CLINICAL STUDY

¹⁸F-fluorodeoxyglucose positron emission tomography as a diagnostic tool for malignancy of adrenocortical tumours? Preliminary results in 13 consecutive patients

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Abstract

Design: This study is a preliminary report on ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) uptake for the characterization of hypersecretory or non-hypersecretory adrenocortical masses in patients without known neoplastic disease, thereby minimizing the presence of adrenal metastases, and without pheochromocytoma, in comparison with computed tomography (CT) scanning and with iodocholesterol scintigraphy.

Methods: Thirteen consecutive patients with an adrenal mass scheduled to have surgery, underwent hormonal exploration, a CT scan for tumour size measurement and an ¹⁸F-FDG positron emission tomography scan. Eleven of these patients also had unenhanced density measurement at CT scan and iodocholesterol scintigraphy.

Results: CT-scanned adrenal masses ranged in size from 2.2 to 10 cm; attenuation value was <10 Hounsfield units (HUs) in two cases and >10 HU in nine. All benign lesions demonstrated iodocholesterol uptake. In the case of malignant tumours, results were non-homogeneous: no uptake, uptake and non-informative scintigraphy. All patients with an adrenocortical carcinoma had positive adrenal ¹⁸F-FDG uptake (*n* = 3), one had a liver metastasis with positive ¹⁸F-FDG uptake, one showed ¹⁸F-FDG uptake in an adrenal metastasis from an unknown primary kidney tumour. All patients with a benign adrenocortical lesion had negative ¹⁸F-FDG uptake (*n* = 9). Patients' lesions were hypersecretory (*n* = 5), or non-hypersecretory (*n* = 8), regardless of the pathology.

Conclusion: This short preliminary study indicates that ¹⁸F-FDG gave a correct classification of tissue characterization with accurate identification of malignant lesions, as well as the disease stage (metastasis or primary). These promising preliminary results on adrenocortical lesions, seldom studied with ¹⁸F-FDG, are to be confirmed in larger series.

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Introduction

Endocrine adrenocortical tumours generate two risks: that associated with hormone hypersecretion (e.g. Cushing's syndrome) and that associated with malignancy. Malignant adrenocortical tumours have a very severe prognosis (20% survival at 5 years); they are often detected late, and their pathological diagnosis may be difficult and require special molecular analysis (1). Early diagnosis is the best opportunity to cure patients with adrenocortical carcinoma (2).

Adrenal tumours are encountered increasingly frequently as 'incidentalomas' by computed tomography

(CT) scans performed for other ('non-adrenal') reasons in up to 4% of patients (3).

Until recently, iodocholesterol scintigraphy was the only diagnostic tool, very useful but not widespread, proposed by nuclear medicine (4, 5). Positron emission tomography (PET) with ¹⁸F-labelled 2-fluoro-2-deoxy-D-glucose (¹⁸F-FDG) has proved to be highly efficient for diagnosing the malignancy of solitary pulmonary nodules (6). However, only a limited number of studies have been applied to adrenal metastatic lesions and very few have been performed on primary adrenal tumours (7–13).

The aim of our study was to prospectively evaluate ¹⁸F-FDG uptake for the diagnosis of adrenocortical

lesions. We compared the results with unenhanced CT scans and iodocholesterol scintigraphy.

Patients and methods

Thirteen patients (12 women, 1 man) aged from 27 to 70 years were studied. An endocrine evaluation looked for steroid oversecretion (baseline urinary cortisol excretion, overnight dexamethasone suppression test, standard aldosterone/renin ratio, baseline and post-corticotrophin androgens and 17OH progesterone); 24 h urinary metanephrines were used to exclude the presence of pheochromocytoma. The presence of adrenal metastases was also minimized since none of the patients had known neoplastic disease. In all cases, adrenal surgery was indicated for the following reasons: hypersecretory tumour, whatever its size, or non-hypersecretory lesion but with suspect imaging features (size > 3 cm, and/or non-homogeneous on CT scan and/or low lipid content as indicated by unenhanced density measurement (attenuation value) above 10 Hounsfield units (HUs) at CT scan). Informed consent was obtained from all patients, in a protocol approved by the local ethics committee. A CT scan evaluated the tumour size and the homogeneity of density in HUs (14).

¹³¹I-6-β-iodomethylnorcholesterol scintigraphy (Norchol; Schering, Gif sur Yvette, France) was performed by injecting 37 MBq iodocholesterol, after suppression of iodine thyroid accumulation and after digestive preparation. Anterior and posterior static views were obtained 4 and 7 days after injection on a dual head gamma camera equipped with high energy collimators (SOPHA DST-XL, Buc, France). ^{99m}Tc-DTPA scintigraphy gave anatomical landmarks for kidneys at day 4. ¹⁸F-FDG images were acquired with a dedicated full-ring PET camera (ADAC-Philips CPET, Cleveland, USA). Patients fasted overnight for glycaemia

control. They were injected with 2.5 MBq/kg ¹⁸F-FDG (Flucis; Schering) in a resting state to avoid muscular tracer accumulation. They were hydrated and systematically given diazepam and mebeverine. Whole body scanning was started 75 min post-injection from the pelvis to the head. Five to seven steps lasting about 10 min per step for emission and transmission acquisition were performed according to the patient's height. Images were reconstructed with an iterative reconstruction algorithm. ¹⁸F-FDG PET images were qualitatively evaluated by two nuclear medicine physicians who were unaware of the final diagnosis. ¹⁸F-FDG adrenal uptake was compared with liver uptake; positive or high uptake was taken into account if adrenal uptake was higher than liver uptake.

Results

Patient characteristics are summarized in Table 1. Tumour sizes (by CT scan) ranged from 2.2 to 10 cm. Out of 13 resected tumours, 9 were benign and 4 were malignant.

The nine benign tumours were all negative for ¹⁸F-FDG uptake, independently of their secretory nature. Although they were small (between 2.2 and 5 cm), these tumours were operated on because of their hypersecretory nature (cases 6, 8 and 11) or because of their size (> 3 cm) or high attenuation values at CT scan (> 10 HU) (cases 5, 6 and 8–13).

The four malignant tumours were all positive for ¹⁸F-FDG uptake. They were also the largest tumours (7–10 cm) (cases 1–4) and when attenuation value was performed, they had high attenuation on CT scans. Two were hypersecretory adrenocortical carcinomas (cases 2 and 3) and one was a non-hypersecretory adrenocortical carcinoma (case 1). In case 3 (Fig. 1), hepatic metastasis depicted by ¹⁸F-FDG uptake was confirmed at pathological examination. In

Table 1 Patient characteristics.

Patient	Age (years)	Gender	Secreting	Size (cm)	Side	Density CT(HU)	Iodo scan	¹⁸ F-FDG	Pathology	Final diagnosis
1	54	F	No	7	R	42	Concordant	+	Malignant	Adrenal carcinoma
2	43	F	Yes	10	L	NA*	Discordant	+	Malignant	Adrenal carcinoma
3	67	F	Yes	10	L	27	NI**	+	Malignant	Adrenal carcinoma
4	27	F	No	10	R	NA*	NA*	+	Malignant	Adrenal metastasis
5	39	F	No	3	R	32	Concordant	–	Benign	Adenoma
6	36	F	Yes	3	L	38.4	Concordant	–	Benign	Adenoma
7	56	M	No	3.5	L	0	Concordant	–	Benign	Adenoma
8	41	F	Yes	2.2	L	40	NA*	–	Benign	Adenoma
9	53	F	No	4	R	10	Concordant	–	Benign	Adrenal cystic lymphangioma
10	41	F	No	3.4	L	11	Concordant	–	Benign	Adenoma
11	41	F	Yes	3 + 1	R + L	47 on L	Concordant	–	Benign	Adenoma
12	70	F	No	5	R	20	Concordant	–	Benign	Adenoma
13	55	F	No	3	R	29	Concordant	–	Benign	Adenoma

*NA: not available; **NI: non-informative.

Concordant: increased uptake on adrenal mass; discordant: no uptake on adrenal mass.

Figure 1 Adrenocortical carcinoma with high ^{18}F -FDG uptake in a left adrenal tumour and increased uptake in the right liver corresponding to a hepatic metastasis (arrow) (case 3).

case 2, CT scan liver lesions which did not demonstrate ^{18}F -FDG uptake were found to be benign lesions at pathological examination. The fourth malignant lesion was an adrenal metastasis. The patient was seen for a large adrenal mass (10 cm), with a biopsy indicating a possible adrenocortical carcinoma. In fact, the ^{18}F -FDG examination showed not only adrenal uptake but also a renal uptake, which allowed us to reconsider the diagnosis: after a re-examination of the CT scan, a primary renal lesion was found (case 4).

Iodocholesterol scintigraphy showed that all the benign adrenocortical tumours had increased uptake in the adrenal mass detected at CT scan and that one of the three malignant adrenal tumours also had concordant uptake.

Discussion

Our preliminary results in adrenal lesions excluding pheochromocytoma and any previous history of cancer, show that all malignant tumours had

^{18}F -FDG uptake, while benign tumours showed no noticeable ^{18}F -FDG uptake.

Results with ^{18}F -FDG were superior to iodocholesterol for malignant tumours. Gross *et al.* (4) studied iodocholesterol scintigraphy in 229 patients with adrenocortical incidentalomas. They report a sensitivity of 71%, a specificity of 100%, a negative predictive value (NPV) of 91% and a positive predictive value of 100%. Lower sensitivity and NPV are due to lesions measuring less than 2 cm in size (4). When only incidentalomas larger than 2 cm are considered, sensitivity is 93% and specificity 100% (5). Nevertheless, we noted a small number of adrenocortical carcinomas measuring over 2 cm, and a high number of false negatives.

In our study, ^{18}F -FDG appears superior to an unenhanced CT scan with attenuation measurements. In the 13 resected lesions, attenuation value was over 11 HU in all the malignant adrenocortical tumours, and in 7 of the benign lesions as well. Moreover, in our study, ^{18}F -FDG provides information on secondary lesions or clarifies CT images (liver lesions, adrenal lesion with attenuation value above 10 HU). Non-hypersecretory adrenocortical adenomas typically have a high mean lipid content in contrast to malignant lesions. The lipid level found by histology is inversely proportional to the attenuation value of the lesion visualized by CT. Boland *et al.* (14) reviewed ten publications; their conclusion, useful for common practice, is that a 10 HU threshold for unenhanced density provides excellent sensitivity for the diagnosis of benign lesions (about 98%) but poor specificity (71%). The fact that our series included hypersecretory benign tumours (three out of nine benign tumours) could explain why attenuation values were high. These data are to be re-evaluated with a combination of unenhanced and delayed enhanced CT scans.

With ^{18}F -FDG, despite the favourable results, most studies have been performed in selected groups of oncology patients and in patients with an expected prevalence of adrenal metastases greater than in the general population, where histology for each lesion could only be evaluated by biopsy specimen and follow-up at CT (7–9).

Maurea *et al.* (10) investigated 26 patients with adrenal incidentaloma compared with CT (but without attenuation data) or magnetic resonance imaging: no significant ^{18}F -FDG uptake was observed in benign adrenal masses. One hundred per cent of malignant adrenal masses including adrenocortical carcinomas and adrenal metastases showed abnormally increased ^{18}F -FDG uptake. ^{18}F -FDG PET showed extra-adrenal locations. However, in this study (10), the adrenal lesions were not all operated on and diagnosis was also established on the basis of biopsy and follow-up. None of these studies gave the attenuation value at CT scan.

In our study, all benign adrenal tumours were ^{18}F -FDG-negative, but in the literature there are some

data concerning positive ^{18}F -FDG uptake and benign adrenal tumour (one case of myelolipoma, one case of adenoma with a sub-clinical Cushing's syndrome and one case of adrenal hyperplasia in Cushing's syndrome) (12, 13, 15). Only larger series will give more details and the prevalence of these findings.

Conclusion

^{18}F -FDG PET seems to be of potential value for the diagnosis of malignant or benign adrenocortical tumours. In malignant tumours, PET examination allows concomitant assessment of the disease stage. It could optimize the indications for surgery, in all cases (benign, malignant, small lesions). Our results need to be confirmed in larger series. As ^{18}F -FDG PET is a costly examination, its true diagnostic performance should be further studied, and evaluated in comparison with CT assessment using dynamic wash-out sequences.

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