Psoas muscle metastases in non-small cell lung cancer

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ABSTRACT Lung cancer is the leading cause of cancer-related death in the U.S. and often spreads via lymphatics or through hematogenous metastasis to the brain, bone and adrenal glands. Isolated metastases to skeletal muscle, including the psoas muscles, are very uncommon. The present report is a case series of three patients with psoas metastases from non-small cell lung cancer (NSCLC) and a review of the relevant literature. Three patients presented with psoas muscle metastases from NSCLC detected on diagnostic imaging. All patients were treated with radiotherapy to the psoas muscle, and two patients were treated with curative intent on an oligometastatic paradigm. Radiotherapy to the psoas muscle was effective and well tolerated.

KEY WORDS Psoas muscle; metastases; lung; carcinoma

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Introduction

Lung cancer ranks as the second most common malignancy in the United States and the number one cause of cancer-related death. In 2007 alone, an estimated 213,000 cases of lung cancer were diagnosed (1). Although significant advances in multimodality therapies have been made, the majority of patients will ultimately develop distant metastases. The patterns of distant failure in lung cancer have been well characterized, with metastases tending to appear in the brain, bone, adrenal glands, liver, contralateral lung and regional lymph nodes (2). By contrast, isolated direct hematogenous metastases to skeletal muscle are rare. Despite the high incidence of lung cancer, there are relatively few reports describing hematogenous metastases to skeletal muscle. In the present report, three cases of non-small cell lung cancer (NSCLC) metastatic to the psoas muscle are described and their treatment and outcomes detailed. Two of the cases represent isolated metastases and one case represents the sole site of skeletal muscle metastasis in the presence of bony metastases. The clinical significance of this finding is discussed in the context of the established literature.

Case reports

Case 1

A 75 year-old man presented with atypical chest pain. During the workup of the pain, a CT scan of the chest showed a left upper lobe mass, and an FNA confirmed NSCLC with squamous differentiation. Further workup yielded a diagnosis of stage IIIA disease, and he was referred for concurrent chemoradiotherapy. PET/CT fusion for treatment planning revealed a single focus of elevated FDG uptake in the left psoas muscle, consistent with metastatic disease (Figure 1). The psoas lesion was asymptomatic. After completion of definitive therapy to the chest, he was treated with radiotherapy (RT) to the left psoas mass to 50 Gy in 20 fractions (Figure 2). Despite aggressive multimodality therapy, he died of progressive metastatic disease nine months after completion of RT. The psoas metastasis remained asymptomatic for the duration of his life.

Case 2

A 66 year-old woman presented with right flank pain. A CT of the chest and abdomen revealed a right lower lobe lung mass and mediastinal lymphadenopathy. Transbronchial biopsy of the

No potential conflict of interest.

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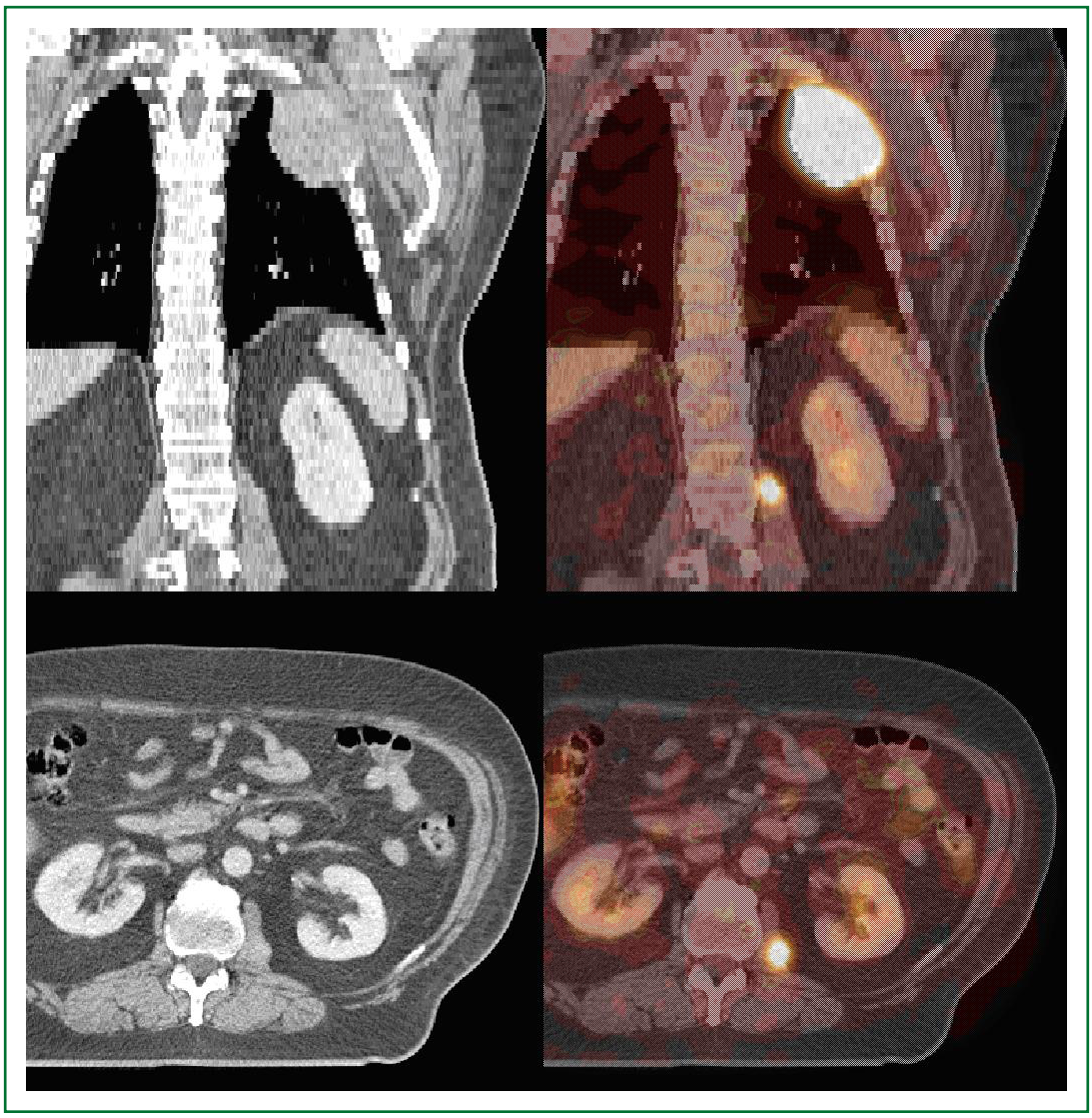

Figure 1. CT images in coronal (upper left) and axial (lower left) cuts paired with PET/CT fused images in coronal (upper right) and axial (lower right) cuts. Both the thoracic primary and the left psoas metastasis can be clearly identified in the PET/CT fusion.

mediastinal nodes showed squamous cell carcinoma. A PET/CT scan identified increased FDG uptake in the right lung mass, mediastinum and right psoas muscle. The patient was treated with curative intent for oligometastatic NSCLC. She received definitive chemoradiotherapy to the chest to 60 Gy with carboplatin and taxol. The right psoas muscle was treated concurrently to 46 Gy in 23 fractions. She is alive with metastatic disease as of eight months after completion of RT and has no symptoms related to the psoas metastasis.

Case 3

A 34 year-old woman presented with palpitations. Although a cardiac workup was unremarkable, a CT scan of the chest revealed a right upper lobe mass and pericardial effusion. A biopsy of the lung lesion provided a diagnosis of adenocarcinoma of the lung. On further staging, multiple foci of bony metastatic disease were detected. She received palliative chest RT and multiple systemic therapy regimens, but later presented with lower back pain recalcitrant to opiate analgesics. A CT scan showed two vertebral body lesions in the lower thoracic and upper lumbar spine and a mass in the left psoas muscle. The psoas mass was confirmed on PET (Figure 3). She was treated with RT to these sites to 40 Gy in 20 fractions while continuing Tarceva. At three week follow-up, her lower back pain had completely resolved. She died of progressive metastatic disease 15 months after completion of psoas RT. She remained asymptomatic in the sites of irradiation for the duration of her life.

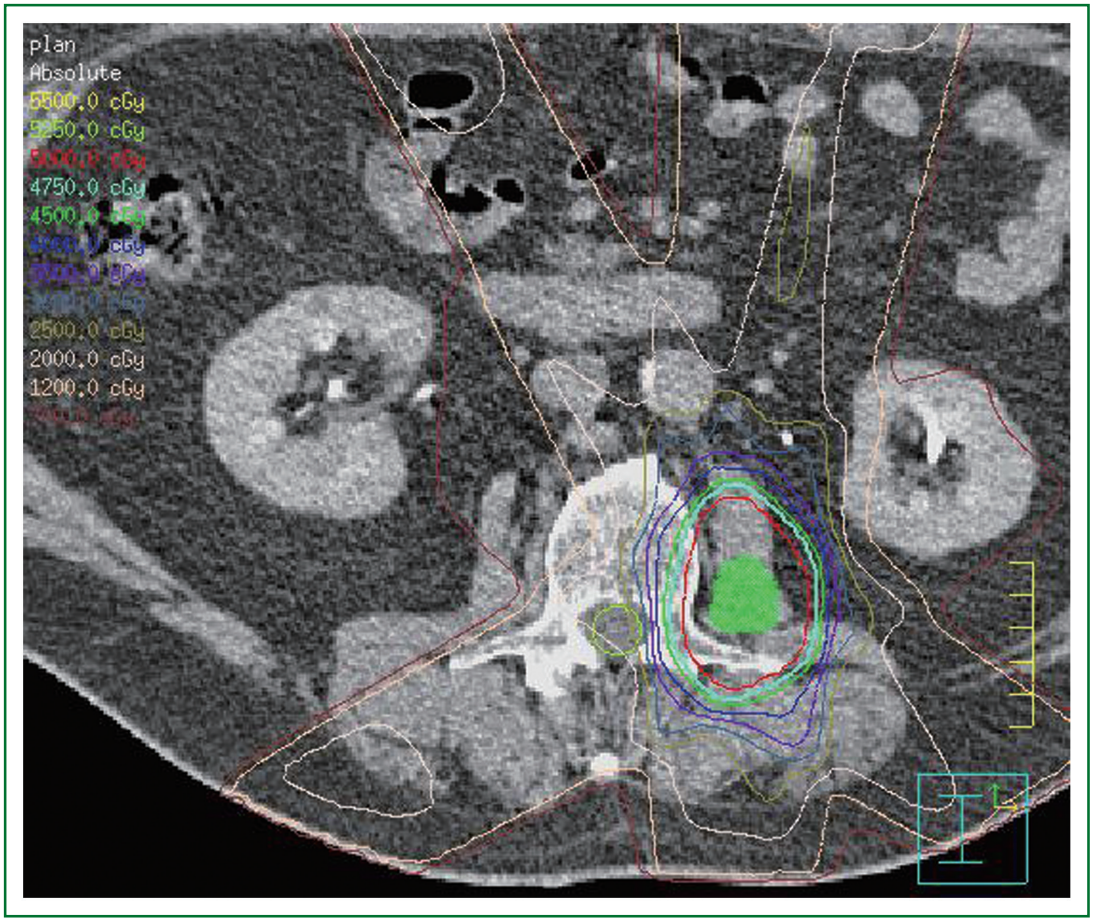

Figure 2. An axial section of the treatment planning CT scan. The green colorwash represents the gross tumor. Radiation isodose lines are described in the key in the upper left.

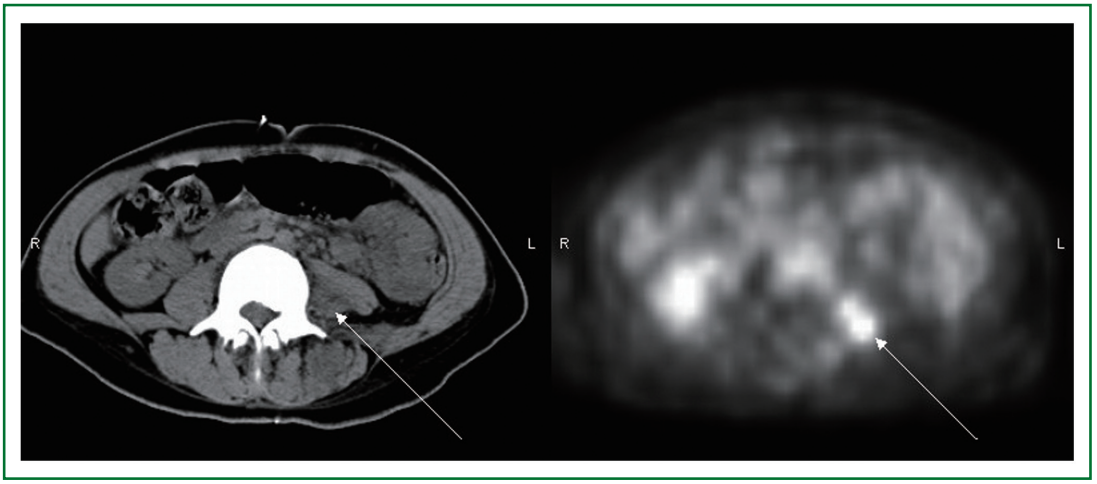

Figure 3. An axial section of a CT scan (left) and a paired axial section of a PET scan (right). The white arrow points to the site of metastatic disease in the left psoas muscle.

Discussion

This case series presents three patients with NSCLC metastatic to the psoas muscle. In two patients, the histology was squamous carcinoma, and one case was an adenocarcinoma. Each patient was treated with RT to the involved area, in addition to systemic chemotherapy. Two patients had isolated psoas metastases and were treated with curative intent for oligometastatic

Table 1. Published series of clinically detected psoas metastases from lung cancer.

Study	# Cases of psoas lesions	# Cases of malignancy	# Cases of lung malignancy
Ampil *et al.* (5)	7	7	1
Nash *et al.* (6)	1	1	1
Damron *et al.* (7)	1	1	1
Sudo *et al.* (8)	1	1	1
Kenny *et al.* (9)	25	2	1

disease; one patient has a single psoas metastasis in addition to bony metastases and was treated palliatively. Ultimately, all three patients developed widespread metastases and two have succumbed to their disease, a finding reflecting the poor prognosis associated with oligometastatic NSCLC and a locally advanced primary (3). However, with follow-up ranging from 8 to 15 months after psoas irradiation, all three patients tolerated treatment well and remained entirely asymptomatic with respect to the psoas lesions.

Case reports of the metastatic spread of cancer to the psoas muscle, though rare, date back over a century, including one case from a pancreas primary published by Flexner in 1894 (4). There are only a few cases in the literature reporting direct hematogenous metastasis of lung cancer to the psoas muscle. Ampil *et al.* describe seven cases of metastatic tumors involving the psoas muscle, including one from a lung primary (5). In two patients, RT to the psoas metastasis provided effective palliation of pain. Nash *et al.* reported on a single case of a biopsy proven psoas metastasis from an adenocarcinoma of the lung (6). Damron *et al.* presented 30 cases of cancer metastatic to soft tissue; this series included one patient with small cell lung cancer metastatic to the psoas muscle (7). Sudo *et al.* described a case of adenocarcinoma of the lung metastatic to the psoas muscle in a patient presenting with pain on hip extension (8). Kenny *et al.* described 25 cases of psoas muscle invasion by malignancy including one adenocarcinoma of a lung primary (9). Of these cases only two represented hematogenous metastasis. Lenchik *et al.* reported on 44 cases of CT identified psoas abnormalities of which 15 were malignancies, two from a primary lung cancer (10). These published series are summarized in Table 1.

Published reports on the use of CT or MRI also suggest that anatomic imaging cannot accurately identify psoas muscle pathology (10,11,12). Cases of metastatic disease masquerading as benign processes such as psoas abscesses have been reported (13,14). While it is possible that these findings could be explained by benign processes or synchronous primary malignancies, this possibility is remote. The three psoas lesions described in this series are unlikely to represent any other disease process except hematogenous metastatis of lung cancer. This contention is supported by several findings: the absence of preceding trauma, the absence of the stigmata of infection, the appearance of psoas masses on CT scans (in two patients), correlated hypermetabolic activity on FDG-PET (in three patients), the resolution of these radiographic findings after RT, and the clinical setting of advanced NSCLC. Given the expense and possible morbidity of surgical biopsy balanced against the high likelihood that these lesions represented metastatic NSCLC, the risks of pathologic confirmation were not deemed to be justified.

Based on the relative paucity of published reports, it appears that very few psoas metastases become radiographically apparent or clinically symptomatic. By contrast, autopsy studies suggest that metastatic infiltration of the psoas muscles is far more common. In one Spanish study, 194 patients with known malignancy underwent postmortem examination (15). At autopsy, 50 were found to have involvement of skeletal muscle with cancer, 16 by direct extension, 34 by metastastic spread. The muscle groups most often involved were the diaphragm (23 patients) and the iliopsoas (10 patients), although this distribution may, in part, represent a sampling bias since these muscle groups were sectioned more often than others. Adenocarcinoma appeared to metastasize to skeletal muscle more frequently than other cancer histologies. Another study of patients with a diagnosis of malignancy found metastases in skeletal muscle in six out of 38 autopsies (16). In four of these cases, cancer was found in the iliopsoas muscles.

It is not known how to reconcile the discrepancy between the rarity of clinically apparent psoas metastases and the high incidence of detection on autopsy, however, the "seed and soil" hypothesis may provide some insight. Paget postulated that the formation of metastases depends on the interaction of specially adapted tumor cells (seeds) and a permissive organ milieu (soil) (17). In more recent formulations of this theory, tumor cells must accumulate specific genetic mutations endowing them with the metastatic phenotype. Once tumor cells acquire the ability to intravasate into the vasculature, they disseminate hematogenously and enter the parenchyma of target organs. Tumor cells then face diverse cellular microenvironments that range from permissive to hostile. Only those cells that are well suited to overcoming obstacles to growth, and find themselves in a suitable milieu, will develop into metastases. Tumor cells in less permissive environments may die or grow in a more indolent fashion (18). It is this set of complex interactions between tumor cells and distant organs that underlies disease specific patterns of distant failure.

The "seed and soil" hypothesis has two important implications for the observations in the present study. First, it explains the finding, universal to all malignant processes, that distant metastases tend to be unevenly distributed throughout the body (19). In the case of lung cancer, clinically evident psoas metastases are extremely rare because the cellular environment of skeletal muscle is less hospitable than other organs. Thus, the interactions between tumor cells and target tissues lead to the preferential development of metastatic disease in more permissive tissue such as the brain, bone and adrenal glands. Second, the "seed and soil" hypothesis may account for the seemingly contradictory observations that metastases to the psoas muscle are rarely identified clinically but are commonly found on autopsy. Due to the resistance of skeletal muscle to tumor implantation, psoas metastases may progress more slowly than tumor deposits elsewhere in the body or present later in the course of disease. The advent of PET imaging may reveal psoas metastases that would have otherwise gone undetected. If true, then the frequency of the detection of psoas metastases in NSCLC may increase in the future.

In the cases presented above, RT was used to treat all psoas metastases. This decision hinged on the poor prognosis associated with skeletal metastasis in lung cancer as well as the morbidity of surgical resection of psoas lesions.

Conclusions

To our knowledge, the current report is the largest case series of clinically detected psoas metastases from NSCLC. On autopsy, metastastic infiltration of the psoas muscles by NSCLC is common, but clinically evident psoas metastases are quite rare. In the future, psoas metastases may be diagnosed with greater frequency due to improved imaging technology. As patients with metastatic disease live longer, slowly growing masses in skeletal muscle may have a greater likelihood of becoming clinically relevant. This series supports the notion that the presence of a psoas metastasis augurs a poor prognosis, discouraging the use of an aggressive local therapy associated with significant toxicity. The patients treated in this series received RT without apparent toxicity and without developing symptoms from the psoas metastases.

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