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Case Series of the Month

Safety and Early Oncologic Outcomes of Lung Resection in Patients with Isolated Pulmonary Recurrent Prostate Cancer: A Single-center Experience

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Abstract

The introduction of novel imaging approaches for recurrent prostate cancer (PC) has paved the way for the use of nonsystemic approaches in patients with recurrent disease. While use of surgery or radiotherapy is standard for men with nodal or bone recurrence only, there are no significant data on the possible curative role of surgery for pulmonary metastases. We aimed to assess the efficacy of lung resection in patients with isolated pulmonary recurrence after radical prostatectomy (RP) for clinically localized PC. Overall, nine patients with biochemical recurrence after RP and either single ($n = 4$) or multiple ($n = 5$) pulmonary uptake spots on fluorodeoxyglugose, choline, or prostate-specific membrane antigen positron emission tomography/computed tomography underwent a total of 20 lung resections between 2011 and 2017 at our institution. No postoperative complications occurred. After lung resection, seven of the nine patients experienced a biochemical response (defined as prostate-specific antigen <0.2 ng/ml at 40 d after surgery). All patients except for one were free of clinical recurrence (CR) at median follow-up of 23 mo. One patient experienced CR and received androgen deprivation therapy at the time of bone recurrence. Although larger prospective studies are needed, our series demonstrates that surgical resection of isolated pulmonary metastases is safe and effective in selected PC patients with recurrent disease.

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1. Case series

After ethics committee approval for data collection, we retrospectively evaluated nine patients with biochemical recurrence and pulmonary uptake as the only site of recurrence detected via fluorodeoxyglucose (FDG), choline, or prostate-specific membrane antigen (PMSA) positron emission tomography (PET)/computed tomography (CT) after radical prostatectomy (RP). All patients underwent lung resection between 2011 and 2017 at our institution. The absence of other metastatic sites was also confirmed via CT and bone scans before lung resection. No patients received systemic therapies such as androgen deprivation therapy (ADT) before metastasectomy. Preoperative, pathologic, and follow-up data were available for all patients. Biochemical response after lung resection was defined as

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Table 1 – Patient characteristics and postoperative outcomes

#	pT stage	pGS	ART or SRT	Imaging tracer	RP to CR (mo)	LMs at imaging (*n*)	LM sites	PSA (ng/ml)		WR to LFU (mo)	CR	WR to CR (mo)	ADT	WR to ADT (mo)	CSM	PSA-DT pre-WR (mo)
								Before	After							
1	pT3bN0 R1	4 + 4	No	FDG	0	3	LLL	23.20	12.19	10	Yes	6	Yes	0	No	NA
2	pT2bN0	5 + 2	Yes + CT	Choline	120	3	RLL	4.11	0.61	85			No		No	26.4
3	pT2bN0	5 + 3	Yes	Choline	66	1	LUL	0.54	0	11			No		No	157
4	pT3aN0	4 + 4	Yes	Choline	144	1	RUL	1.02	0	47			No		No	35.7
5	pT3aN0	4 + 4	Yes	Choline	96	1	LLL	1.78	0	23			No		No	26.6
6	pT2cN0	4 + 3	Yes + BAT	PSMA	94	1	RUL	1.66	0.02	17			No		No	34.6
7	pT2bN0	3 + 4	No	FDG	10	2	RUL, RLL	0.60	0	77			No		No	27.3
8	ypT3aN0	4 + 4	Yes	FDG	48	6	LUL, LLL	0.28	0	26			No		No	26
9	pT3aN0	4 + 4	Yes	FDG	35	2	RLL	2.60	0.02	12			No		No	6.1

pGS = pathologic Gleason score; RT = radiotherapy; ART = adjuvant RT; SRT = salvage RT; CT = chemotherapy; BAT = B-mode acquisition and targeting; FDG = fluorodeoxyglucose; PSMA = prostate-specific membrane antigen; RP = radical prostatectomy; CR = clinical recurrence; LMs = lung metastases; RUL = right upper lobe; RLL = right lower lobe; LUL = left upper lobe; LLL = left lower lobe; PSA = prostate-specific antigen; WR = wedge resection; LFU = last follow-up; ADT = androgen deprivation therapy; CSM = cancer-specific mortality; DT = doubling time; NA = not available.

prostate-specific antigen (PSA) <0.2 ng/ml at 40 d after surgery [1]. Clinical recurrence (CR) was defined as positive molecular imaging outside the area of the resection. Follow-up consisted of PSA testing 40 d after surgery, at 3, 6, 9, and 12 mo after RP, and biannually thereafter. Conventional imaging with abdominal CT was performed at 6 and 12 mo and yearly thereafter, and ^{11}C-choline and ^{68}Ga-PSMA PET/CT scans were exclusively considered for patients who experienced biochemical recurrence (two or more PSA values ≥0.2 ng/ml) according to the treating physician's preference. In selected cases, FDG PET/CT was considered to better characterize lung nodules. Follow-up visits, physician correspondence, and death certificates were used to assess vital status and cause of death.

Table 1 lists the preoperative and postoperative characteristics of our population. The median age at prostate cancer (PC) diagnosis was 61 yr. Pathologic stage was pT2, pT3a, and pT3b/4 in 44%, 44%, and 11% of patients, respectively. Overall, 66% patients had Gleason score 8–10 and none presented lymph node invasion at final pathology. Seven out of nine patients received adjuvant or salvage radiotherapy after RP. Overall, four patients underwent choline, one ^{68}Ga-PSMA, and four FDG PET/CT at the time of biochemical recurrence (defined as two consecutive PSA values >0.2 ng/ml). Overall, four and five patients presented with a single (Fig. 1) and multiple metastases (Figs. 2 and 3) at imaging, respectively. A total of 20 wedge lung resections were performed. Nodules were located mainly in the same lobe, with higher frequency in the lower lobes. In two patients, metastases were distributed between the upper and lower lobes. However, all nodules were amenable to wedge resection. Six patients underwent video-assisted thoracoscopic (VAT) lung resection, while a standard thoracotomy was performed in three cases. Thoracotomy was preferred on the basis of localization of metastases. Metastases located centrally in the lung

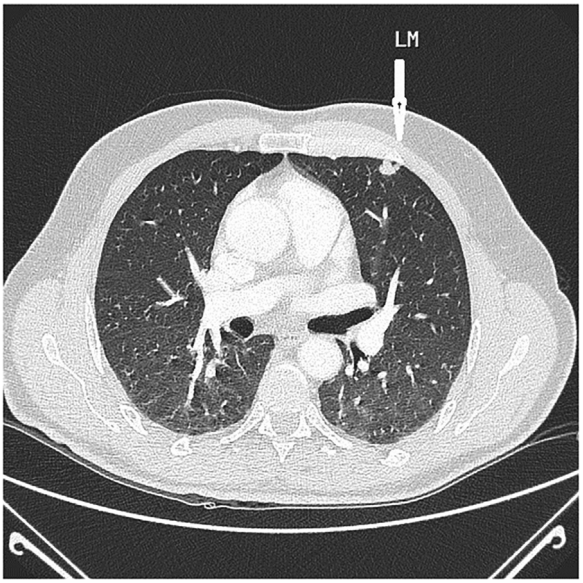

Fig. 1 – Chest computed tomography scan showing a single lung metastasis (LM) in the left upper lobe.

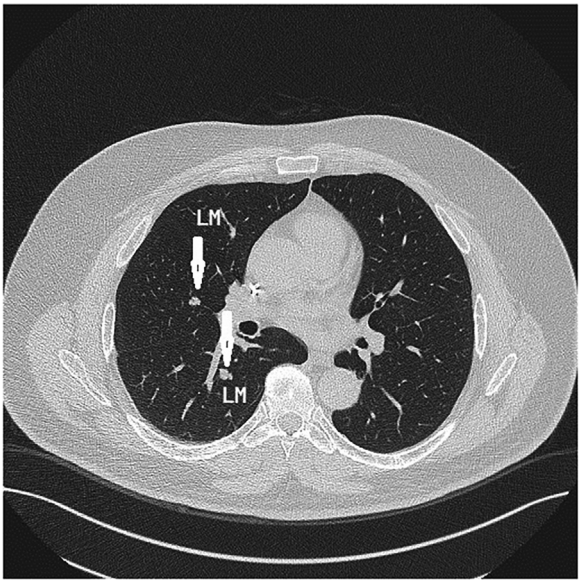

Fig. 2 – Chest computed tomography scan showing multiple lung metastases (LM) in the right upper and lower lobes.

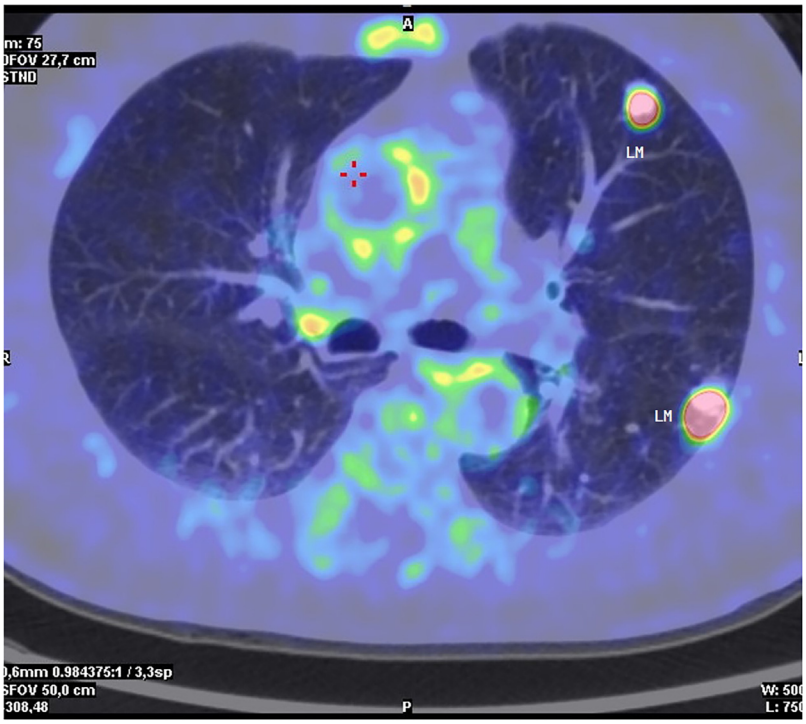

Fig. 3 – Fluorodeoxyglucose positron emission tomography scan showing uptake by lung metastases (LM).

parenchyma are not usually amenable to VAT resection and require manual palpation for identification and resection with adequate margins. Peripheral nodules, even if multiple, were excised via VAT. The median operative time for lung resection was 55 min and the median hospital stay was 6 d. Final pathology confirmed lung metastasis from PC (Fig. 4). No postoperative complications occurred. Median PSA was 1.66 ng/ml (interquartile range [IQR] 2.7) before and 0 ng/ml (IQR 0.3) after wedge resection. The median PSA doubling time from RP to lung resection was 26.9 ng/ml (IQR 9.3). After lung resection, seven out of nine patients experienced a biochemical response. The median follow-up for survivors was 23 mo. Patients #1 and #2 did not experience a biochemical response after lung metastasectomy. Patient #1 experienced CR consisting of bone metastases and received ADT at the time of recurrence. Patient #2 did not experience a biochemical response although PSMA PET/CT did not show pathologic uptake during follow-up. No cancer-specific death has been recorded.

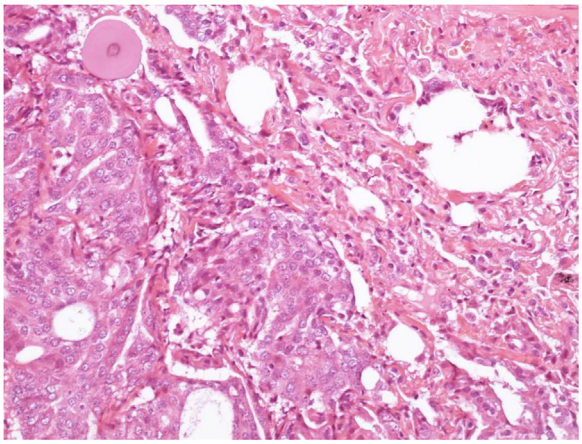

Fig. 4 – Histological slide of prostate cancer lung metastases with associated normal lung parenchyma.

2. Discussion

Although lymph nodes and bone represent the most common sites of metastatic spread of PC [2], the incidence of visceral metastases is increasing, and up to 5% of men with metastatic PC have lung involvement at presentation [1]. A recent prospective trial demonstrated a benefit of image-guided metastases-directed therapies compared to observation in PC patients with recurrence after primary treatment [3]. Nonetheless, the majority of men had nodal metastases and the vast majority of patients with visceral recurrence underwent stereotactic radiotherapy. Therefore, the role of surgical resection of pulmonary metastasis in the recurrence setting is still unclear, with only few cases of lung resection for PC metastases reported in the literature [4–10].

In the face of this paucity of data, we aimed to analyze outcomes for lung resection of isolated pulmonary metastases in a series of PC patients who experienced recurrence after RP. We were able to report excellent results in this setting, and virtually all of the patients with lung metastases included in our cohort experienced a biochemi-

cal response and were free from CR at median follow-up of 23 mo without the need for additional therapies. Only one patient with multiple lung metastases experienced disease relapse and received ADT. Lung resection was not associated with postoperative complications after a reasonable operative time and length and hospital stay. Although these results are promising, further studies with larger cohorts and longer follow-up are needed to comprehensively assess the role of lung resection in PC patients with pulmonary recurrent disease.

Other authors reported promising results for lung resection in PC patients experiencing lung recurrence [4–10]. However, these case series involved a maximum of three patients with short follow-up data, highlighting the rarity of this situation [4–9]. Lack of a preoperative noninvasive diagnosis is also uncommon and the most appropriate PET examination for PC lung metastases has not been clearly identified. The increasing use of ^{68}Ga-PSMA PET/CT might improve the therapeutic setting for these patients [4]. Our study represents the largest series to assess the role of curative-intent surgical resection in men with recurrent pulmonary PC, albeit with a small number of strictly selected patients. However, despite the bias resulting from patient selection, from a clinical standpoint our findings could support the feasibility, safety, and oncologic efficacy of metastasis-directed therapies in the context of recurrent PC. In particular, surgery alone might represent an effective option and might delay the use of systemic therapies such as ADT and their short- and long-term side effects, provided that surgical resection does not impair patient quality of life. Thus, we would not recommend major lung surgery beyond a wedge resection for metastases.

Our study is limited by the lack of a control group undergoing observation and these results should be considered preliminary. Nonetheless, the current series seems to suggest a role for lung resection without concomitant ADT as a possible treatment option for selected PC patients experiencing isolated pulmonary recurrent disease after primary treatment.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Gandaglia G, Abdollah F, Schiffmann J, et al. Distribution of metastatic sites in patients with prostate cancer: a population-based analysis. Prostate 2014;74:210–6.

[2] Bubendorf L, Schöpfer A, Wagner U, et al. Metastatic patterns of prostate cancer: an autopsy study of 1,589 patients. Hum Pathol 2000;31:578–83.

[3] Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. J Clin Oncol 2018;36:446–53.

[4] Große Hokamp N, Kobe C, Linzenich E, et al. Solitary PSMA-positive pulmonary metastasis in biochemical relapse of prostate cancer. Clin Nucl Med 2017;42:406–7.

[5] Goto T, Maeshima A, Oyamada Y, et al. Solitary pulmonary metastasis from prostate sarcomatoid cancer. World J Surg Oncol 2010;8:101.

[6] Wallis CJ, English JC, Goldenberg SL. The role of resection of pulmonary metastases from prostate cancer: a case report and literature review. Can Urol Assoc J 2011;5:E104–8.

[7] Gago JP, Câmara G, Dionísio J, et al. Pulmonary metastasis as sole manifestation of relapse in previously treated localised prostate cancer: three exceptional case reports. Ecancermedicalscience 2016;10:645.

[8] Reinstatler L, Dupuis J, Dillon JL, et al. Lung malignancy in prostate cancer: a report of both metastatic and primary lung lesions. Urol Case Rep 2017;16:119–22.

[9] Fukuoka T. Prostate cancer in a patient with multiple pulmonary metastases alone and respiratory symptoms. J Rural Med 2014;9:27–31.

[10] Suardi N, Gandaglia G, Gallina A, et al. Long-term outcomes of salvage lymph node dissection for clinically recurrent prostate cancer: results of a single-institution series with a minimum follow-up of 5 years. Eur Urol 2015;67:299–309.