FDG PET/CT in the Evaluation of Late Manifestation of Adrenal Metastasis after Radical Nephrectomy in Patients with Renal Cell Carcinoma: A Report of Four Cases and Review of Literature

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Abstract: *Purpose:* Presence of distant metastasis is a strong independent predictor of poor survival in patients with renal cell carcinoma (RCC). Positron emission tomography using F-18 fluorodeoxyglucose (FDG) has been reported to be superior to conventional anatomic imaging modalities for detecting distant metastases from RCC.

Methods: The authors report the findings of four patients who underwent FDG positron emission tomography / computed tomography (PET/CT) at varying periods after radical nephrectomy for RCC.

Results: FDG PET/CT detected increased tracer concentration in the adrenal glands in all four patients and subsequent fine needle aspiration confirmed metastatic RCC. While the adrenal was the only site of metastasis in one patient, additional metastases were detected in lymph nodes and lungs in the others.

Conclusions: RCC metastatic to the adrenal gland is usually a vascular tumour and there is an intrinsic risk of haemorrhage during CT-guided needle biopsy. This small series of cases suggests that FDG PET/CT is a useful non-invasive investigation in identifying malignant adrenal lesions in patients with RCC presenting after nephrectomy.

Keywords: FDG PET/CT, Renal cell carcinoma, Adrenal metastasis.

INTRODUCTION

The role of F-18 fluorodeoxyglucose positron emission tomography (FDG PET) in the detection of renal cell carcinoma (RCC) is limited by low sensitivity [1]. Renal excretion of FDG may hamper the detection of renal cell carcinoma. Presence of distant metastasis is a strong independent predictor of poor survival in patients with RCC. Patients with metastatic disease have a 5-year survival rate of 0 to 20% [2-3]. A 5-year survival rate of 25-50% has been reported for patients with solitary metastases from RCC that can be completely resected [4-5]. Currently available anatomic imaging techniques have limited accuracy for the detection of distant metastases. The sensitivity of computed tomography (CT) for detection of lung metastases from extra-thoracic malignancies ranges from 75-95% and can be as low as 48-69% for metastases less than 6 mm in size [6]. FDG PET has been reported to be superior to conventional anatomic imaging modalities for detecting distant metastases from RCC [7]. We report a series of four cases where FDG PET/CT was useful in characterising ipsilateral and contralateral adrenal lesions in patients with RCC at varying periods after nephrectomy.

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CASE 1

A 54-year-old man underwent left radical nephrectomy for clear cell adenocarcinoma of the left kidney (stage T2N0M0). The tumour was 10 cm in size, involving the upper pole of the left kidney with no capsular invasion and the left adrenal gland was free of tumour. He presented to our institute one year later with a right adrenal mass and left-sided pleural effusion detected on CT imaging of the chest and abdomen. He was referred for FDG PET/CT to assess for any involvement of the right adrenal gland and any other metastasis. The images (Figure **1A-C.**) showed a focus of FDG uptake in the enlarged right adrenal gland as well as in multiple enlarged axillary and mediastinal nodes. Fine needle aspiration cytology (Figure **1D.**) confirmed metastatic RCC. Treatment with Sunitinib was started and he is currently on follow up.

CASE 2

A 53-year-old man presented with CT scan of the chest and abdomen showing a soft tissue density mass in relation to the inferior part of the lateral limb of the left adrenal gland. He had previously undergone left radical nephrectomy 2 years earlier for clear cell adenocarcinoma in the mid-part of the left kidney with no capsular invasion. FDG PET/CT (Figure **2.**) showed a focus of tracer uptake in the enlarged left adrenal

gland as the only site of involvement, which was confirmed as metastasis on CT-guided FNAC.

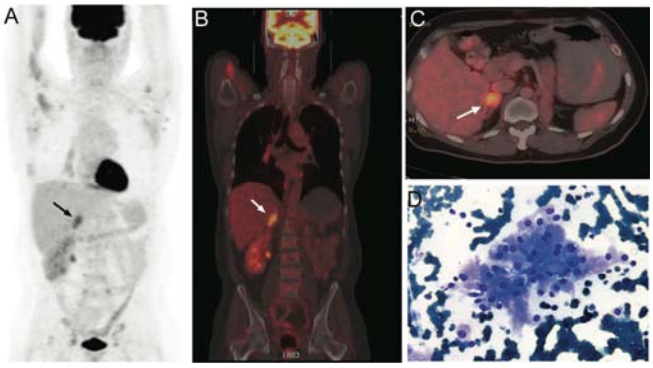

Figure 1: FDG PET/CT images: the maximum intensity projection (MIP) image **(A)** coronal PET/CT **(B)** and axial PET/CT **(C)** show a focus of intense tracer uptake (SUVmax 7.3) in the enlarged right adrenal gland (arrow) and in multiple enlarged axillary and mediastinal nodes. Fine needle aspiration cytology **(D)** from the right adrenal gland show a cluster of tumor cells with a moderate amount of vacuolated cytoplasm, moderate nuclear pleomorphism and prominent nucleoli.

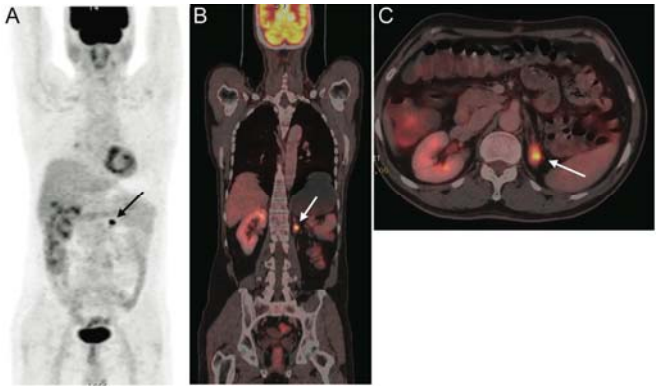

Figure 2: FDG PET/CT images: the maximum intensity projection (MIP) image **(A)**, coronal PET/CT **(B)** and axial PET/CT **(C)** show a focus of intense tracer uptake (SUVmax 8.2) in the enlarged left adrenal gland (arrow) as the only site of involvement.

CASE 3

A 65 year old man who had undergone right radical nephrectomy for clear cell adenocarcinoma 3 years previously presented with abdominal pain. He underwent CT scan of the abdomen, which showed a large lesion in the right adrenal gland. FDG PET/CT (Figure **3.**) showed intense tracer uptake in the enlarged right adrenal gland and multiple mediastinal lymph nodes. He was confirmed to have metastasis in the adrenal gland on CT-guided FNAC and started on chemotherapy.

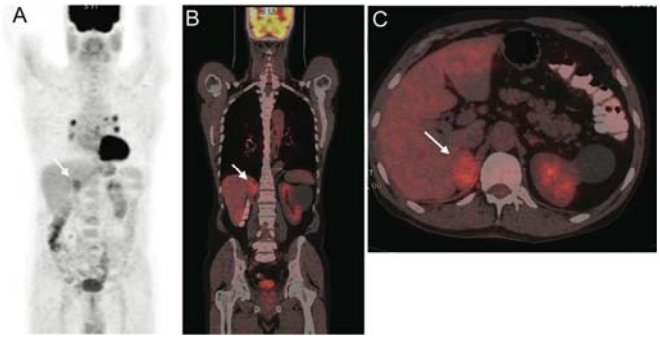

Figure 3: FDG PET/CT images: the maximum intensity projection (mip) image **(A)** coronal pet/ct **(B)** and axial pet/ct **(C)** show intense tracer uptake (suvmax 5.2) in the enlarged right adrenal gland (arrow) and multiple mediastinal lymph nodes.

CASE 4

A 74 year old man who underwent radical nephrectomy for clear cell adenocarcinoma in the lower pole of the left kidney two years ago presented with pain in the abdomen. He underwent CT scan of the chest and abdomen, which showed a soft tissue lesion in the upper lobe of the left lung and another lesion in the left adrenal gland. He was referred for FDG PET/CT (Figure **4.**) to characterize the lung and adrenal lesions. FDG PET/CT showed intense tracer uptake in the upper lobe of the left lung and the left adrenal gland, which was confirmed as metastatic RCC. He was started on chemotherapy.

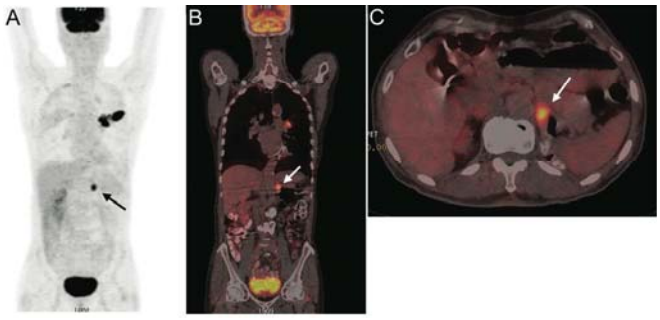

Figure 4: FDG PET/CT images: the maximum intensity projection (MIP) image **(A)**, coronal PET/CT **(B)** and axial PET/CT **(C)** show intense tracer uptake (SUVmax 10.3) in the upper lobe of the left lung (arrowhead) and the left adrenal gland (arrow).

DISCUSSION

Although RCC can metastasize to almost any organ, the most common metastatic sites are the lungs, abdomen, bones and brain [8]. While metastasis of RCC to different sites is not uncommon, contralateral adrenal metastasis (CAM) is rare. In one autopsy study

of more than 400 patients who had undergone nephrectomy for RCC [9], the contralateral adrenal gland was the sole site of metastatic involvement in only 2.5%. Among those with widespread RCC metastases identified at autopsy, the contralateral adrenal gland was involved in 12.7% of patients. In addition to being able to metastasize to different organs, RCC can recur many years after resecting the primary tumor [10]. In a recent study, a series of 1179 patients were treated for RCC and it was found that the global incidence of adrenal metastasis among those patients was 3.7%, of which 1.9% were ipsilateral, 1.5% contralateral, 0.3% bilateral, 2.7% synchronous with the renal tumor and only 1% metachronous metastasis [11].

The behaviour of RCC is unpredictable. Metastasis may be found synchronously with the primary tumor or in various organs many years after treating the primary malignancy. Metastasis of RCC to the contralateral adrenal gland has been diagnosed as late as 23 years after nephrectomy [11]. Adrenal metastases are usually anatomically and functionally silent and patients rarely have symptoms or signs of adrenal insufficiency. Thus, abdominal imaging is not always used routinely during the follow-up and an isolated contralateral adrenal gland metastasis from RCC is rarely diagnosed during life. The underlying biological pathway for secondary involvement of the contralateral adrenal gland by RCC is unknown.

The optimal diagnostic approach to a solitary contralateral adrenal tumor in patients with a history of RCC is controversial and differs from the management of adrenal 'incidentalomas.' Radiological studies cannot determine with certainty whether an adrenal tumor in a patient with RCC is a primary adrenal neoplasm (the most common type), an adrenal cortical adenoma, or a metastasis. In these patients, presence of a solitary adrenal tumor with no elevation in serum adrenocortical hormones is strongly suggestive of a metastatic lesion to the adrenal gland. RCC metastatic to the adrenal gland is usually a vascular tumor, compared with the more hypovascular adrenal cortical adenoma or carcinoma. Biopsy of adrenal masses may be helpful in doubtful cases, although in general the diagnosis of RCC by biopsy has been problematic [12]. Because of the vascular structure of the tumor, there is an intrinsic risk of haemorrhage during CT-guided needle biopsy. All of our patients underwent FNAC to confirm metastasis and they have no complication of hemorrhage. The mediastinal lymph node metastasis in one of the patient and lung metastasis in another patient was confirmed on follow up evaluation.

The overall sensitivity and specificity of FDG PET for detection of primary RCC has been reported to range from 31-95% and 33-90%, respectively [1]. FDG PET has not been extensively studied for evaluation of distant metastases from RCC. Reported studies of FDG PET in metastatic RCC have involved few patients, and most series have compared the results of FDG PET with clinical outcome determined by follow-up with conventional anatomic radiologic techniques. Pathologic confirmation of metastatic disease, if performed, was usually combined with radiological follow-up for reporting results. Using FDG PET for restaging 36 patients with advanced RCC, Safaei *et al.* biopsied 25 suspicious lesions from 20 patients and demonstrated a sensitivity and specificity of 87% and 100%, respectively [13]. FDG PET accurately identified 84% (21 / 25) of the biopsied lesions. FDG PET had an overall diagnostic accuracy of 89% for restaging residual/recurrent RCC. Park *et al.* [14] evaluated the role of FDG PET/CT for the surveillance of patients with RCC who have a high risk of local recurrence or distant metastasis, by comparing the results with those of conventional imaging methods. Isolated local recurrences after radical nephrectomy for renal cell carcinoma occur in 2% to 3% of cases. FDG PET/CT accurately classified the presence of a recurrence or metastasis in 56 (89%) patients. FDG PET/CT showed an 89.5% sensitivity, 83.3% specificity, 77.3% positive predictive value, 92.6% negative predictive value, and 85.7% accuracy in detecting recurrence or metastasis, which was not significantly different from the results with conventional methods.

CONCLUSION

RCC metastatic to the adrenal gland is usually a vascular tumor, compared with the more hypovascular adrenal cortical adenoma or carcinoma. Because of the vascular structure of the tumour, there is an intrinsic risk of haemorrhage during CT-guided needle biopsy. This small series of cases suggests that FDG PET/CT is a useful non-invasive investigation in identifying malignant adrenal lesions in patients with RCC presenting after nephrectomy and avoiding risk of biopsy causing hemorrhage.

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