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Original Article

Leydig cell tumor with lung metastasis diagnosed by lung biopsy

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Abstract: Leydig cell tumors are very rare and account for only 3% of testicular tumors and are generally benign. Only less than 0.2% of all testicular cancers were evidenced by metastatic spread. We report a 34-year-old man visited hospital because of coughing sputum mixed with blood. His chest CT showed bilateral patch clouding opacity. He was suspected with allergic alveolitis and treated with methylprednisolone. However, his symptoms and general condition deteriorated, and he visited our hospital. He had no abnormal findings on physical examination. A chest radiograph showed pneumonia in whole lung and CT showed multiple nodules and diffused ground glass opacities in both lung fields. Lung biopsy confirmed a diagnosis of Leydig cell tumor with lung metastasis. The diagnosis is based on the histopathology and immunohistochemistry.

Keywords: Leydig cell tumors, lung metastasis, lung biopsy, immunohistochemistry

Introduction

The interstitial Leydig cells of testis, developing from the mesenchyme located between the seminiferous tubules. The majority of Leydig cell tumors are found in men, usually at 5-10 years of age or in middle adulthood (30-60 years). Leydig cell tumors (LCTs) are very rare tumors and account for 1-3% of all testicular malignancies. Majority of these tumors are benign. Malignant LCT accounts for less than 0.2% of all testicular cancers as evidenced by metastatic spread and poor survival [1, 2]. We report an interesting case of malignant LCT with lung metastasis in 34-year-old man who presented with coughing sputum mixed with blood for 7 months. The final diagnosis of LCT with lung metastasis was made by lung biopsy.

Case presentation

A 34-year-old man who had been complaining of coughing sputum mixed with blood for 7 months was admitted to a local hospital. His chest CT showed bilateral patch clouding opacity. Percutaneous lung biopsy (PCNA) was performed by the local hospital, but the result was negative. The allergic alveolitis was suspected, and administration of methylprednisolone for 2 months.

However, his symptoms and general condition deteriorated, and she was admitted to our hospital. He was diagnosed Leydig cell tumor and a high left inguinal orchiectomy was performed one month ago. He had no prior history of lung disease, and no exposure to dust or occupational hazards. Chest auscultation was normal, and there were no lymphadenopathy, skin lesions or neurological signs. The full blood count findings showed moderate anemia (red blood cells (RBCs) 3.08×10^{12}/L, hemoglobin 82 g/L) with increased white blood cells (13.0×10^{9}/L: 90.7% neutrophils, 0.4% eosinophils, 5.0% lymphocytes, and 3.1% monocytes) and normal platelets counts (262×10^{9}/L). The rest of the biochemical findings were normal. Chest X-ray showed pneumonia in whole lung (**Figure 1A**). CT showed multiple nodules and diffused ground glass opacities in both lung fields (**Figure 1B**).

Infection, rheumatic diseases and lymphoproliferative diseases were suspected as the primary

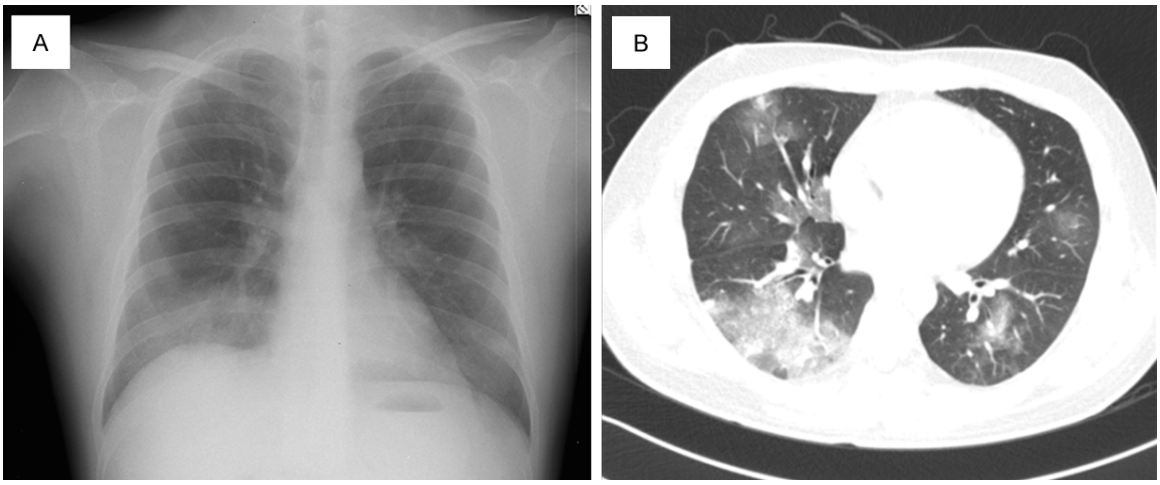

Figure 1. A. Chest X-ray at the time of admission showed pneumonia in whole lung. B. CT showed multiple nodules and diffused ground glass opacities in both lung fields.

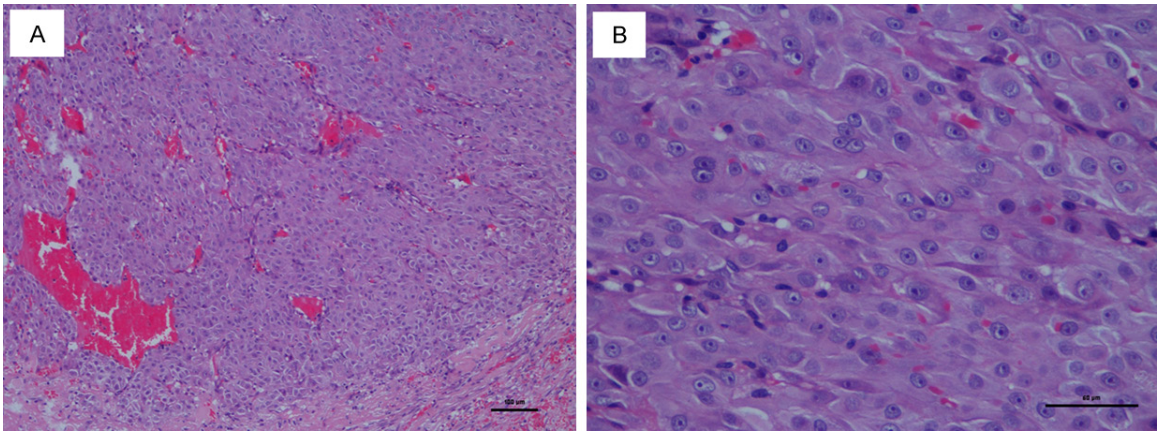

Figure 2. A. Low power view showed solid nests of tumor cells and the tumor vessels (100×). B. Tumor cells are large and polygonal with round nuclei and abundant eosinophilic cytoplasm (400×).

disease causing coughing sputum mixed with blood. However, microbiological examinations, such as sputum, blood culture and urine were negative.

We suspected metastatic disease to lungs because the patient was diagnosed LCT before. Histological confirmation was very important for the diagnosis of LCT with lung metastasis. To obtain a diagnosis, lung biopsy (from the left upper lobes) was performed.

Tissue sections were fixed in 10% formalin and hematoxylin and eosin (H&E) stains. Low power view showed solid nests of tumor cells and the tumor vessels (**Figure 2A**). The individual tumor cells showed abundant eosinophillic cytoplasm with central round to oval nucleus with round nuclei (**Figure 2B**). Immunohistochemical studies were conducted in selected formalin-fixed, paraffin-embedded blocks of case. The tumor cells were diffusely positive for Vimentin (**Figure 3**) and CK (**Figure 4**). The tumor cells showed no immunoreactivity for PAX-8, HMB45, CD31, P63, TIF-1, NapsinA, S100, CD34 and CK5/6. LCT with lung metastasis was the final diagnosis. The patient has had chemotherapy treatment in another hospital after this diagnosis was made.

Discussion

LCT is derived from the interstitial Leydig cells, which are designated by the name of the

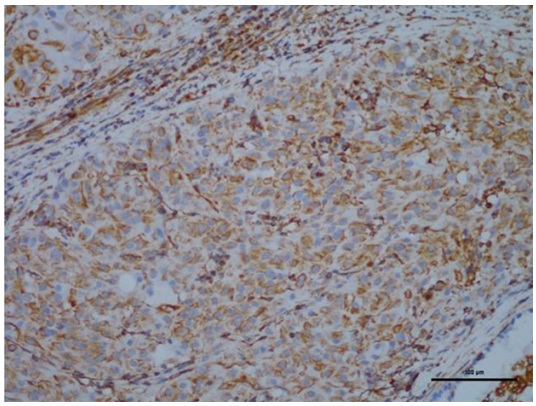

Figure 3. Immunohistochemical staining demonstrated that tumor cells were positive for Vimentin (200×).

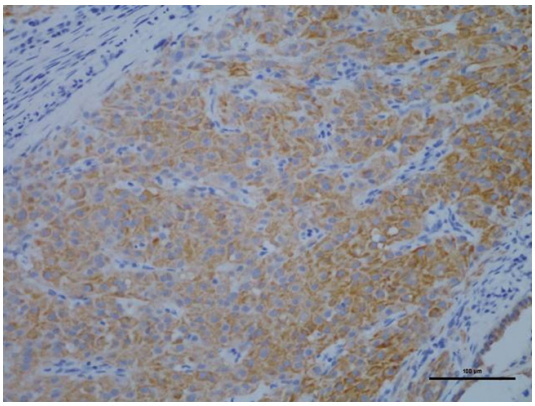

Figure 4. Immunohistochemical staining demonstrated that tumor cells were positive for CK (200×).

German anatomist Franz Leydig who first described them in 1870 [3, 4]. Leydig cells share the same mesodermal origin and the same phenotype with adrenocortical cells. LCT is the most common sex cord-stromal tumor, representing no more than 40% of all nongerm cell testicular tumors, and affects both testes in equal rate [5-7].

Adults with LCT usually complain of testicular swelling [5]. A small proportion is associated with endocrine manifestations, including gynecomastia and decreased libido. Gynecomastia is the main clinical manifestation in male adults but may be also clinically significant in affected children who undergo precocious puberty. Some cases of LCT were merely revealed by Gynecomastia [8, 9], and these patients often had raised plasma oestradiol concentrations.

Although LCTs are usually clinically benign, about 10% of the reported cases have been associated with a malignant course [10, 11]. In general, it is difficult to diagnose malignant Leydig cell tumors histologically. The most accepted criterion of malignancy remains the presence of metastasis. Metastatic LCT occurs in patients between 20 and 82 years, with a mean age of 58 years [12]. About 20% patients had metastatic disease at the time of initial diagnosis, with another 40% having metastatic disease with 2 years. Most frequent sites of metastasis are the regional lymph nodes (70%), followed by liver (45%), lung (40%), and bones (25%) [1].

The survival after diagnosis of the primary LCT disease ranged from 2 months to 17 years. Median survival is 2 years [13]. Survival after diagnosis of metastatic disease ranged from less than 1 month to 9 years. However, two-third patients die within 2 years after they are diagnosed LCT. For malignant tumors, the surgery may be radical and usually is followed by adjuvant chemotherapy, sometimes by radiation therapy. Radiation therapy only relieves the pain of LCT patients who have had bony and retroperitoneal metastasis. Chemotherapy with the bleomycin-etoposide-platinum regimen used for germ cell malignancies has limited efficacy in managing malignant LCTs [13]. The tyrosine kinase inhibitor imatinib has shown some chemotherapeutic activity in animal models [14], but this is not demonstrated in human trials [15].

Lung biopsy plays a very important role in the diagnosis of lung infection or lung with unexplained nodules. Percutaneous lung biopsy (PCNA) technique is a high precision minimal risk clinical procedure to extract abnormal tissue growth in the lungs [16]. The PCNA procedure is conducted by highly qualified professionals with the help of CT scan or ultrasound. The utility of the PCNA is the possibility of diagnosing specifically the patients with lung diseases and avoiding a surgical lung biopsy. In our case, we did not perform PCNA, because the tiny specimens obtained by PCNA may not be sufficient to diagnose lung diseases and surgical lung biopsy is considered the best way to obtain enough tissue for pathological study.

In our case, the patient has been misdiagnosed in the past with allergic alveolitis. Allergic alveolitis represents a group of pulmonary disorders

mediated by inflammatory reaction to inhalation of an allergen. These may be organic or inorganic particles (microbes, animal or plant proteins, and certain chemicals) that form haptens by sensitized individuals. The chest CT of this disease often shows homogeneous ground-glass opacity and numerous round centrilobular opacities which is usually less than 5 mm in diameter [17, 18]. The homogeneous ground-glass opacity is bilateral and symmetric but sometimes patchy and concentrated in the middle part and base of the lungs or in a bronchovascular distribution. The chest CT of pulmonary metastases shows soft tissue attenuation well circumscribed rounded lesions, more often in the periphery of the lung. They are usually of variable size, a feature which is of some use in distinguishing them from a granuloma [19]. A prominent pulmonary vessel has frequently been noted heading into a metastasis. The ground-glass opacity representing hemorrhage can be seen, particularly surrounding haemorrhagic pulmonary metastases. In our case, the CT of the patient showed multiple nodules and diffused ground glass opacities in both lung fields. It is very difficult to distinguish allergic alveolitis and pulmonary metastases only via CT. Therefore, lung biopsy plays a very important role in the diagnosis of this lung disease.

In summary, the possibility of pulmonary metastases might be considered in some cases diagnosed as allergic alveolitis or interstitial pneumonia. It is important to encourage the use of lung biopsy by clinicians and cytopathologists for investigating an abnormality found on a chest X-ray or CT scan.

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Disclosure of conflict of interest

None.

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