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A 58-Year-Old Man with a Painful Gluteal Mass as the First Presentation of Metastatic Adenocarcinoma of the Lung

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Male, 58-year-old
Final Diagnosis: Metastatic lung adenocarcinoma
Symptoms: Gluteal mass
Medication: —
Clinical Procedure: —
Specialty: Oncology • Pulmonology

Objective: Unusual clinical course

Background: Lung cancer is the second most common cancer, with the highest mortality rate. It frequently metastasizes to the nervous system, bone, adrenal gland, and liver. Rarely, it metastasizes to soft tissues, including cutaneous, subcutaneous, and skeletal muscles, with an overall prevalence rate of 2.3%. In most cases, soft-tissue metastases develop after an initial diagnosis of the primary internal malignancy and late in the disease course. In exceedingly rare cases, they may coincide with or occur before primary cancer has been detected. In our case, the initial manifestation of primary lung adenocarcinoma was a gluteal mass.

Case Report: We present the case of a 58-year-old man with no other medical comorbidities other than a 40-pack-year smoking history, who initially presented with a solitary painful right-buttock mass. Imaging revealed a solid right gluteal soft-tissue mass along with lumbar, lung, hepatic, bilateral renal, and adrenal lesions concerning for an underlying metastatic pathology. A gluteal mass biopsy showed poorly differentiated adenocarcinoma with immunohistochemistry (TTF-1+CK7+CD20–) favoring primary lung cancer.

Conclusions: Although it is an unusual and uncommon presenting entity of lung cancer, our case report accentuates how a simple solitary cutaneous palpable mass can be an alarming sign of a serious underlying occult malignancy. Moreover, our case report also highlights the diagnostic and prognostic value of immunohistochemistry characteristics of the tumor and how it can guide the clinician to identify the primary site, which, in this case, was adenocarcinoma of the lung.

Keywords: Immunohistochemistry • Lung Neoplasms • Smoking • Neoplasm Metastasis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/928122

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Background

Worldwide, approximately 1.8 million patients had lung cancer in 2012, with an estimated 1.6 million deaths [1]. Multiple environmental factors (eg, asbestos, radon, arsenic, nickel), lifestyle factors (eg, antioxidants, smoking, alcohol, phytoestrogens, cruciferous vegetables), radiation therapy, HIV, and pulmonary fibrosis are associated with the subsequent development of lung cancer. However, smoking remains the prime risk factor, accounting for approximately 90% of all lung cancers. A 40-pack-year smoking history increases lung cancer risk by 20-fold [1-3]. The clinical manifestations of lung cancer can be due to: (a) extra-thoracic metastases, (b) intrathoracic effects of the tumor (eg, cough, hemoptysis, pleural disease), or (c) paraneoplastic phenomena (eg, digital clubbing, hypercalcemia, hypercoagulability disorders, Cushing syndrome, various neurologic syndromes) [4-7]. However, unless already locally advanced or metastasized, most lung cancer patients remain clinically silent [8]. As our patient initially presented with no complaints other than a progressively worsening gluteal mass and was later found to have diffusely metastatic lung adenocarcinoma. Lung cancer frequently metastasizes to the liver, adrenal glands, brain, kidneys, and bone. However, in contrast to bony metastasis, soft-tissue (ST) metastasis is rare, with the reported overall prevalence of 2.3% among lung cancer patients [9]. Therefore, we emphasize that physicians must consider metastasis as a differential diagnosis, especially in high-risk patients presenting with new and rapidly growing subcutaneous lesions, as timely diagnosis can have profound implications for patient prognosis and therapeutic management.

Case Report

A 58-year-old man with a more than 40-pack-year of smoking history and no known medical comorbidities initially presented to the hospital for a painful right gluteal mass, growing for 1 month. It had become increasingly painful over this period and ultimately became unbearable 1 day before the presentation, limiting his regular activities, such as walking and sitting. He tried over-the-counter ibuprofen, without any relief. He reported chronic persistent dry cough, which he attributed to smoking, and denied any generalized constitutional symptoms, including hemoptysis, unintentional weight loss, night sweats, or chills. A review of systems was also significant for right upper-quadrant pain and lower back pain with bilateral lower-extremity paresthesia. Results of a physical exam were significant for a non-ulcerative and firm right inguinal lymphadenopathy and a right gluteal mass of approximately 10×5 cm, which was tender to palpation, discrete, firm, immobile, and non-erythematous (**Figure 1**). It started as a small, painless lump, which progressively worsened over 3-4 months. The patient was also found to have bilateral nail clubbing. Computed

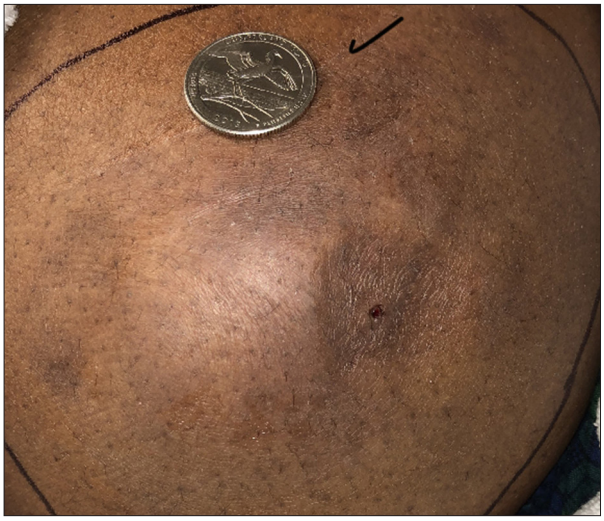

Figure 1. Photograph of the metastatic lesion on the right gluteal mass. A flesh-tone, discrete, firm, immobile, non-erythematous, and non-ulcerative nodule measuring 10×5 cm.

tomography (CT) of the abdomen and pelvis with contrast was done for further characterization, which showed a solid right gluteal soft-tissue mass, destructive lesion of L1, bilateral adrenal and renal masses, intra-hepatic lesions, and pelvic soft-tissue mass with slight ascites. Given the suspected metastatic disease, further imaging was done. A CT head was negative for any mass lesions, CT chest with contrast showed a poorly defined left upper-lobe mass measuring 10.3×7.9×9.3 cm with obstruction of left upper-lobe bronchus, and a small left pleural effusion (**Figures 2, 3**). Results of a tumor markers panel including alpha-fetoprotein (AFP), cancer antigen-19-9 (Ca 19-9), carcinoembryonic antigen (CEA), and prostate-specific antigen (PSA) were negative except for an elevated cancer antigen-125 (CA-125) of 176 u/mL. Antibiotics were started for possible pneumonia, and an ultrasound-guided biopsy of the gluteal mass was done. Pathology reported poorly differentiated adenocarcinoma with features of tumor favoring primary lung cancer given the positive immunohistochemistry for cytokeratin 7 (CK7), thyroid transcription factor 1 (TTF-1), and was negative for cytokeratin 20 (CK20), caudal type homeobox 2 (CDX2), CA19-9, napsin-A, and arginase-A antibodies (**Figures 4, 5**). The patient said he had undergone a recent screening colonoscopy, which was unremarkable for any pathology. However, he denied receiving any prior low-dose CT chest done for lung cancer screening. He was subsequently discharged with pulmonary and oncology outpatient follow-up for further management. However, the patient refused and opted for hospice care.

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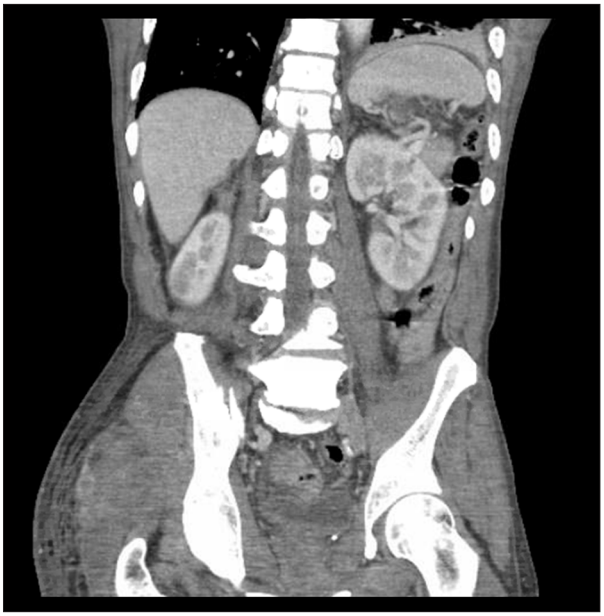

Figure 2. Coronal view computed tomography (CT) abdomen and pelvis with contrast showing right-buttock solid 6.7-cm mass with adjacent subcutaneous edema indenting the gluteus muscle and bilateral adrenal and renal masses.

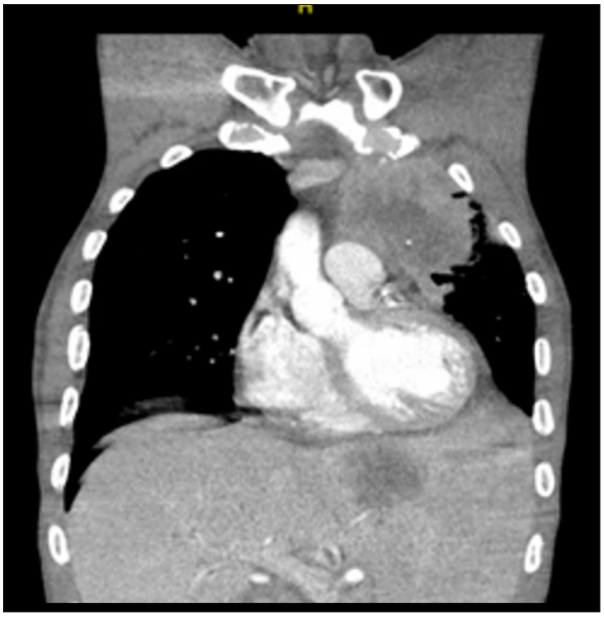

Figure 3. Coronal view CT chest showing 10.3×7.9×9.3 cm left upper-lobe poorly defined mass with central necrosis and calcification with the obstruction of the left upper-lobe bronchus, and a 6.3-cm left hepatic-lobe mass with peripheral nodular enhancement.

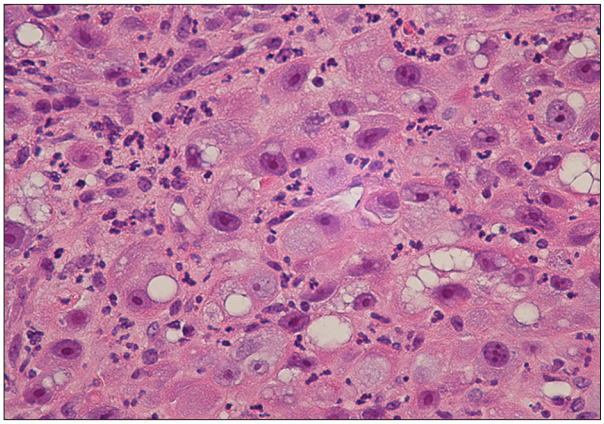

Figure 4. Gluteal mass biopsy showing a poorly differentiated tumor composed of large round-to-oval cells, arranged in sheets. The cells have abundant cytoplasm, round nuclei, and prominent nucleoli.

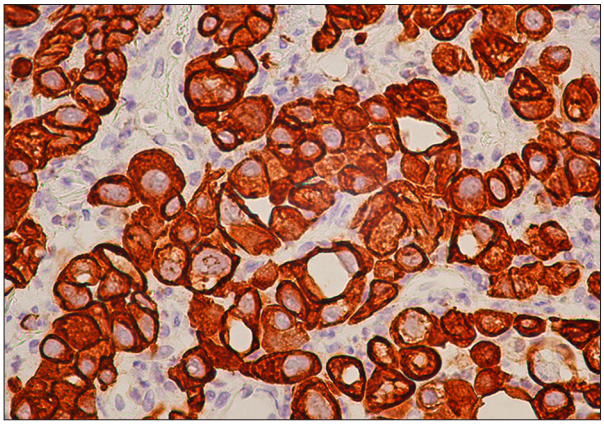

Figure 5. Gluteal mass biopsy (immunohistochemistry, magnification ×400) showing tumor cells are strongly immunoreactive to cytokeratin 7 (CK 7).

Discussion

Unless already locally advanced or metastasized, most lung cancer patients remain clinically silent. Around 70% of newly diagnosed lung cancer cases are already metastatic at the time of initial presentation [10]. Lung cancer frequently metastasizes to the liver, adrenal glands, brain, kidneys, and bone. However, in contrast to bony metastasis, soft-tissue (ST) metastasis, including cutaneous, subcutaneous, and skeletal muscle, are rare, with the reported overall prevalence of 2.3% among lung cancer patients [9]. In a retrospective analysis of 500 cancer patients, only 1.8% were found to have soft-tissue metastasis; 54% of those lesions were skeletal and 46% were subcutaneous [11].

The pathophysiology involves the lymphovascular, hematogenous, or direct extension of the primary tumor as a local or distant metastasis [12]. A painful palpable mass is the most

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common clinical manifestation of ST metastasis. Sometimes, it even presents with a painless, asymptomatic, and incidental lump. It warrants a high clinical suspicion of underlying malignancy and low threshold for biopsy in any patient presenting with a new soft-tissue lump, as missing such a diagnosis can be life-threatening and can become a serious professional liability.

The most common ST metastasis sites from primary lung cancer are the abdomen, chest, neck, and head. However, these lesions can appear anywhere. Zhu et al and Khaja et al (2019) found that patients who initially presented with progressively worsening discrete painless nose tip lesion and ulcerated wart-like hand lesion, respectively, had primary squamous cell carcinoma [13,14]. Generally, ST metastasis is the late presentation of the primary occult malignancies. According to a study done over 6 years, 10 out of 4385 lung cancer patients developed skin metastasis, with 16 months average time from diagnosis to discovery of cutaneous metastasis [15,16]. However, in exceedingly rare cases, these lesions present simultaneously with or even before lung cancer is diagnosed. According to retrospective studies done in 1990 and 2012, cutaneous metastases were the initial presentation in only 0.8% of 7316 cancer patients with internal malignancies and only in 2.8% of 2130 advanced non-small-cell lung cancer (NSCLC) patients, respectively [17,18].

There was no known primary cancer in our patient, and we had to rely on ancillary diagnostic tests, including a physical exam, tumor markers, and immunohistochemistry. Our patient was found to have bilateral digital cubing, which is the most common paraneoplastic manifestation of primary lung cancer. In 90% of digital clubbing cases, the etiology is underlying pulmonary malignancy, especially NSCLC. It has rarely been associated with extrapulmonary carcinomas [19]. Moreover, our patient had elevated CA-125 levels, which is known to be associated with ovarian adenocarcinoma. However, recent studies have shown its existence on the peritoneum and pleural ectodermal cells and its increased association with poor prognosis of lung cancer. Kimura et al showed elevated CA125 levels in 38% of lung cancer patients and 68% of those with advanced adenocarcinomas [20].

Histological and immunohistochemical analysis is another valuable tool to establish the primary origin. Lung origin can be proven with positive CK7, TTF-1, and napsin-A staining pattern [18,21]. TFF-1 is associated with regulating the expression of Clara cell secretory proteins and surfactant protein. Ye et al found that out of 120 primary lung adenocarcinoma cases, 79% had TFF-1+/napsin-A+ staining, 8% had TFF-1–/napsin-A+, and only 3% had TFF-1+/napsin-A–, suggesting that both TFF-1 and Napsin-A are highly sensitive and specific for detecting primary lung adenocarcinoma [22]. Another analysis, of 102 samples, showed that the CK7+/CK20– vs CK20+/CK7– pattern was able to identify lung vs colorectal adenocarcinoma, respectively, in 95% of cases. According to Yue et al, an antibody panel combining CK7, TTF-1, and CK20 has high sensitivity and specificity for differentiating primary lung adenocarcinomas from extrapulmonary adenocarcinomas of breast or colon origin. Analysis of 66 patients with lung adenocarcinoma showed that TTF-1 was expressed by 73% of primary lung adenocarcinomas, whereas all non-pulmonary adenocarcinomas lacked TTF-1 staining. None of the patients with extrapulmonary adenocarcinoma expressed TTF-1+CK7+CD20– panel [23,24]. Another study, done to evaluate the efficacy of immunohistochemical markers in subtyping poorly differentiated NSCLC, showed 100% of biopsies of pulmonary adenocarcinoma expressed CK7, and 80% were positive for TTF-1, whereas p63 was extremely sensitive for pulmonary SCC [25]. We were unable to obtain a lung biopsy because our patient refused further workup. Our patient's pertinent >40-pack-year smoking history, digital clubbing, and gluteal mass biopsy positive for TTF-1+CK7+CD20– panel are highly suggestive of primary pulmonary adenocarcinoma.

Prognosis, treatment, and therapeutic goals of primary lung cancer are determined by multiple factors, including (a) patient's age and functional status, (b) tumor staging, and (c) tumor grading based on histology and immunochemistry. Age <70, female sex, well-differentiated tumors, and TFF-1 expression are associated with good overall prognosis, whereas pretreatment weight loss, active smoking, poor differentiation, advanced staging, and ST metastasis suggest a poor prognosis. Surgical resection remains the mainstay curative treatment, especially for early-stage lung tumors. The therapeutic goal for locally advanced and metastatic cancer is to improve survival and reduce disease-related adverse events, and are mostly treated with chemotherapy with concurrent radiation [10,26,27].

Conclusions

Our patient presented merely with a solitary painful palpable mass and was later found to have diffusely metastatic and poorly differentiated adenocarcinoma. Even though ST metastasis is a rare and uncommon manifestation of underlying occult malignancies, our case report highlights the high clinical suspicion and low threshold for biopsy, especially in high-risk patients presenting with new soft-tissue lesions. These lesions can provide accessible biopsy sites and thus help avoid invasive procedures. Furthermore, a timely biopsy of the lesion can have help in establishing the diagnosis, prognosis, and therapeutic management. Our case report also highlights the diagnostic and prognostic value of immunohistochemistry characteristics of the tumor.

Conflict of Interest

None.

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