Bronchogenic carcinoid tumours that are 18F-fluorodeoxyglucose avid on positron emission tomography

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Received 8 April 2013; received in revised form 6 June 2013; accepted 25 June 2013

Abstract

OBJECTIVES: Bronchogenic carcinoid tumours are widely cited as non-fluorodeoxyglucose (FDG) avid. However, three case reports of FDG-avid bronchogenic carcinoid tumours have been published, leading to speculation as to which clinicopathological factors may be associated with increased activity on FDG-positron emission tomography. We reviewed a series of cases from our institution and compared them with the available reports in the literature, to attempt to identify the factors associated with FDG avidity in bronchogenic carcinoids.

METHODS: We performed a single-institution retrospective review.

RESULTS: One patient was identified at our institution who had a typical carcinoid tumour with a standardized uptake value (SUV) of 26, oncocytic features on histology and positive staining for glucose transporter 1 (GLUT1). Three additional patients were identified in the literature with typical bronchogenic carcinoids with SUVs of 39, 38 and 33. Two of these tumours stained positive for GLUT1, and the remaining patient was not tested. Two of these patients had oncocytic features on histology, and results on the remaining patient are not reported.

Additionally, 4 patients at our institution were identified with bronchogenic carcinoids with average SUV of 2.6. All were GLUT1 negative, and none had oncocytic features.

In the reported literature, excluding the four most FDG-avid tumours described above, atypical carcinoids had a higher mean SUV than typical carcinoids (5.7 vs 3.4, P = 0.02), but size was not correlated with SUV (r = 0.7, P = 0.3).

CONCLUSIONS: FDG uptake is commonly associated with worse prognosis in malignancy; however, bronchogenic carcinoids, particularly oncocytic typical carcinoids, are a possible source of extremely high SUVs on FDG-PET.

Keywords: Bronchogenic carcinoid • FDG-PET • Oncocytic • GLUT1

INTRODUCTION

Increased glucose metabolism as measured by 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is used to stage a wide variety of malignancies, including lung cancer [1]. The high metabolic activity of malignant tissue is theorized to result in rapid uptake of FDG, which is a radioactive glucose analogue that can be imaged with PET. Initial reports suggested that FDG-PET has a low sensitivity for bronchogenic carcinoids [2, 3]. More recently, it has been recognized that FDG uptake in bronchogenic carcinoids is variable [4]. Despite several reports that bronchogenic carcinoids can be FDG-avid, they are still commonly cited as negative on FDG-PET in major textbooks [1]. The aims of this study are to raise awareness that bronchogenic carcinoids can be FDG-avid and to determine the clinical significance of FDG-avidity in this group of tumours.

MATERIALS AND METHODS

A single-institution retrospective review was performed in patients with bronchogenic carcinoids in whom preoperative FDG-PET and pathological glucose transporter 1 (GLUT1) data were available. A PubMed search for bronchogenic carcinoids with reported standardized uptake value (SUV) values on FDG-PET was conducted. Search terms were ‘carcinoid’ combined with ‘FDG’, ‘fluorodeoxyglucose’, ‘PET’ and/or ‘Positron Emission Tomography.’ Abstracts and manuscripts were reviewed for bronchogenic carcinoids, and bibliographies were reviewed for additional relevant papers. Group means were compared with the Student’s t-test. A linear regression analysis was used to correlate SUV with tumour size. All statistical tests were performed with the R software (www.r-project.org).

RESULTS

A 58-year old male ex-smoker presented with a round, smooth, well-demarcated 2 cm left lower lobe lung nodule. FDG-PET was obtained to further characterize the lesion, and the SUV was markedly elevated at 26 (Fig. 1). There were no other areas of abnormal tracer uptake concerning for metastasis. A transbronchial biopsy was performed, which showed a typical carcinoid with oncocytic histology. A lung-sparing anatomical resection (superior...
segmentectomy) was performed. Final pathological stage was T1aN0M0R0. The tumour was a 2.1 cm typical carcinoid tumour with appropriate strong reactivity with chromogranin and synaptophysin by immunohistochemistry and oncocytic features on histology (Fig. 2A). A GLUT1 stain was diffusely positive (Fig. 2B). The patient is asymptomatic with no evidence of recurrence on repeat imaging 7 years later.

Four additional patients with carcinoid tumours who had undergone FDG-PET were identified from our institution, all with moderately elevated FDG-avidity (average SUV 2.6), and the resected specimens were stained for GLUT1. All were negative. The specimens were also re-examined for histological evidence of oncocytic features, and none were present (Fig. 2C). All these tumours displayed appropriate strong reactivity with chromogranin and synaptophysin by immunohistochemistry.

**DISCUSSION**

An influential early series of patients with bronchogenic carcinoid reported low FDG avidity (average SUV 2.4) and a high rate of negative FDG-PET scans; 86% (6/7) of patients had SUV below 2.5 [2]. Low FDG uptake in carcinoids was confirmed by other authors [3], and carcinoids became well-known as a common cause of false-negative FDG-PET scans [1]. More recently, however, three cases of extremely FDG-avid bronchogenic carcinoids with SUVs of 39 [5], 38 [6] and 32.9 [7] have been reported in the literature, and the patient who prompted this series is the fourth (SUV = 26). Three of these four tumours stained positive for GLUT1 (the fourth was not stained), and three tumours have the oncocytic histotype (unspecified in the fourth tumour). All four of the extremely FDG-avid tumours are typical carcinoids. The long-term follow-up is available on 2 of the patients, and both had a favourable outcome [5 and the current report].

Excluding the four cases of extremely FDG-avid bronchogenic carcinoids from the dataset, the pooled available literature describing patients with carcinoid tumours in whom FDG-PET results were reported supports the view that atypical carcinoids are more FDG-avid than typical carcinoids (Table 1). Mean SUVs were higher in the atypical group (5.7 vs 3.4, *P* = 0.02). There was no correlation between tumour size and SUV (*r* = 0.7 and 0.3). Not enough data on clinical outcomes were available to make comparisons between outcome and SUV in the literature.
Various predictors of FDG activity in bronchogenic carcinoids have been suggested. Atypical carcinoids might be more metabolically active and therefore more FDG-avid than typical carcinoids [4, 11–18], as we found to be the case in this review. An association has been suggested between FDG-avidity and tumour size [2, 4, 13], but this hypothesis was not supported by the current analysis. Lesions that are metastatic might have higher FDG-avidity [7], but data on metastasis were not available in this study. Expression of the GLUT1 glucose transport protein might predict glucose uptake and, therefore, FDG avidity [5, 7, 19]. This was found to be the case in at least three of the four most FDG-avid carcinoids in the literature. However, several cases of less extremely FDG-avid bronchogenic carcinoids (SUVs 4.9 and 6.0) have stained negative for GLUT1 expression [12].

We found extremely high levels of FDG uptake on PET in carcinoid tumours with the oncocytic histotype. Since an oncocytic appearance on histology is due to an abundance of mitochondria in the cytoplasm, and mitochondria are a main site of glucose metabolism, it is not surprising that these tumours have increased glucose uptake resulting in increased FDG avidity. High SUVs on FDG-PET have also been reported in oncocytic tumours of the pancreas, an oncocytic Schneiderian papilloma, and an oncocytic tumour of the parotid.

Bronchogenic carcinoids have a wide range of FDG-avidity. Based on published studies reviewed here, typical carcinoids often have lower SUVs than atypical carcinoids, and a mild elevation in SUV in a tumour that otherwise appears to be a bronchogenic carcinoid should raise the suspicion of an atypical carcinoid. Markedly elevated SUVs (20s–30s), on the other hand, appear to be associated with the oncocytic histotype of typical carcinoid tumour and positive staining with GLUT1, but not with a poor prognosis.

### CONCLUSIONS

High FDG uptake is commonly associated with more aggressive malignancies, but it is important to remember that some indolent tumours (e.g. typical carcinoids) can also be very FDG-avid. Oncocytic typical carcinoids should be kept in mind as a possible source of extremely high SUVs on FDG-PET.

### Funding

The authors acknowledge the support of the Ryan Hill Foundation and the Foundation for Surgical Fellowships.
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