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Pozytonowa tomografia emisyjna (^{18}FDG-PET) w poszukiwaniu przerzutów raka rdzeniastego tarczycy

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Streszczenie

Wstęp: Rak rdzeniasty tarczycy zwykle jest rozpoznawany w stadium bardziej zaawansowanego guza niż raki zróżnicowane i często z przerzutami. Leczeniem z wyboru jest całkowite wycięcie tarczycy i regionalnych węzłów chłonnych. Skuteczność tych zabiegów bywa ograniczona, co wiąże się z agresywnością choroby i jej zaawansowaniem w momencie operacji. Utrzymujące się lub ponownie podwyższone stężenia kalcytoniny (CT) i antygenu rakowo-płodowego (CEA) wskazują na obecność resztkowej choroby lub wznowę procesu. Jednak nie zawsze rutynowo wykonywane badania obrazowe (USG, TK, MRI, scyntygrafia MIBI) prowadzą do znalezienia źródła kalcytoniny. Większą czułość wykazuje scyntygrafia DMSA, receptorów somatostatynowych i pozytonowa tomografia emisyjna (PET).
Celem niniejszej pracy była ocena przydatności badania PET w celu zlokalizowania ognisk wznowy i/lub przerzutów raka rdzeniastego u chorych z podwyższonymi stężeniami kalcytoniny po leczeniu operacyjnym, u których rutynowymi metodami nie znaleziono ogniska nowotworu.
Materiał i metody: Badanie PET z wykorzystaniem ^{18}F-fluoro-2-deoksy-D-glukozy, połączone z tomografią komputerową (^{18}FDG-PET/CT), przeprowadzono w Zakładzie Medycyny Nuklearnej Centrum Onkologii w Bydgoszczy między styczniem a październikiem 2004 roku. Badanie to wykonano u 5 chorych, u których obserwowano podwyższone pooperacyjne stężenia kalcytoniny (164,0 – > 2000,0 ng/l; norma < 10,0 ng/l), a rutynowe badania obrazowe nie lokalizowały podejrzanych ognisk.
Wyniki: U 4 spośród 5 chorych wykazano w tym badaniu obecność ognisk o zwiększonym metabolizmie ^{18}FDG, które wskazywały na umiejscowienie zmiany nowotworowej. W jednym przypadku nie stwierdzono wyraźnego ogniska wzmożonego metabolizmu znacznika, mimo wysokich stężeń kalcytoniny. Rozpoznane ogniska zlokalizowane były w dwóch przypadkach na szyi i w śródpiersiu, w jednym w płucu i lewym nadnerczu, a w jednym na szyi i w wątrobie. W wyniku przeprowadzonych powtórnych operacji, u wszystkich chorych potwierdzono histopatologicznie prawidłowość rozpoznania, a w 3 przypadkach stwierdzono obniżenie stężeń kalcytoniny i CEA, co świadczy o skuteczności leczenia chirurgicznego opartego na obrazach z badania PET/CT.
Wnioski: Pozytonowa tomografia emisyjna stanowi cenną metodę diagnostyki obrazowej w poszukiwaniu przerzutów raka rdzeniastego tarczycy o trudnej do ustalenia lokalizacji.

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Słowa kluczowe: *rak rdzeniasty tarczycy, pozytonowa tomografia emisyjna, przerzuty*

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Positron emission tomography (^{18}FDG-PET) in the detection of medullary thyroid carcinoma metastases

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Abstract

Introduction: Medullary thyroid carcinoma (MTC) is usually more advanced at presentation than differentiated thyroid cancers and often has distant metastases. The primary treatment of MTC is total thyroidectomy and regional lymph node dissection. The efficacy of these procedures has been limited by the aggressiveness of the disease and metastatic spread at the time of surgery. Persistently elevated levels of calcitonin (CT) and carcinoembryonic antigen (CEA) or their increase postoperatively are indicative for residual or recurrent disease. Conventional imaging methods such as ultrasonography, computed tomography, magnetic resonance imaging and MIBI scintigraphy usually fail to find the source of calcitonin. Better imaging properties have been shown by DMSA scintigraphy, somatostatin receptor scintigraphy or by positron emission tomography (PET).

The aim of the study was to evaluate the diagnostic accuracy of PET for the localisation of occult MTC in patients after surgery with increased concentrations of CT, in whom conventional imaging procedures have not been successful.

Material and methods: The PET investigation using ^{18}F-fluoro-2-deoxy-D-glucose combined with computed tomography (^{18}FDG-PET/CT) was performed at the Department of Nuclear Medicine (Oncology Centre in Bydgoszcz) between January and October 2004. In five patients with postoperative calcitonin ranging from 164 to > 2000 ng/l (normal < 10 ng/l) no tumour lesions were found using other imaging methods.

Results: In four of five cases, responsible lesions with a higher metabolism of FDG, indicating MTC tissue (remnants or metastases), were localised. In one patient no focus of FDG accumulation was found despite high CT concentration. PET detected tumour manifestations in the neck and the mediastinum in two patients, in the lung and the left adrenal gland in one case and in the neck and the liver in another patient. As a result of surgery for the removal of a residual tumour or metastases the accuracy of diagnosis was confirmed by histopathology in all four cases and a decrease in CT and CEA levels was observed in 3/4 cases. The metabolic imaging findings by PET/CT ensured that the surgery on these patients was successful.

Conclusions: For the detection of occult residual or metastatic MTC lesions, ^{18}FDG-PET is a valuable procedure in imaging diagnostics.

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Key words: *medullary thyroid carcinoma, positron emission tomography, metastases*

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Introduction

Medullary thyroid carcinoma (MTC) is a neoplasm of the thyroid parafollicular C cells that accounts for 5–8% of all thyroid cancers [1]. MTC produce calcitonin (CT), a specific marker, and carcinoembryonic antigen (CEA), a non-specific tumour marker. MTC may occur either sporadically or in a hereditary form as familial MTC including multiple endocrine neoplasia type 2A or type 2B and isolated familial MTC [2]. Both forms of MTC are characterised by relatively slow tumour growth but early lymphatic metastatic spread. Of the well differentiated thyroid carcinomas MTC is the most aggressive, with survival rates of 40–50% at 10 years [3]. Neck lymph node metastases are detected in at least 50% of patients, and metastases outside the neck, in the liver, lungs or bones, are present initially in 20% of cases [1]. The primary treatment of MTC is total thyroidectomy and bilateral lymph node dissection. Several studies have shown that survival in patients with MTC is dependent upon the adequacy of the initial surgical procedure. Unfortunately, even with aggressive surgery, most patients with MTC do not achieve normalisation of postsurgical serum CT and CEA levels. Biochemical cure is obtained in only 20–30% of patients with lymph node metastases, and

rarely in patients with extensive lymph node involvement or distant metastases [4].

In patients with persistently elevated or again increased CT levels, the challenge to find the site of the residual or recurrent disease, since surgical resection is at the moment the only curative treatment. Tumour localisation techniques include ultrasonography (US) of the neck and liver, computed tomography or magnetic resonance imaging (MRI) of the neck, chest and liver. The scintigraphic studies used in the evaluation of MTC such as ^{99m}Tc-sestamibi (MIBI), pentavalent ^{99m}Tc-dimercaptosuccinic acid (DMSA), ^{123}I/^{131}I-metaiodobenzylguanidine (MIBG), and somatostatin analogues labelled with ^{111}In (SRS) are poorly sensitive, especially for small lesions [5]. ^{18}F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (^{18}FDG-PET), as a functional imaging technique that relies on *in vivo* visualisation of lesional glucose metabolism, differs from conventional imaging procedures [6]. FDG-PET scanning in patients with MCT offers a potential approach to the detection of recurrent or metastatic disease [7–9]. The aim of the present study was to evaluate the diagnostic accuracy of PET for the localisation of occult MTC in patients after surgery with increased concentrations of CT, in whom conventional imaging procedures have been failed.

Material and methods

PET investigation using ^{18}F-fluoro-2-deoxy-D-glucose combined with computed tomography (^{18}FDG-PET/CT) was performed at the Department of Nuclear Medicine (Oncology Centre in Bydgoszcz) between January and October 2004. In five patients (three women and two men, aged 43–83 years) with postoperative CT ranging from 164.0 to > 2000.0 ng/l (normal < 10 ng/l), no tumour lesions were found using other imaging methods. All our patients had been diagnosed earlier using US of the abdomen, computed tomography and MRI of the neck and the chest and whole body SRS.

Results

In four of five cases the lesions responsible, with a higher metabolism of ^{18}FDG indicating MTC tissue (remnants or metastases), were localised. In one patient no focus of FDG accumulation was found, despite high CT and CEA concentrations. PET/CT detected tumour manifestations in the neck and the mediastinum in two patients and in the neck and liver an another patient. In a male with confirmed MEN2A syndrome [10] after earlier right adrenalectomy, foci of increased metabolism of ^{18}FDG were identified in the lung and in the left adrenal gland. In only one PET study the diameter of a focus of 12 mm in the neck region was given precisely. In another PET investigations only the localisation of the MTC remnants and/or metastases, without information concerning their diameters, was suggested by radiology. On the basis of the results of histopathological studies, the tissues removed were found in one case to be a local recurrence in the neck and metastatic lymph nodes. In other patients the source of CT and CEA were the cervicomediastinal lymph nodes with neoplastic infiltration of the capsule. Four of the patients investigated underwent surgery for the removal of a residual tumour or metastases. The accuracy of the diagnosis was confirmed by histopathology in all four cases. Postoperatively, a significant decrease in CT and CEA levels was observed in three cases.

Discussion

Conventional radiographic and radionuclide imaging often fail to localise recurrent or metastatic medullary thyroid carcinoma, resulting in poor outcome of the disease. In the search for a more reliable method ^{18}FDG-PET has been applied to detect MTC tissue, which has a high potential for metastasis. Studies of the clinical role of FDG-PET in the diagnosis and staging of recurrent and metastatic MTC have shown encouraging results. Musholt et al. [7] compared the accuracy of FDG-PET with that of computed tomography and MRI scans and found that PET imaging was more sensitive in the detection of cervicomediastinal MTC metastases. A study by Szakall et al. [8] suggested that FDG-PET was a highly sensitive method for localising metastases in MTC patients with elevated postsurgical CT levels. PET demonstrated more lesions in the neck and the mediastinum than were found by other imaging methods, but it failed to detect many small lesions in the lung and liver. The lack of attenuation correction in their study and the relatively low sensitivity of PET for small pulmonary metastases were probable reasons for a decreased tumour detection rate in the lung and liver. However, in contrast to this, we found on PET scans one metastatic focus in the liver in one case and one lesion of increased FDG metabolism in the lung in an another patient. The metabolic imaging findings by PET in these patients have been observed to result in a higher biochemical cure rate obtained by further surgery.

A recent prospective study of 26 patients reported that ^{18}FDG-PET is superior to conventional imaging techniques for the detection of recurrent or metastatic MTC [9]. The sensitivity was 96% for FDG-PET, 41% for ^{111}In-SRS, 57% for DMSA, and 87% for morphological imaging (US, computed tomography, MRI) combined with bone scintigraphy. In our study positive ^{18}FDG-PET findings led to more radical surgical intervention in four out of five patients. In three of them

meticulous lymph node dissection and the removal of distant metastases resulted in a decrease in CT and CEA levels, which are sensible markers of active MTC. Although the diagnosis of disseminated MTC was confirmed by histopathology of the removed tissues in all four cases, it was suggested that undiagnosed foci of the disease remained in one patient without a postsurgical decrease in CT and CEA. Interestingly, retrospective analysis of computed tomography and MRI scans revealed the presence of MTC foci in the neck, which were later found in one case by the PET study.

As the most recent nuclear medicine imaging procedure ^{18}FDG-PET appears to be a promising diagnostic technique for the detection of recurrent or metastatic MTC. Despite the high cost and lack of availability of PET, this method may serve to increase the cure rate and to prolong survival in patients with MTC.

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