pink cytoplasm. The

nuclei were prominent and usually contained one or two large nucleoli, and had prominent nuclear membranes [Figure 1d]. The immunohistochemical results showed ki67 (+70%; Figure 1e) and Sal-like protein 4 (+; Figure 1f). Finally, the biopsy pathology revealed that was seminoma, a kind of GCTs. Alveolar lavage fluid was evaluated by tuberculous smear and exfoliated cytology. Acid-fast bacilli were not detected while suspected cancer cells were present. The patient started chemotherapeutic treatment consisted of four cycles of cisplatin combined with etoposide and ifosfamide. He achieved complete remission after the first and third cycles of chemotherapy. However, the metastases progressed rapidly to involve brain, skin, eye socket, and other tissues after the fourth cycle. Subsequent therapy using apatinib was also suspended due to the presence of soy sauce color urine suggestive of gross hematuria. Radiotherapy was then applied as strongly requested by the patient, but it was ineffective. The patient gradually lost consciousness during the treatment. It only took 4 months from the diagnosis of primary pulmonary GCT to the abandonment of treatments.

EGCTs are very rare neoplasms that have been described in mediastinum, pineal gland, retroperitoneum, and sacrococcygeal region. Pulmonary GCTs are the least common GCTs in EGCTs displaying similar symptoms to other types of lung tumor, including cough, sputum, hemoptysis, and fever. Dyspnea is also present when accompanied with obstructive pneumonia. There are two hypotheses for the mechanism of EGCTs: The germ cells migrate along the genitourinary ridge during embryonic period to extragonadal sites, or second, they might be mediators that are assigned to specific organs to perform

Address for correspondence: Prof. Zhen-Xiang Yu,
Department of Respiration, The First Hospital of Jilin University,
Changchun, Jilin 130021, China
E-Mail: yuzhenxiang2005@sina.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

© 2018 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

Received: 23-11-2017 **Edited by:** Peng Lyu

How to cite this article: Li TT, Yan X, Zhou T, Liu Y, Yu ZX. Primary Pulmonary Germ Cell Tumor with Bone Metastasis. Chin Med J 2018;131:624-5.

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.4103/0366-6999.226071

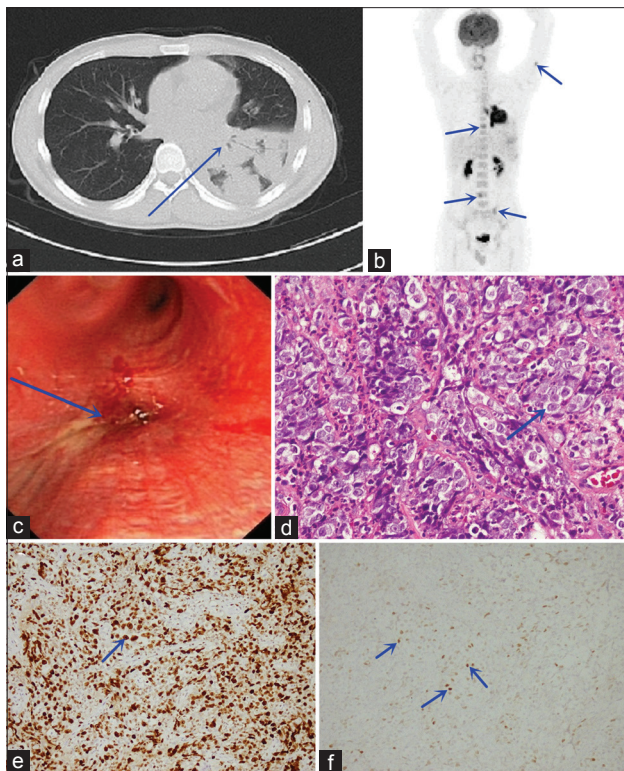


Figure 1: The representative images of the patient. (a) The lung CT showed a lesion with obstructive pneumonia in the inferior lobe of the left lung; (b) PET-CT showed the primary lesion, multiple bone metastasis; (c) bronchoscopic examination showed that the bronchial openings of the lower lobe of left lung was rough, hyperemic, edema, and the lumen was close to occlusion and it was soft and easy to bleed on touch; (d) The germ cell tumor was confirmed by pathology: (hematoxylin-eosin staining, $\times 400$); (e): Ki67 (+70%) (immunohistochemical staining, $\times 200$); (f): SALL 4 (+) (immunohistochemical staining, $\times 200$). PET-CT: Positron emission tomography-computed tomography; SALL4: Sal-like protein 4.

specific functions or transmit-specific information based on the physiological and metabolic conditions of the organs. Approximately 80% of patients with metastatic GCTs have increased levels of serum AFP or human chorionic gonadotropin.^[1] The EGCTs can be diagnosed only if the original tumor at testis or ovary is excluded.^[2] Bone metastasis is rare in testicular GCTs. It usually occurs in the late stages of disease progression, and systemic chemotherapy should be considered an emergency oncology once discovered.

EGCTs should be treated by a multidisciplinary approach including systemic chemotherapy, radiotherapy, and surgery regardless of the tumor location.^[2] The rapid development of cancer driver genes provides a novel targeted therapy for patients with lung cancer.^[3] Kinase inhibitors targeting epidermal growth factor receptor (EGFR), human epidermal growth factor receptor-2 (HER2), and vascular endothelial growth factor receptor are proved to be effective in many solid

tumors. Schaffrath *et al.*^[4] demonstrated that kinase inhibitors targeting EGFR, HER2, mammalian target of rapamycin, and insulin-like growth factor-1 receptor were effective in testicular GCTs. Meanwhile, anti-programed death 1 (PD1) has been indicated to be standard immunotherapy for various kinds of cancers and expression of its ligand PD-L1 has been confirmed in testicular GCTs.^[5] The long-term survival rate can reach more than 90% if a primary lesion has a pathological characteristics with good prognosis or can be removed surgically. Metastatic or surgically unresectable tumor represents a poor prognosis. Currently, cisplatin-based chemotherapy shows to significantly improve the prognosis of patients.

This report is about a case of primary pulmonary GCT with bone metastasis. The patient had no history of orchitis or testicular tumor and normal testes as evidenced by PET-CT scan. This case suggests that pulmonary space-occupying lesion in adolescents with elevated AFP should be alert to the possibility of primary pulmonary GCT after the primary tumor of common locations is excluded from the study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s)/patient's guardians has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients/patient's guardians understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This study was supported by a grant from Provincial and Ministerial Fund Project (No. 2015Y036-3).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Ebi H, Nakata M, Tahara M, Igarashi T, Kawada K, Itoh K, *et al.* Extragonadal germ cell tumors in Japan. *Cancer Sci* 2003;94:1107-11. doi: 10.1111/j.1349-7006.2003.tb01408.x.
2. Ait Benali H, Lalya L, Allaoui M, Benmansour A, Elkhanoussi B, Benjelloun S, *et al.* Extragonadal mixed germ cell tumor of the right arm: Description of the first case in the literature. *World J Surg Oncol* 2012;10:69. doi: 10.1186/1477-7819-10-69.
3. Ni J, Zhang L. Evaluation of three small molecular drugs for targeted therapy to treat nonsmall cell lung cancer. *Chin Med J* 2016;129:332-40. doi: 10.4103/0366-6999.174484.
4. Schaffrath J, Schmoll HJ, Voigt W, Müller LP, Müller-Tidow C, Mueller T, *et al.* Efficacy of targeted drugs in germ cell cancer cell lines with differential cisplatin sensitivity. *PLoS One* 2017;12:e0178930. doi: 10.1371/journal.pone.0178930.
5. Shah S, Ward JE, Bao R, Hall CR, Brockstein BE, Luke JJ, *et al.* Clinical response of a patient to anti-PD-1 immunotherapy and the immune landscape of testicular germ cell tumors. *Cancer Immunol Res* 2016;4:903-9. doi: 10.1158/2326-6066.CIR-16-0087.