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SHORT COMMUNICATION

CT-guided percutaneous core biopsy for assessment of morphologically normal adrenal glands showing high FDG uptake in patients with lung cancer

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Objective: Increased fludeoxyglucose (FDG) uptake in morphologically normal adrenal glands on positron emission tomography-CT (PET-CT) is a diagnostic challenge with major implications on treatment. The purpose of this retrospective study was to report our experience of CT-guided percutaneous core biopsy of morphologically normal adrenal glands showing increased FDG uptake in a context of lung cancer.

Methods: Biopsies for non-enlarged adrenal glands showing increased FDG uptake in lung cancer patients performed at our institution from December 2014 to December 2016 were retrospectively analyzed. Six biopsies were performed in five patients during the study period. All procedures were performed with the patients in the prone position, using a posterior approach and coaxial 17-gauge needles with 18-gauge automated cutting needles. Patient characteristics, procedural

details and final pathological diagnosis were analyzed, as well as the duration of hospitalization.

Results: Five of the six biopsies (83.3%) confirmed adrenal metastasis from the primary lung cancer. No complications were reported and the patients were discharged the day after the procedure.

Conclusion: The high confirmation rate of metastasis and lack of complications support performing CT-guided percutaneous biopsy of non-enlarged adrenal glands showing increased FDG uptake, for optimal management in lung cancer patients.

Advances in knowledge: Morphologically normal adrenal glands showing high FDG uptake in patients with lung cancer are metastasis. This manuscript shows that CT-guided percutaneous biopsy should be proposed. Increased FDG uptake in morphologically normal adrenal glands may indicate metastasis.

INTRODUCTION

The utility of whole body ¹⁸F-fluorodesoxyglucose -positron emission tomography/CT (FDG-PET/CT) for lung cancer staging has been recognized for years and this technique is now part of the standard work-up. Patients with metastatic, Stage IV disease are often not amenable to curative treatment and among them, patients with extra thoracic metastases have a poorer outcome.¹ FDG-PET/CT offers better sensitivity and specificity than standard CT for the detection of adrenal metastases,² but up to 28% of cases demonstrating increased adrenal uptake are false positives.³ Adrenal masses with maximal standard uptake value (SUV_{max}) greater than that of the liver have been usually considered as malignant. However, recent studies have shown that normal adrenal glands may demonstrate higher uptake than the liver.^{4,5} Thus, several cut-off values for SUV_{max} have been recently suggested to

differentiate between benign masses and adrenal metastases due to lung cancer.^{3,4} Rarely, adrenal metastases can also be encountered without any adrenal enlargement on CT.^{2,6,7} Thus, FDG increased uptake of morphologically normal adrenal glands is a diagnostic challenge with major implications for treatment. Pathological analysis is the gold standard for assessment of adrenal metastases. CT-guided fine needle aspiration and percutaneous core biopsy are less invasive procedures than adrenalectomy and have shown good diagnostic accuracy for characterization of adrenal masses,^{6,8,9} with complication rates from 2.8 to 11.3%. Regarding biopsy of morphologically normal adrenal glands, very few data are available.⁸ The purpose of this retrospective study was to report our experience of CT-guided percutaneous core biopsy of morphologically normal adrenal glands showing high FDG uptake in the context of lung cancer.

METHODS AND MATERIALS

This retrospective study was approved by our local ethics committee.

We retrospectively analyzed all adrenal biopsies of non-enlarged adrenal glands presenting increased FDG uptake in patients with confirmed or suspected lung cancer from December 2014 to December 2016. During the study period, five patients had a total of six biopsies of non-enlarged adrenal glands showing increased FDG uptake in a context of lung cancer. Increased FDG uptake was defined on qualitative assessment by comparing adrenal FDG uptake with the normal FDG uptake in the liver. We retrospectively measured SUV mean value of the liver.

All procedures were performed by the same operator ((blinded for review) having 15 years experience in interventional radiology. Patients were placed in prone position, and a posterior approach was used. Coaxial 17-gauge needles with 18-gauge automated cutting needles (Bard Monopty, Bard, Covington, GA) were used and three to four samples were obtained. Hydrodissection was not used.¹⁰ All patients had normal laboratory parameters.

Initial CT, FDG-PET/CT, and biopsy guidance CT images were retrospectively reviewed to confirm the absence of mass or enlargement of the adrenal glands at time of the percutaneous biopsy. Patient characteristics, procedure details and final pathological diagnosis were analyzed as well as the hospitalization duration.

RESULTS

Results are presented in Table 1. Five patients (one female and four males), aged from 47 to 73 years (mean: 62.4 years) with no other potential metastatic site according to PET/CT and brain MRI findings were included. One of the patients underwent two separate biopsy procedures, one for each of the two adrenal glands, starting with the left side. The second biopsy was performed 2 weeks after the first one, because adrenalectomy is considered only for a solitary metastasis at our institution. All procedures had been decided during multidisciplinary meetings, as part of the initial staging (patient 2–5) or because of a suspected recurrence after radiation therapy (patient 1).

The interval between FDG-PET/CT examination and percutaneous biopsy ranged from 2.1 to 8.9 weeks. The needle path crossed the pleura, lung parenchyma, and diaphragm in all three right biopsies (Figure 1), whereas the left retroperitoneal space was reached below the diaphragm in the three left adrenal procedures.

No complications were reported and the patients were discharged the day after the procedure.

Five of the six biopsies (83.3%) confirmed adrenal metastatic spread of the primary lung cancer (Table 1). The sixth biopsy result was negative, showing normal adrenal tissue, in a patient with a cavitary lung mass, highly suspicious for lung cancer, for which the percutaneous biopsy had only shown necrosis. This patient was lost to follow-up.

DISCUSSION

We report here that CT-guided biopsy of morphologically normal adrenal glands showing increased FDG uptake in a context of lung cancer is a safe procedure, allowing confirmation of metastasis in 83% of cases. This malignancy rate is comparable to the 72 to 87% malignancy rates reported for hypermetabolic adrenal masses in patients with known malignancy.^{3,11,12} Only one procedure failed to demonstrate metastatic spread, which was probably a false negative, although pathological confirmation of lung cancer could not be obtained. Our results agree with those of Vilelli *et al*, who reported that CT-guided core biopsies had 86% sensitivity for malignancy, without on-site evaluation.¹³ Several etiologies for 18-FDG PET-CT false positives have been reported in literature, including adrenal adenoma, cortical hyperplasia, sarcoidosis, histoplasmosis or tuberculosis.¹⁴ Nevertheless, these etiologies are usually associated with an adrenal mass or at least an enlargement of the adrenal gland. In a context of lung cancer, high FDG uptake in morphologically normal adrenal glands more likely corresponds to the early detection of microscopic metastatic foci.

The definition of abnormal FDG uptake is mainly based on visual assessment in the absence of reliable SUV cut-off values for discriminating benign diseases from malignancies.¹⁵ All the

Table 1. Characteristics of the six procedures

Patient	Sex/Age	Primary lung cancer	Adrenal SUV _{max} value	Side	Liver SUV _{mean} value	Needle path length (cm)	Adrenal biopsy pathological result
1	M/64	TTF1 +adenocarcinoma	6.9	Left	3.6	12	Metastasis
2	F/47	Unknown	2.8	Right	1.9	8.4	Normal adrenal parenchyma
3	M/65	Squamous cell carcinoma	2.7	Left	2	12	Metastasis
4	M/63	TTF1 +adenocarcinoma	4.2	Right	2.1	11	Metastasis
5	M/73	TTF1- adenocarcinoma	3	Left	1.8	11	Metastasis
		TTF1- adenocarcinoma	4.8	Right	1.8	11	Metastasis

SUV, standard uptake value.

Figure 1. CT-guided percutaneous core biopsy of a morphologically normal adrenal gland showing increased FDG uptake in a 63-year-old male. (a) PET-CT shows increased FDG uptake of the right adrenal gland (arrow). (b) On the corresponding CT image, the gland is not enlarged (arrow). (c) CT image of the percutaneous biopsy showing the coaxial needle through the pleura and right lower lobe lung parenchyma. (d) Photomicrograph of histopathological specimen obtained during the biopsy shows adenocarcinoma, consistent with metastatic lung adenocarcinoma (original magnification, Hematoxylin-Eosin staining, $\times 20$). FDG, fludeoxyglucose; PET-CT, positron emission tomography.

biopsied adrenal glands in our series showed FDG uptake higher than that of the liver. CT-guided biopsies of morphologically normal adrenal glands in lung cancer patients have been previously reported by Pagani. In that study, which did not include the use of FDG-PET/CT, metastatic spread was confirmed in only 12% of patients.⁷

Sampling error can be a limitation when biopsy is performed on morphologically normal adrenal glands. It is reported to occur in 11% of cases but can be avoided by on-site pathological evaluation.¹³ We used a coaxial 18-gauge needle, obtained at least three biopsy samples, and recovered adrenal tissue in all six procedures, even on the technically more difficult left side.⁸ Endoscopic transgastric ultrasound-guided fine needle aspiration has

been suggested as an alternative method, offering good diagnostic accuracy with a low complication rate.^{6,16} However, it is only applicable to the left adrenal gland.

Our study is limited by the small number of cases and, probably, by one false negative result. Nevertheless, the high positive rate for metastasis and the lack of complications support performing CT-guided percutaneous biopsy of non-enlarged adrenal glands demonstrating high FDG uptake, for optimal management in lung cancer patients.

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