

MULTIMEDIA ARTICLE - Clinical Imaging

Positron Emission Tomography with 2-Deoxy-2-[¹⁸F] Fluoro-D-Glucose in the Detection of Malignancy in Intraductal Papillary Mucinous Neoplasms of the Pancreas

Brian KP Goh¹, Yaw-Fui Alexander Chung^{1,4}, David CE Ng², Sathiyamoorthy Selvarajan³, Khee-Chee Soo^{1,4}

Departments of ¹Surgery, ²Nuclear Medicine, and ³Pathology, Singapore General Hospital; ⁴Department of Surgical Oncology, National Cancer Centre. Singapore, Singapore

Summary

A 79-year-old Indian male was admitted with upper abdominal discomfort of 1-year duration which was associated with loss of weight and appetite. Serum tumor markers, including carcinoembryonic antigen and carbohydrate antigen 19-9, were within normal limits. A computed tomographic scan demonstrated a cystically dilated and tortuous pancreatic duct measuring 1.9 cm, suggestive of an intraductal papillary mucinous neoplasm. Fusion positron emission tomography/computed tomography with 2-deoxy-2-[¹⁸F] fluoro-D-glucose positron emission tomography (FDG-PET/CT) which was subsequently performed confirmed a metabolically active focus within the pancreatic head mass with a standard uptake value (SUV_{max}) of 3.5 compatible with carcinoma. A total pancreatectomy was performed and the final histology demonstrated a main-duct type intraductal papillary mucinous neoplasm with a focus of high-grade dysplasia compatible with carcinoma-in-situ. These images illustrate the emerging utility of FDG-PET/CT in the preoperative detection of malignancy in intraductal papillary mucinous neoplasm.

A 79-year-old Indian male was admitted with upper abdominal discomfort of 1-year duration which was associated with loss of weight and appetite. Clinical examination of the abdomen did not reveal any palpable masses. Laboratory investigations including a complete blood count, liver function tests and serum amylase were unremarkable. Standard serum tumor markers were within normal limits: carbohydrate antigen (CA) 19-9, 13.4 U/mL (reference range: 3-45 U/mL); carcinoembryonic antigen (CEA), 1.4 µg/L (reference range: 0.5-3.5 µg/L) and alpha-fetoprotein, 1.3 µg/L (reference range: 1-10 µg/L). A contrast-enhanced computed tomographic (CT) scan demonstrated a cystically dilated and tortuous pancreatic duct measuring 1.9 cm, suggestive of an intraductal papillary mucinous neoplasm (IPMN). The common bile duct was dilated up to the level of the ampulla and a 3.2x2.0 cm heterogeneous soft tissue mass was observed in the head of the pancreas which extended into the duodenum, suggestive of a malignant lesion (Images 1 and 2). Fusion positron emission tomography/computed tomography (PET/CT) was subsequently performed with 12.7 mCi of 2-deoxy-2-[¹⁸F] fluoro-D-glucose (¹⁸F-FDG) administered intravenously. A whole body PET/CT scan



Image 1

was performed 60 minutes later with CT data used for attenuation correction and anatomical correlation. This confirmed a metabolically active focus within the pancreatic head mass with a standard uptake value (SUV_{max}) of 3.5 compatible with carcinoma (Image 3).

The patient underwent exploratory laparotomy whereby the entire pancreas demonstrated features compatible with IPMN. A 3.0 cm hard nodule was also found within the head of the pancreas. A total pancreatectomy was performed and the final histology revealed a main-duct type IPMN with a focus of high-grade dysplasia compatible with malignant IPMN with carcinoma-in-situ (Image 4). There were no invasive features and the resected margins were free of tumor. The surrounding pancreatic parenchyma was markedly atrophic with fibrosis and chronic inflammation compatible with chronic

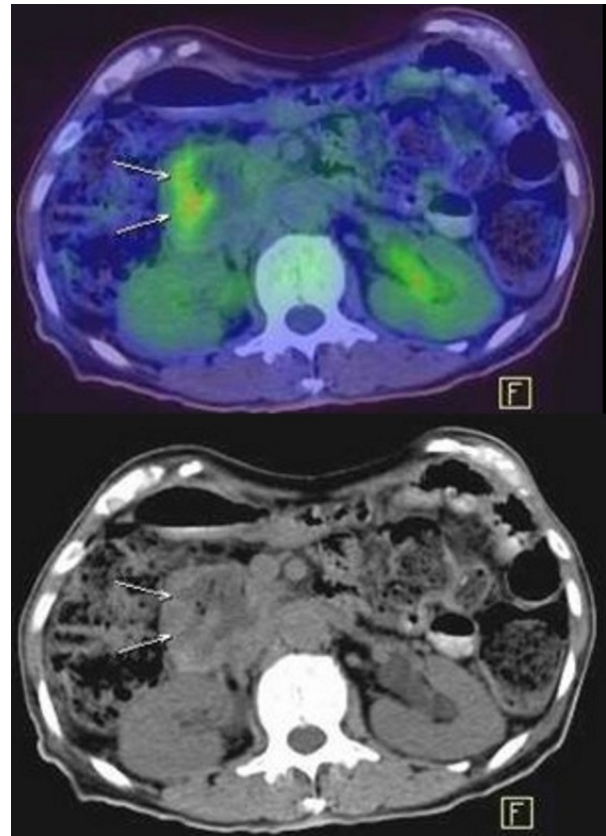


Image 3

pancreatitis. The patient's postoperative recovery was uneventful and he was discharged on the 8th postoperative day.

Discussion

IPMNs have a wide-spectrum of histological grades ranging from benign to malignant neoplasms [1]. Presently, most investigators



Image 2

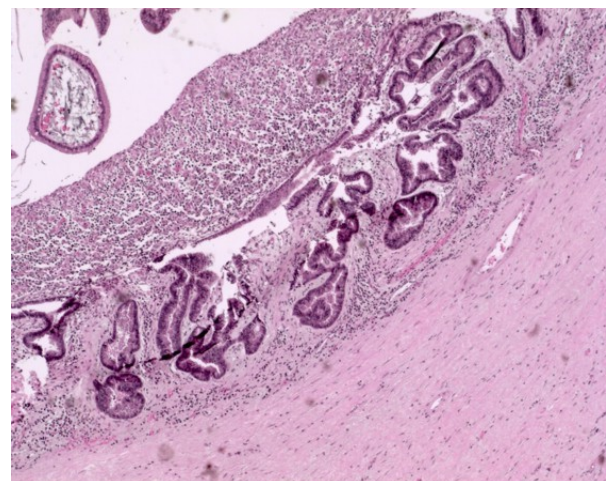


Image 4

consider IPMNs at the very least pre-malignant and hence surgical resection is advocated in most instances especially for a main-duct type IPMN. However, the preoperative determination of malignancy of IPMN remains important as the extent of surgical resection may be dependent on the degree of malignancy. 'Less radical' organ-preserving resections, such as duodenum-preserving pancreatic head resection and spleen-preserving distal pancreatectomy, may be performed for non-malignant lesions [2]. Moreover, conservative management may be a viable option for benign or borderline lesions in high-risk patients with a shorter life-expectancy as observational studies suggest a time-lag of at least 5 years for the progression from benign to malignant IPMNs [3]. Currently, the preoperative determination of malignancy in IPMNs remains difficult if not impossible. Studies have demonstrated that preoperative factors such as the presence of diabetes, mural nodules, large tumor size, marked dilatation of the pancreatic duct and main duct-type tumors are predictive of malignancy in IPMN but these are usually not sufficiently accurate [2, 4].

FDG-PET/CT is a functional/anatomical imaging modality which detects abnormalities in glucose metabolism using a glucose analogue together with anatomic correlation [5]. Studies have demonstrated the accuracy of this imaging in the diagnosis of pancreatic carcinoma with results comparable or even superior to conventional methods [5, 6, 7, 8]. However, experience with FDG-PET in the evaluation of cystic lesions of the pancreas including IPMNs is presently limited. Presently, only 4 studies addressing the role of FDG-PET in the evaluation of IPMNs have been reported in the English literature [9, 10, 11, 12]. As a whole, these studies have successfully demonstrated the accuracy of FDG-PET in distinguishing malignant from benign or borderline IPMNs.

The use of FDG-PET in the management of cystic lesions of the pancreas was first reported by Sperti *et al.* from Padua [9]. They retrospectively evaluated 56 patients with cystic lesions of the pancreas comparing

FDG-PET and CT scans using a standardized uptake value (SUV) greater than 2.5 as positive for malignancy. FDG-PET had sensitivity, specificity, positive and negative predictive values, and accuracy in detecting a malignant cyst of 94%, 97%, 94%, 97%, and 96%, respectively, as compared to CT with values of 65%, 87%, 69%, 85%, and 80%, respectively. The same group subsequently performed a follow-up prospective study of 50 patients with virtually identical results [10]. The sensitivity, specificity, positive and negative predictive values and accuracy of FDG-PET in the second study were 94%, 94%, 89%, 97%, and 94%, respectively, as compared to the figures for CT (65%, 88%, 73%, 83%, and 80%, respectively). When we carefully analyzed their results for IPMNs alone, FDG-PET correctly distinguished all IPMNs as benign (8/8) or malignant (1/1) in their initial study [9]. In their second study, FDG-PET correctly diagnosed 8/8 benign and 8/8 malignant IPMNs [10]. However, a recent study from the Sloan-Kettering Memorial Cancer Center addressing the utility of FDG-PET in 68 patients with cystic lesions of the pancreas demonstrated a sensitivity and specificity of only 57% and 85%, respectively, in detecting a malignant cystic lesion [12]. FDG-PET correctly diagnosed 3/3 benign and 1/2 malignant IPMNs [12].

Besides these three studies, Yoshioka *et al.* from Japan reported two cases of histologically-proven invasive malignant IPMNs successfully diagnosed via FDG-PET [11]. The first patient had a 4.5 cm cystic lesion with a 1.5 cm solid mass visible on CT. This was confirmed as malignant on FDG-PET demonstrating a SUV_{max} of 6.0. In the second case, on CT, a 3 cm cystic lesion with no solid components was demonstrated. FDG-PET demonstrated an area of increased uptake in the cyst with a SUV_{max} of 2.6. Hence, from a review of the literature including our current case [9, 10, 11, 12], FDG-PET is extremely accurate in the preoperative evaluation of malignancy in IPMNs. FDG-PET utilizing a SUV_{max} cut-off of 2.5 was correct in 32/33 cases of IPMNs (19 benign) reported previously with only one false negative result.

However, in the absence of large controlled trials, it is possible that the overall results which have been published may be somewhat over-optimistic due to reporting bias.

It is known that potential limitations of the specificity of PET/CT in the diagnosis of pancreatic carcinoma includes its use on patients with chronic pancreatitis who had previously undergone upper gastrointestinal surgery, patients with an acute exacerbation of chronic pancreatitis, patients with pancreatitis-related complications such as intracystic hemorrhage which can lead to non-specific FDG accumulation and patients who have undergone recent interventional procedures (stent, probe placement) [13]. These limitations may potentially exist in IPMNs as patients with IPMNs frequently have pathologic evidence of concomitant pancreatitis secondary to ductal occlusion from the abundant mucin-production [1, 3]. A potential false negative in the use of FDG-PET/CT is the presence of diabetes mellitus as the values of tumor uptake of FDG are lower in insulin-dependant diabetes patients as compared to non-diabetics [8]. As patients with IPMNs frequently have diabetes due to their advanced age and tumor involvement of the pancreas, one should be aware of this potential confounding factor in these patients. However, although false-positive results of FDG-PET have been reported with other cystic lesions of the pancreas such as mucinous cystic neoplasms, Tangier's disease and pancreatic pseudocysts [9, 10], to the best of our knowledge, this has never been reported for IPMNs.

In conclusion, this case illustrates the emerging utility of FDG-PET/CT in the preoperative detection of malignancy in IPMNs which may be important in preoperative planning. Further studies are required to determine the accuracy of FDG-PET/CT in demonstrating malignancy preoperatively in patients with IPMN.

Received March 5th, 2007 - Accepted March 25th, 2007

Keywords Diagnosis; Pancreatic Neoplasms; Positron-Emission Tomography

Abbreviations ¹⁸F-FDG: 2-deoxy-2-[¹⁸F] fluoro-D-glucose; SUV: standard uptake value

Correspondence

Brian KP Goh
Department of Surgery
Singapore General Hospital
Outram Road
Singapore 169608
Singapore
Phone: +65-632.140.51
Fax: +65-622.093.23
E-mail: bsgkp@hotmail.com

Document URL: <http://www.joplink.net/prev/200705/11.html>

References

1. Goh BK, Tan YM, Cheow PC, Chung YF, Chow PK, Wong WK, Ooi LL. Cystic neoplasms of the pancreas with mucin-production. *Eur J Surg Oncol* 2005; 31:282-7.
2. Jang JY, Kim SW, Ahn YJ, Yoon YS, Choi MG, Lee KU, et al. Multicenter analysis of clinicopathologic features of intraductal papillary mucinous tumor of the pancreas: is it possible to predict the malignancy before surgery? *Ann Surg Oncol* 2005; 12:124-32.
3. Goh BK, Tan YM, Cheow PC, Chung YF, Chow PK, Wong WK, Ooi LL. Cystic lesions of the pancreas: an appraisal of an aggressive resectional policy adopted at a single institution during 15 years. *Am J Surg* 2006; 192:148-54.
4. Lai EC, Lau WY. Intraductal papillary mucinous neoplasms of the pancreas. *Surgeon* 2005; 3:317-24.
5. Rose DM, Delbeke D, Beauchamp RD, Chapman WC, Sandler MP, Sharp KW, et al. 18Fluorodeoxyglucose-positron emission tomography in the management of patients with suspected pancreatic cancer. *Ann Surg* 1999; 229:729-38.
6. Balci NC, Semelka RC. Radiologic diagnosis and staging of pancreatic ductal adenocarcinoma. *Eur J Radiol* 2001; 38:105-12.
7. Kalra MK, Maher MM, Mueller PR, Saini S. State-of-the-art imaging of pancreatic neoplasms. *Br J Radiol* 2003; 76:857-65.
8. Goh BK, Tan YM, Chung YF. Utility of fusion CT-PET in the diagnosis of small pancreatic carcinoma. *World J Gastroenterol* 2005; 11:3800-2.

9. Sperti C, Pasquali C, Chierichetti F, Liessi G, Ferlin G, Pedrazzoli S. Value of 18-fluorodeoxyglucose positron emission tomography in the management of patients with cystic tumors of the pancreas. *Ann Surg* 2001; 234:675-80.

10. Sperti C, Pasquali C, Decet G, Chierichetti F, Liessi G, Pedrazzoli S. F-18-Fluorodeoxyglucose positron emission tomography in differentiating malignant from benign pancreatic cysts: a prospective study. *J Gastrointest Surg* 2005; 9:22-9.

11. Yoshioka M, Sato T, Furuya T, Shibata S, Andoh H, Asanuma Y, et al. Positron emission tomography with 2-deoxy-2-[¹⁸F] fluoro-d-glucose for diagnosis

of intraductal papillary mucinous tumor of the pancreas with parenchymal invasion. *J Gastroenterol* 2003; 38:1189-93.

12. Mansour JC, Schwartz L, Pandit-Taskar N, D'Angelica M, Fong Y, Larson SM, et al. The utility of F-18 fluorodeoxyglucose whole body PET imaging for determining malignancy in cystic lesions of the pancreas. *J Gastrointest Surg* 2006; 10:1354-60.

13. Friess H, Langhans J, Ebert M, Beger HG, Stollfuss J, Reske SN, Buchler MW. Diagnosis of pancreatic cancer by 2[¹⁸F]-fluoro-2-deoxy-D-glucose positron emission tomography. *Gut* 1995; 36:771-7.