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# TUMOUR-TO-TUMOUR METASTASIS: A RARE CASE OF PROSTATE CANCER METASTASISING TO PRIMARY LUNG ADENOCARCINOMA

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## ABSTRACT

Tumour-to-tumour metastasis (TTM) is a rare phenomenon that clinicians should be aware of when evaluating patients with a history of prostate cancer. We present the diagnosis and management of an 80-year-old former smoker with high-risk prostate cancer, who developed a lung nodule consistent with TTM. The patient had concurrent primary lung adenocarcinoma and metastatic prostate cancer, making this a unique case of dual primary and metastatic malignancies. The complexity of this case highlights the need for comprehensive evaluation and interdisciplinary management in patients with multiple malignancies. The literature review reveals that these are extremely rare occurrences, with most cases involving metastasis to the second primary tumour. Despite the challenges in diagnosing preoperatively, it is important to consider TTM as a possibility in patients with prostate cancer who present with a lung nodule. This report presents one of the few documented cases of TTM. It also reviews relevant cases in the literature and discusses the current situation in relation to established criteria for classifying combination tumours.

## KEYWORDS

Prostate cancer, lung adenocarcinoma, tumour-to-tumour metastasis, case report

## LEARNING POINTS

- Isolated lung metastasis with prostate cancer is exceptionally rare in the literature.
- Tumour-to-tumour metastasis cases present challenges in sampling and interpreting histopathology.
- In instances of tumour-to-tumour metastasis, it is vital to consider the patient's clinical history, perform thorough gross examination and obtain appropriate samples to distinguish between the separate tumour components.

## INTRODUCTION

Tumour-to-tumour metastasis (TTM) is an infrequent medical phenomenon where one tumour infiltrates the tissue of another. This occurrence shows an incidence of 0.2%–3.5% as reported in autopsy series[1,2]. Identifying TTM can be pathologically challenging especially if cells' architecture

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is similar. On literature review, a few cases of TTM are reported; for instance, breast cancer metastasising to myxoid liposarcoma, prostate cancer to soft tissue sarcoma and renal cell carcinoma to synchronous contralateral renal cell carcinoma[3-5]. However, while metachronous prostate cancer and lung cancer is not uncommon, associated TTM is rarely published[6]. We present a unique case of prostate cancer metastasising to malignant primary lung lesion.

## CASE DESCRIPTION

This is a case of an 80-year-old African American male with a medical history of prostate cancer, chronic kidney disease, atrial fibrillation and osteopenia.

His prostate cancer was initially non-metastatic castrate-sensitive prostate cancer treated with radical retropubic prostatectomy followed by adjuvant radiotherapy for positive margins. He presented again after 7 years of remission with biochemical recurrence; his prostate specific antigen (PSA) had risen to 1.56 and the workup for metastasis was negative. He was then started on bicalutamide (androgen signalling inhibitors) and leuprolide (gonadotropin-releasing hormone (GnRH) agonist), and his PSA went down to 0.09. Two years later, the PSA trended up to 1.67, making it a castrate-resistant prostate cancer. A positron emission tomography-computed tomography scan (PET CT) scan with piflufolastat F18 to look for metastasis was negative; however, the computed tomography (CT) scan showed a 1.7 x 1.7 cm non-tracer avid.

Bicalutamide was stopped and a novel hormonal therapy – a competitive androgen receptor inhibitor, darolutamide – was started, and PSA subsequently went down to 0.09.

On a follow-up a year later a F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET CT) scan showed a now suspicious metabolically right-middle lobe nodule measuring 2.2 x 2.3 cm. A decision was made to perform a biopsy on this lesion. The biopsy showed two different types of neoplasms: an invasive lung adenocarcinoma and metastatic prostate adenocarcinoma, representing an unusual metasynchronous primary lung adenocarcinoma and metastatic prostate cancer within the lung *(Fig. 1-4)*.

The case was discussed in a multidisciplinary meeting with cardiothoracic surgery; subsequently, the patient underwent a robotic right-middle lobectomy, right lower lobe wedge resection and lymphadenectomy. Pathology confirmed the previous findings and showed the following: grossly two foci of tumour (3 cm and 2 mm) invasive lung adenocarcinoma with papillary and acinar patterns moderately differentiated with close margins <0.1 cm to visceral pleura (TTF1+, Napsin A+, P40-, P63-) and metastatic prostate adenocarcinoma (NKX3.1+, PSAP+, PSMA+, TTF1−, Napsin A−). A total of 16 lymph nodes were examined; one lymph node was positive for metastatic prostate adenocarcinoma and the rest were negative. The patient was assessed at stage IA pT1cpN0M0 for lung adenocarcinoma and the prostate is now a metastatic castrate-resistant prostate cancer.

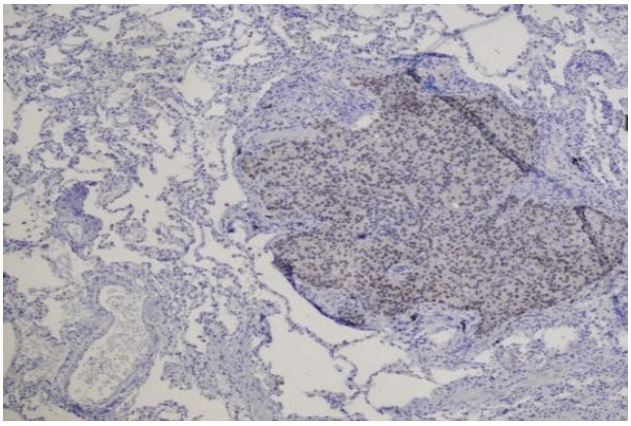

*Figure 1. IHC prostate adenocarcinoma.*

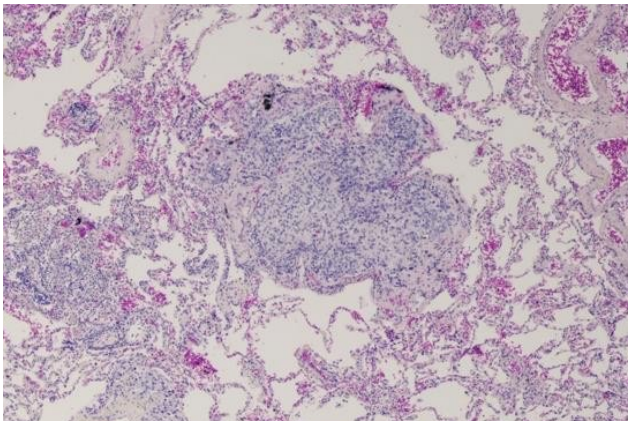

*Figure 2. Metastatic prostatic adenocarcinoma.*

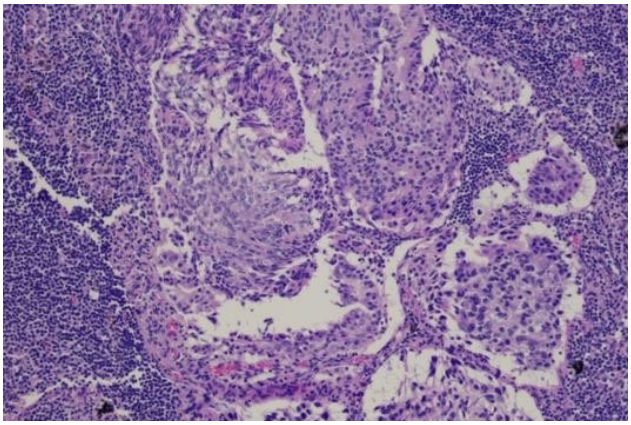

*Figure 3. IHC lung adenocarcinoma.*

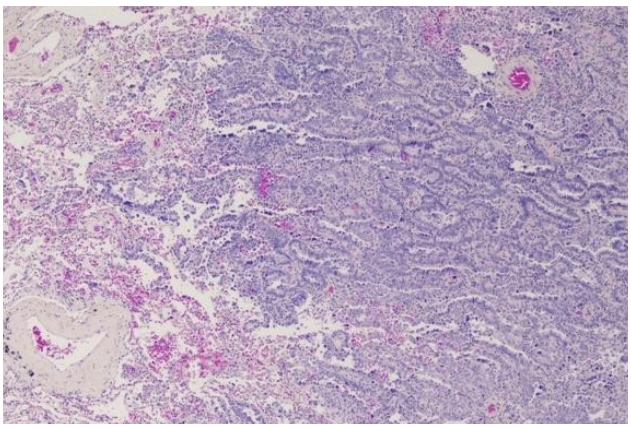

*Figure 4. Lung invasive adenocarcinoma (TTF1+, Napsin A+, P40-,P63-).*

Next-generation sequencing (NGS) was done on peripheral blood and showed low tumour burden 1 Muts/Mb ctDNA tumour fraction low at <1% and MSI high not detected. Tumour profiling results showed NBN p495fs*34 variant (49.5%), TP53 C141Y (0.2%) and DNMT3A S837* (19.9%). NGS was not performed on the tissue sample from the lymph node because the prostate cancer cells are too few and too admixed with the lung cancer to be able to get any meaningful results from the lung or concurrent lymph node specimen.

## DISCUSSION

Prostate cancer is the most prevalent malignancy in men with incidence of 112 per 100,000 males. It has a predilection to metastasise to lymph nodes, bones and lungs. Typically, pulmonary metastases from prostate cancer manifest after bone and lymph node involvement. However, there have been isolated cases where lung involvement was the initial sign of metastasis. Isolated lung metastases without concurrent bone or lymph node involvement develops in 5 to 27%[7,8].

The coexistence of primary lung adenocarcinoma and metastatic prostate cancer within the lung is also uncommon. Immunohistochemical staining for tumour markers is an essential distinguishing feature between primary lung and metastatic prostate adenocarcinoma as presented in the above case[9].

TTM is a rare occurrence in the medical field. Campbell et al. have established specific criteria for diagnosing this phenomenon[2]. These criteria include the presence of multiple primary tumours, the recipient tumour being a genuine benign or malignant growth, confirmed metastatic development within the recipient tumour and the exclusion of tumours that have spread to the lymphatic system. Essentially, TTM refers to the situation where one primary malignancy (donor tumour) spreads to another distinct primary tumour (recipient tumour). This phenomenon has been observed in various cancers, with lung adenocarcinoma being a common donor tumour followed by breast, gastrointestinal, prostate and thyroid carcinomas. For instance, lung adenocarcinoma has been found to metastasise to vestibular schwannoma, emphasising the importance of 18F-fluorodeoxyglucose positron emission tomography (PET) in identifying rapidly growing cerebellopontine angle tumours in patients with a history of cancer[10]. Furthermore, there have been reports of lung adenocarcinoma metastasising into a renal angiomyolipoma, highlighting the need for morphological and immunohistochemical investigations to differentiate between primary and secondary tumour origins[11]. Different tumour types have varying tendencies to spread to other parts of the body, and their ability to serve as hosts for secondary tumour deposits also varies. For example, clear cell renal cell carcinoma is often the most common recipient of metastases, followed by sarcomas, meningiomas and thyroid cancers, which also serve as hosts for metastatic involvement.

Collision tumours occur when two different types of cancer grow in the same location without any mixing of their histological features. While cases of collision tumours involving primary lung adenocarcinoma and metastatic prostate cancer in the lung are not frequently reported, understanding this concept is important in recognising the potential for multiple unrelated cancer processes to affect the same organ or tissue site. Mixed tumours are characterised by the presence of two or more distinct cellular populations that originate from the same neoplastic clone but exhibit different morphological and histological characteristics. While mixed tumours are commonly discussed in the context of salivary gland tumours, the concept can also provide insights into the complex histopathological dynamics seen in cases with concurrent primary and metastatic malignancies.

The 'seed and soil' theory suggests that specific tumour cells (referred to as 'seeds') have a preference for the environment of particular organs (known as 'soil'), which can facilitate the spread of cancer. In our case, it is possible that the lung provides a suitable environment for prostate cancer cells to metastasise and grow alongside a primary lung adenocarcinoma. This theory helps to explain the rare occurrence of TTM, where metastatic prostate cancer cells find a hospitable environment within the lung adenocarcinoma tissue. This metastatic process involves a selective mechanism that allows only cells capable of successful invasion, embolisation, circulation, arrest within capillary beds, penetration of host cells and proliferation within the organ parenchyma[12].

The interaction between tumour cells and their microenvironment, known as the tumour-microenvironment interaction, plays a significant role in tumour growth and metastasis. Factors such as immune response, stromal support and angiogenesis in the lung may create a niche that supports the coexistence and growth of both primary lung adenocarcinoma and metastatic prostate cancer cells. It is important to note that the microenvironment of different organs is unique, and the ability of metastatic cells to survive within the host is influenced by various factors such as the surrounding microenvironment, the presence of growth factors and the presence of cell surface receptors that promote the spread of metastases[12]. Therefore, therapeutic approaches should not only target the primary tumour cells, but also consider the factors that affect cell growth, survival, blood vessel formation and invasion. Genetic and molecular factors play a crucial role in determining the specific sites where tumour metastasis occurs, as recent research suggests. For example, changes in certain genes can increase the likelihood of prostate cancer cells spreading to the lungs, even before the more common spread to the bones and lymph nodes occurs.

## CONCLUSION

The concurrent diagnosis of primary lung adenocarcinoma and metastatic prostate cancer in the lung is a complex interaction of neoplastic processes, including TTM,

collision tumours and mixed tumours. Although rare, these phenomena have significant implications for diagnosis, treatment and prognosis. The simultaneous diagnosis of primary lung adenocarcinoma and metastatic prostate cancer in the lung prompts a discussion about the underlying mechanisms of such rare occurrences. In these cases, it is crucial to have a detailed clinical history, conduct careful gross examination and perform accurate sampling to identify the individual tumour components. This literature review emphasises the importance of awareness and understanding of these rare oncological events, which can lead to improved diagnostic accuracy and inform therapeutic strategies.

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