The role of resection of pulmonary metastases from prostate cancer: a case report and literature review

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Abstract

We report a case of a 53-year-old man who presented with two nodules in the lower lobe and one nodule in the upper lobe of the right lung almost 7 years after radical prostatectomy for pT3aN0M0, Gleason 4+5 disease, without evidence of osseous or lymphatic spread. Surgical resection of the lower lung nodules confirmed metastases, but prostate-specific antigen did not drop to undetectable levels. Isolated pulmonary metastases from prostate cancer are rare with only 33 previously described cases in the English-language literature, 18 of which were solitary metastases. We review the principles of management, including metastasectomy and long-term prognosis.

Case report

A 53-year-old man with a positive family history of prostate cancer presented with clinical stage T2NXM0 prostate cancer, a prostate-specific antigen (PSA) of 14.7 ng/mL and Gleason 3+4 adenocarcinoma in 6 of 8 cores. In 2002, he was treated with 6 months of neoadjuvant hormone withdrawal followed by an open radical prostatectomy and bilateral pelvic node dissection. The pathology specimen demonstrated bilateral disease, Gleason Score 4+5 (Fig. 1), one focus of extraprostatic extension, negative surgical margins and negative pelvic lymph nodes (pT3aN0M0). Postoperatively, his PSA level decreased to an undetectable level.

In January 2004, his PSA was 0.08 ng/mL, but remained stable for 4 years. In July 2008, however, the PSA rose to 0.21 ng/mL and he was treated with 64 Gy of salvage radiation therapy in 33 fractions. Post-radiation, his PSA decreased to a nadir of 0.19 ng/mL.

In 2009 (6 years, 10 months postoperatively), a chest computed tomography (CT) demonstrated a solitary pulmonary nodule (6 mm) in the upper lobe of the right lung and 2 further nodules (5 mm and 1 cm) in the right lower lobe (Fig. 2). Percutaneous biopsy of the largest lower pole nodule suggested metastatic prostate cancer (Fig. 3), and since there was no evidence of metastatic disease in the remaining workup, the patient elected to undergo a right lower lobe wedge resection, with planned observation of the upper pole. Post-resection PSA was 0.41 ng/mL 2 weeks postoperatively, 0.28 ng/mL at 5 months, 0.30 ng/mL at 9 months and 0.34 ng/mL at 1 year. Repeated surveillance chest CT at 6-month intervals demonstrated a stable 6-mm nodule in the right upper lobe.

Literature review

Solitary or multiple pulmonary metastases from prostate cancer, in the absence of gross osseous or lymphatic involvement, is an unusual presentation and begs the question of metastasectomy. We searched English-language MEDLINE for cases (Table 1). In a series of 1290 patients with metastatic prostate cancer, Fabozzi and colleagues found radiologic evidence of pulmonary metastases in 48, with 11 (0.86%) being a solitary pulmonary nodule.[1] Our literature review found a total of 18 cases of solitary metastatic prostate cancer to lung and 15 cases of multiple metastases without osseous or lymphatic involvement.

A. Solitary metastasis

Surgical excision of a solitary metastasis contributed to a complete response in only 4 cases. Smith and colleagues report the case of a 70-year-old male whose radical prostatectomy specimen was pT2N0M0, Gleason 4+5=9 with negative margins.[2] The patient's postoperative PSA was initially undetectable, but at 2 years it rose to 2.1 ng/mL. Bone scan, magnetic resonance imaging skeletal survey and abdominal and pelvic CT were negative, but a chest x-ray and subsequent chest CT scan showed a 2-cm solitary nodule in the right lower lobe of the lung. Surgical excision

Table 1. Reports of isolated solitary pulmonary metastases from prostate cancer†

Authors	Age, yr	Initial tumour characteristic	Initial treatment	Metastatic characteristic	Metastatic treatment	Outcome
Smith et al.	70	pT2N0M0, Gleason 4+5	RP	2 cm right lower lobe nodule, rising PSA	Surgical resection	PSA ↓ to undetectable
Chao et al.	69	cT2aN0, Gleason 4+3, PSA 6.7 ng/mL	RP	1.2 cm pulmonary nodule	Wedge resection	12 years disease-free follow-up
Pruthi et al.	72	pT2bN0M0, Gleason 3+3, PSA 4.1 ng/mL	RP, salvage RT	2 cm left lower lobe lung mass	LHRH agonist without success then surgical resection	PSA ↓ to undetectable levels for 3 years of follow-up
Khandani et al.	78	Unknown	RT	Left lower lobe lung mass	Surgical resection, mediastinal LND	PSA ↓ to a nadir of 0.2 ng/mL
Hofland and Bagg	49	pT2cN0M0, Gleason 4+5, PSA 1.4 ng/mL	RP, LND, pelvic radiation, total androgen deprivation, bilateral orchiectomy	Left lower lobe lung nodule, rising PSA	Surgical resection – lobectomy	Development of further metastases and lost to follow-up
Boyer and Boyer	65	pT2, Gleason 3+3, PSA 3.0 ng/mL	RP	2.8 cm left upper lobe lung nodule, rising PSA	Surgical resection followed by leuprolide	PSA ↓ to nadir of 0.07 ng/mL
Rockey and Graham	83	Unknown	RT	Left lower lobe nodule	Surgical biopsy followed by bilateral orchiectomy	No follow-up available
Varkarakis et al.	1 case: no information available					
Fabozzi et al.	11 cases: no information available					

RP: radical prostatectomy; RT: radiation therapy; LND: lymph node dissection; PSA: prostate-specific antigen; LHRH: luteinizing hormone-releasing hormone.

of the mass, accompanied by regional lymphadenectomy, resulted in a return to undetectable PSA levels. Chao and colleagues report a 69-year-old patient with a single 1.2-cm pulmonary nodule that was successfully treated with resection followed by 12 years of remission without further adjuvant therapy.[3] Pruthi and colleagues describe the case of a 72-year-old male who presented 6 years post-radical prostatectomy and salvage radiation therapy, with a climbing PSA and a biopsy proven 2-cm right lower lobe pulmonary metastasis.[4] The patient had a transient response to hormonal therapy, but metastasectomy resulted in the PSA falling to undetectable levels for more than 3 years of follow-up. In a fourth case report, a 78-year-old with a history of prostate cancer, treated with radiation therapy 15 years prior, presented with a rising PSA, chest pain and hemoptysis.[5] A positron emission tomography-CT scan showed uptake in a lung mass and no other foci of increased uptake. Surgical resection of the lung mass with mediastinal lymph nodes confirmed metastatic prostate cancer with a single, positive subcarinal lymph node. Postoperatively, the PSA decreased to, and remained at, a nadir of 0.2 ng/mL.

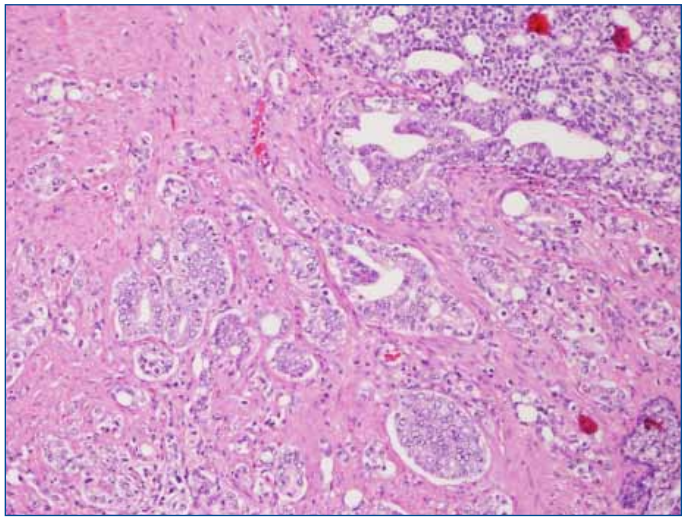

Fig. 1. Representative section from the original prostatectomy specimen showing high-grade infiltrating prostatic adenocarcinoma and intraductal carcinoma (overall Gleason score 4+5). Hematoxylin and eosin, original magnification 100×.

In other case reports of solitary pulmonary metastasis, surgical excision with or without androgen withdrawal, resulted in partial[6] or no[7] response, and one case of an 83-year-old treated successfully with lung biopsy and bilateral orchiectomy.[8]

B. Multiple metastases

In other reports, multiple pulmonary metastases are present in the absence of other bone, lymphatic or visceral lesions.

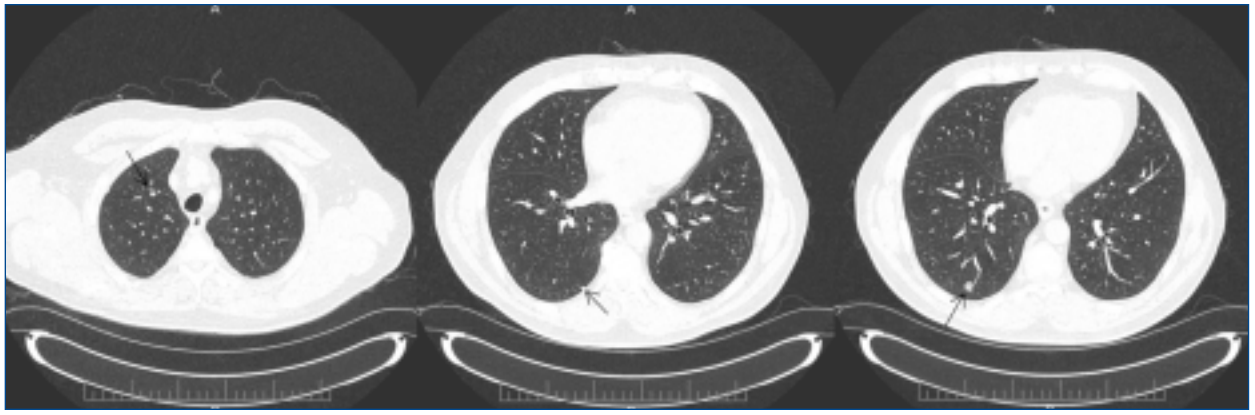

Fig. 2. Chest computed tomography. Left panel demonstrates a 6-mm nodule in the upper lobe of the right lung. Middle and right panels demonstrate a 5-mm and 1-cm nodule in right lower lobe, respectively.

There are two radiological patterns of pulmonary metastases: multinodular (likely due to hematologic spread),[9-11] and a diffuse interstitial pattern[1,10,13-21] representative of lymphatic spread. Other isolated intrathoracic manifestations of metastatic prostate cancer include endobronchial metastasis[22] and malignant pleural effusions.[23-25] Treatment of both low burden (2 nodules) and more disseminated pulmonary metastases with metastasectomy and hormonal therapy was successful in 3 case reports.[9,10,13] Hormone therapy alone has been used successfully for some cases of multiple isolated pulmonary metastases.[14-21]

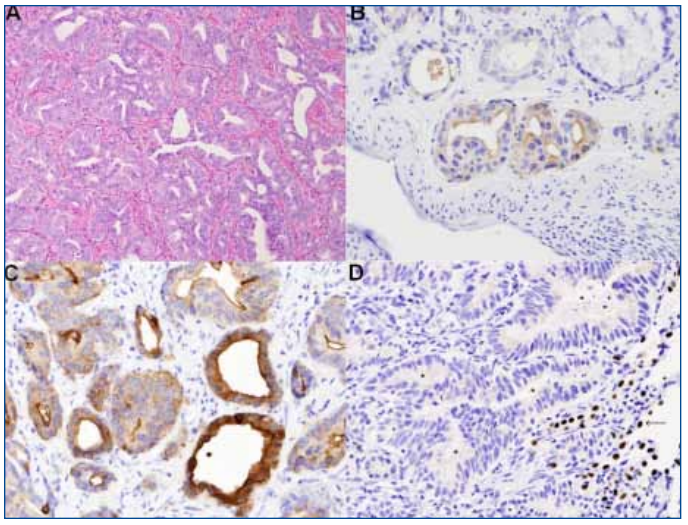

Fig. 3. A: Representative section from the pulmonary metastasis showing growth of malignant glands filling acinar spaces. Many of the tumour cells exhibit prominent nucleoli; the architectural pattern in this view is predominately cribriform with fused glands showing irregular slit-like spaces. Hematoxylin and eosin, original magnification 100×. B: Immunohistochemical staining for prostatic acid phosphatase within tumour cells. Original magnification 200×. C: Immunohistochemical staining for prostatic-specific antigen within tumour cells. Original magnification 200×.
D: Imunohistochemical stain for the lung-specific marker TTF-1. The tumour cells (asterix) are negative while the resident normal alveolar epithelial cells (arrow) exhibit positive nuclear staining. Original magnification 200×.

Discussion

Lung metastases in late-stage prostate cancer are uncommon and the clinical incidence is significantly lower than autopsy rates. In a series of terminal patients, pulmonary metastases were clinically and autopsy detectable in 5.7% and 25%, respectively.[26] Saitoh and colleagues found 1367 cases of metastatic disease in the autopsy results of 1885 prostate cancer patients.[27] While metastases to the lungs were found in 49.1% of all patients with metastatic disease, only 4 of 1367 (0.3%) had metastases isolated to the lungs. In two other retrospective series of stage D prostate cancer, only 1 patient had clinically apparent lung metastasis without concurrent bony or lymph metastases.[10,28] Thus, the finding of an apparently solitary pulmonary metastasis from prostate cancer, with an otherwise negative metastatic workup is unusual and presents a therapeutic question of the role of metastasectomy. Our literature review provides some evidence that in a specific subset of patients with a low burden of metastases, even if it is usually regarded as a manifestation of systemic disease, surgery (especially minimally invasive surgery lobectomy or metastasectomy) may be an option.

Based on their study of patients with T1-T3a, N0-NX, M0 treated with radiation therapy, Singh and colleagues have shown that patients with a low burden of metastatic disease (<5 lesions) have significantly improved survival as compared to those patients with >5 lesions.[28] They suggest that the number of metastases may reflect the biological progression of the tumour, with oligometastatic disease being less aggressive than its more disseminated counterpart. Based on this assertion, they suggest that this subset of patients would be suitable for aggressive local treatment of metastatic lesions. Several cases reports of long-term survival from resection of pulmonary lesions have been reported.[2-5,11]

Saitoh and colleagues discuss two potential patterns of metastatic dissemination: (1) a single-step process in which all metastatic cancer cells originate from the primary tumour;

Table 2. Reports of isolated multiple pulmonary metastases from prostate cancer

Authors	Age, yr	Initial tumour characteristic	Initial treatment	Metastases characteristics	Metastatic treatment	Outcome
Bromberg et al.	71	Stage B1, Gleason 3+3=6	RP, LND	3 nodules in left upper lung field	Pulmonary wedge resection, bilateral orchiectomy	Resolution of unresected nodule within 1 year
Maeda et al.	71	T2bN0M0	RP	1 nodule in upper lobe, attenuation in lower lobe left lung	Resection of upper lobe, open biopsy lower lobe	Not reported
Cusan et al.	60	Stage C, moderately differentiated	External beam RT	Bilateral pulmonary nodules	Unsuccessful treatment with LHRH agonist and flutamide; right lower lobe resection and flutamide only	PSA ↓ to a nadir of 0.5 μg/L
Allen and van Velden	59	Well differentiated, PSA >1000 ng/mL	N/A	Multiple round pulmonary opacities, present at diagnosis	Bilateral orchiectomy	Regression of pulmonary deposits. PSA ↓ to 157 ng/mL
Behrakis and Koutsilieris	71	Moderately differentiated, acid phosphatase 20 ng/mL	TURP (prostate cancer diagnosed on TURP specimen)	2 or 3 nodules on chest x-ray	Open lung biopsy, GnRH-agonists	Resolution of pulmonary nodules within 8 months
Eastham et al.	69	Gleason 3+4=7, PSA 117 ng/mL	N/A	Diffuse bilateral lung nodules	Bilateral orchiectomy	Resolution of nodules within 8 months, PSA 1.6 ng/mL.
Harris and Cowley	76	Moderately differentiated, PSA 42.6 μg/L	N/A	Scattered round lesions in both lungs	Cyproterone	Improved pulmonary nodules. PSA < 0.5 μg/L
Kirby	59	pT3, Gleason 4+5=9	RP, goserelin and salvage radiation, bicalutamide	Multiple pulmonary metastases	Bicalutamide	Regression of pulmonary nodules
Kume et al.	56	Moderately differentiated	N/A	Multiple 5-10 mm pulmonary metastases	Bilateral orchiectomy	Resolution of pulmonary nodules
Petras and Wollett	59	Not reported	N/A	Bilateral pulmonary nodules	Bilateral orchiectomy, DES	Resolution of pulmonary nodules
Jacobson and Edeiken	76	Not reported	Radiation, bilateral orchiectomy, chemotherapy	Multiple pulmonary nodules	Not reported	Not reported
Liebman et al.	78	T2cNxM0 Gleason 3+4=7	RP, LND	2 right sided, 1 left sided lung masses	Hormonal and chemotherapy	Brain metastasis and death within months

RP: radical prostatectomy; RT: radiation therapy; LND: lymph node dissection; PSA: prostate-specific antigen; LH-RH: luteinizing hormone-releasing hormone; TURP: transurethral resection of the prostate; GnRH: gonadotropin-releasing hormone; DES: drug-eluted stents.

and (2) a cascade process in which metastases metastasize.[27] In the second theory, early removal of metastases could potentially improve patient outcome, which in the case of prostate cancer, could be monitored by PSA. If PSA decreases to an undetectable level following a simple, minimally invasive lobectomy or metastasectomy, the patient could potentially benefit from a prolonged survival. If, as in our patient, the PSA does not become undetectable, there are likely other sites of metastases. In our case, the patient did not suffer significant morbidity from the attempt at cure and his PSA remains very low with a very slowly rising trend and the remaining lung lesion has been stable on 6 monthly chest CT scans.

Rusch thoroughly discusses the indications for pulmonary metastasectomy.[29] The criteria she describes include eradication of the primary tumour, ability to resect all metastatic disease and the absence of extrathoracic lesions. The more conventional approach[1] in hormone-naïve patients would

be first-line androgen-deprivation therapy, though in at least 2 cases patients had good responses to lobectomy following failure of androgen withdrawal.[4,13]

It is most likely that the few cases of successful metastasectomy are exceptions to "normal" tumour biology and, as such, not generalizable. But patients need to be fully informed that such an intervention may or may not alter the natural history of their disease, and if they are otherwise healthy, likely only result in significant short-term perisurgical morbidity. It bears pointing out that numerous studies report a high incidence of recurrent lung metastases following lung metastasectomy (Table 2). Laisaar and colleagues report an incidence of 21%,[30] Rena and colleagues report an incidence of 30.6%[31] and Saito and colleagues describe an incidence of 44.8%.[32] Despite these data, Laisaar and colleagues strongly advocate for the role of surgical resection in cases of solitary pulmonary nodules.[30] Furthermore, they recommend reoperation if and when new nodules develop.

Conclusion

Though pulmonary metastases are unusual, we recommend that chest x-ray or chest CT scan be considered in a patient with rising PSA following primary therapy in whom all other studies are negative. We present a case report of low burden pulmonary metastases from a previously well-controlled prostate cancer. In this patient, we proceeded to a pulmonary wedge resection of his largest lesions and ongoing surveillance of the remaining nodule; however, his PSA failed to reach undetectable levels postoperatively. In this well-informed individual, he continues to have an excellent quality of life and no regrets.

There is minimal evidence in the literature, only 4 cases,[2-5] to suggest that surgical metastasectomy may provide for disease eradication in a unique subset of patients. A similar number of other cases[8,10,13] demonstrate that metastasectomy in combination with hormonal therapy can resolve pulmonary metastases. On the other hand, there are many cases in which the incidence of recurrent pulmonary metastases after metastasectomy is high. Therefore, in otherwise healthy men, metastasectomy may be considered following careful counselling.

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This paper has been peer-reviewed.

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