



# Testicular Pain is the First Symptom of Lung Squamous Cell Carcinoma Metastasizing to the Testis

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A 67-year-old male presented with a two-month history of left-sided testicular pain of unknown etiology. Color Doppler ultrasonography revealed a hypoechoic area in the left testis, measuring approximately 3.1 x 2.2 cm, with ill-defined borders and heterogeneous internal echogenicity; blood flow signals were also observed within the lesion (Figure 1a). The sagittal T2-weighted sequence on pelvic magnetic resonance imaging (MRI) demonstrated a solid mass in the left testis (Figure 1b). Concurrently, laboratory tests revealed elevated levels of high-sensitivity C-reactive protein (9.33 mg/l), white blood cell counts ( $15.00 \times 10^9/l$ ), and neutrophil percentage (86.5%). Additionally, the serum tumor marker, Ca19-9, was measured as 67.60 U/ml. The urine examination revealed a negative result for occult blood, but proteinuria was detected; also, a white blood cell count of 13/ $\mu l$  and the presence of squamous epithelial cells (count =3/ $\mu l$ ) were detected in the urinalysis. Based on these findings, an initial diagnosis of left orchitis was made, and treatment with cefdinir and dexamethasone was initiated, which yielded no response.

Subsequently, a testicular biopsy was performed to confirm the diagnosis, which surprisingly revealed a moderately and poorly differentiated squamous cell carcinoma (Figure 2a). Immunohistochemical analysis of the biopsy sample demonstrated positivity for CK7, p40 (Figure 2b), p63 (Figure 2c), and CK5/6 (Figure 2d), whereas staining was negative for CK20, Villin, TTF-1, NapsinA, SALL4, Oct-3/4, CD30, Glypican-3, AFP, and CD117. The Ki67 proliferation index was approximately 40%.

Further chest and abdominal computed tomography (CT) examinations were recommended, which revealed a mass in the patient's left lung (Figure 3a) in addition to evidence of bony destruction in the left scapula and multiple vertebral bodies (Figure 3b). A biopsy of the lung mass was taken, and the histopathology confirmed it as squamous cell carcinoma.

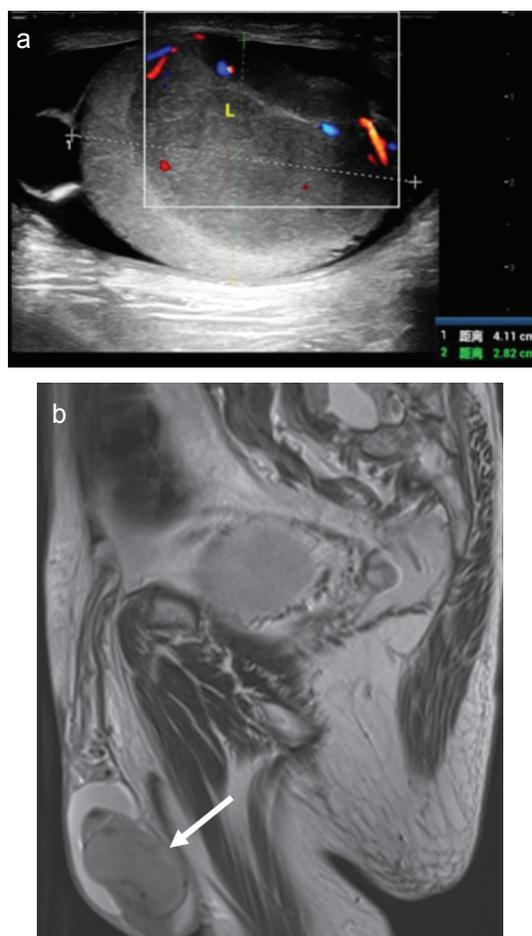


FIG. 1. Color Doppler ultrasonography (CDUS) and magnetic resonance imaging (MRI) findings. (a) CDUS examination of the left testis; (b) MRI sagittal T2-weighted image of the left testis.



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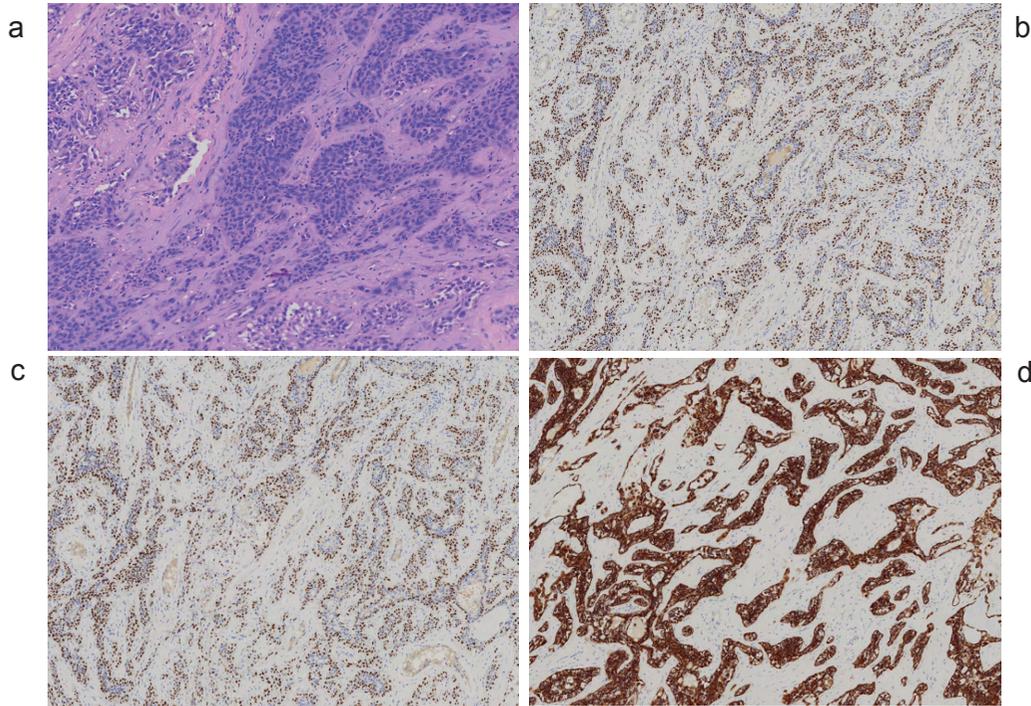


FIG. 2. Pathological findings of the biopsy specimen. **(a)** The lesion exhibited nests of squamous cell carcinoma characterized by enlarged nuclei, intense staining, and cellular atypia (hematoxylin and eosin staining x200); **(b)** p40, **(c)** p63, and **(d)** CK5/6 were positive (x100).

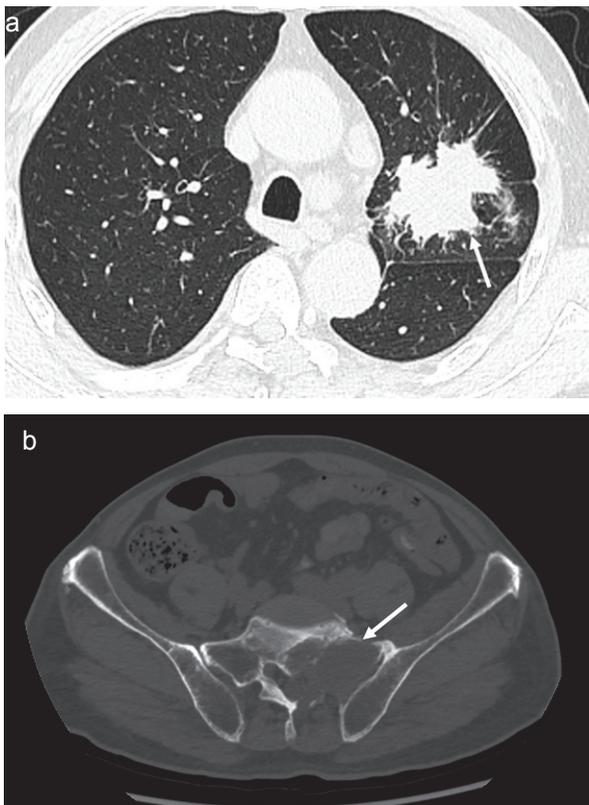


FIG. 3. Chest and abdominal computed tomography (CT) findings. **(a)** An irregular mass seen in the left lung; **(b)** bony destruction on the left side of the sacrum.

The immunohistochemical analysis showed positive staining for CK5/6, CK7, p63, and p40 and negative staining for TTF-1. The Ki67 proliferation index was approximately 20%. Accordingly, the left testicular mass was diagnosed as a metastatic lung squamous cell carcinoma. The patient is currently undergoing chemotherapy with tislelizumab (200 mg), paclitaxel micelle (390 mg), and carboplatin (0.5 g).

Metastatic testicular cancer is a rare phenomenon, comprising only 3.6% of all testicular tumors; over 90% of these germ-cell tumors originate from mature testicular epithelial cells. While prostate cancer is the most common primary malignant tumor that metastasizes to the testes, other cancers, such as gastrointestinal, renal, and bladder cancer, can also metastasize to the testes. In contrast, metastasis of non-small cell lung cancer is typically seen in the brain, bones, adrenal glands, and liver; only a few cases involving the testes have been reported so far.<sup>1,2,3</sup> There is uncertainty regarding the exact reason for the rarity of testicular metastasis, with some studies proposing hematogenous spread as the pathway for lung cancer metastasizing to the testes.<sup>1,4,5</sup> In our patient, we considered both the lymphatic and hematogenous routes for metastasis; however, no suspicious metastatic lymph nodes were observed in the vicinity of the aorta. Additionally, multiple osseous metastases sites on the left side, including the scapula, the adnexa of the fifth thoracic vertebra, the sacrum, and the ilium, were detected along with the left testicular metastasis suggesting a progressive top-to-bottom spread of metastases. Notably, osseous metastasis in lung cancer is a known complication of hematogenous spread, strongly supporting the plausibility of hematogenous metastasis in our patient. Orchitis, testicular

torsion, and testicular tuberculosis are the foremost differential diagnoses; however, in cases where anti-inflammatory treatment fails to alleviate testicular pain, a pathological examination of the testis supplemented with a comprehensive radiological whole-body examination is recommended to exclude the possibility of a primary or metastatic testicular neoplasm.

While testicular metastasis is rare in lung cancer, it should not be overlooked. In our patient, although both lymphatic and hematogenous routes were initially considered as possible pathways for metastasis, the presence of multiple osseous metastases strongly supported the possibility of hematogenous spread. This case report highlights the importance of conducting thorough diagnostic investigations for testicular pain and the need to suspect rare malignancies, such as squamous cell carcinoma, even when the initial diagnosis suggests inflammation or infection. Accurate diagnosis is crucial for appropriate management and treatment planning.

**Informed Consent:** Informed consent was obtained from the patient for the anonymous use and publication of clinical, imaging, and histologic data.

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**Conflict of Interest:** No conflict of interest was declared by the authors.

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