^{18}F-FDG PET/CT, ^{123}I-MIBG and ^{99m}Tc-MDP whole-body scans, in detecting recurrence of an adult adrenal neuroblastoma

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Abstract
Neuroblastoma is the most common extracranial solid malignancy in children, but is rare in adults. *We report* the case of a 33 years old man with recurrence of neuroblastoma, 2 years after the excision of the primary tumor in the right adrenal gland. The iodine-123-radioiodinated metaiodobenzylguanidine (^{123}I-MIBG) and ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) bone scans and the fluorine-18-fluorodeoxy glucose-positron computed tomography (^{18}F-FDG PET/CT) findings in this patient are presented. First, *we applied* ^{123}I-MIBG scintigraphy that detected increased uptake at the right adrenal gland region and probably at liver lesions and in several bones. Then, the ^{99m}Tc-MDP bone scan also revealed increased uptake of the radiopharmaceutical in bones, but there was a discrepancy between these two studies concerning the number and location of the lesions. Then, ^{18}F-FDG PET/CT scan was performed, which showed increased uptake of ^{18}F-FDG at the right adrenal gland region with extension to the liver and also in multiple bones. Additionally, an aortocaval lymph node was detected. *In conclusion*, this case indicated that ^{18}F-FDG PET/CT had defined the extent of the recurrence of neuroblastoma in a better way than ^{123}I-MIBG and ^{99m}Tc-MDP together.

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Introduction

Neuroblastoma is the most common extracranial solid malignancy in children [1]. The mean age of diagnosis is 2 years, with 35% of the cases occurring before the age of 1 year. The incidence in adulthood is only 0.12-0.2 cases per million inhabitants per year [2]. Due to the rareness of neuroblastomas in adults, the data about their prognosis are scarce. Its ultimate outcome is poor, regardless of the initial disease stage [3, 4]. Biologic characteristics in adults differ from those in children [4]. The most common site of origin of neuroblastoma is within the abdomen, with the adrenal gland being the primary tumor site in 38% of cases [5].

In this article we report a rare case of neuroblastoma in a 33 years old man examined by ^{123}I-radioiodinated metaiodobenzylguanidine scintigraphy (^{123}I-MIBG), ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) and the fluorine-18-fluorodeoxy glucose-positron computed tomography (^{18}F-FDG PET/CT) scans after recurrence, 2 years after the excision of the primary tumor in the right adrenal gland. The findings between these three scans are discussed.

Description of the case

A 33 years old man presented with persistent pyelonephritis. Renal ultrasonography was performed which revealed a mass of 7x7x6.5cm of the right adrenal gland. He underwent a complete surgical right adrenal gland resection. Histopathology showed the presence of neuroblastoma, with clear surgical margins. The patient was diagnosed as stage I, according to the international neuroblastoma staging system (INSS) [6]. Chemotherapy and/or radiotherapy had not been applied after the surgery. The patient entered a follow-up program and two years later, urine dopamine and homovanillic acid were increased: 873μg/24h (normal range: 65-400μg/24h) and 17.1mg/24h (normal value<6.2mg/24h), respectively. Imaging, with CT and magnetic resonance imaging (MRI), demonstrated equivocal findings in the abdomen and could not differentiate between scarring, fibrosis or relapse at the surgical field area.

Then, the patient underwent imaging with nuclear medicine imaging modalities: ^{123}I-MIBG, ^{99m}Tc-MDP bone scan and ^{18}F-FDG PET/CT. These three methods were performed within 20 days. First, ^{123}I-MIBG scintigraphy showed increased uptake at the anatomic region of the right adrenal gland with possible liver lesions in the same area, in two thoracic vertebrae and in one rib (Fig. 1). Then, the ^{99m}Tc-MDP bone scan showed increased uptake in three ribs and in one thoracic vertebra (Fig. 2). As there was a discrepancy between these results, concerning bone metastases, ^{18}F-FDG PET/CT scan was performed. Although the delivered radiation dose of the ^{18}F-FDG PET/CT scan was about 21mSv and increased the accumulative dose of all three methods of nuclear medicine to 31mSv, it was asked by the oncologists because accurate staging was required as probable surgical or radiotherapy interventions would be needed in the course of treatment protocol. The total radiation dose of all imaging methods, including CT scan, was 41mSv.

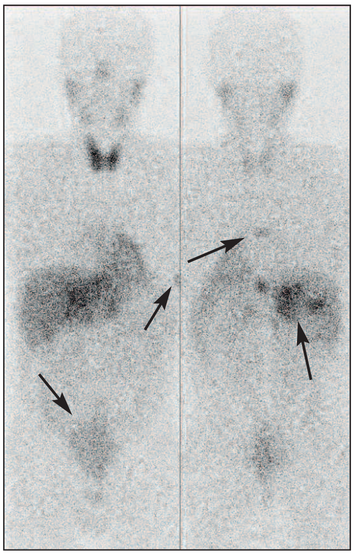

Figure 1. The ^{123}I-MIBG scans,anterior and posterior view, showed increased uptake at the anatomic region of the right adrenal gland with possible lesions in the liver, in one of the middle and in one of the lower thoracic vertebrae and in one of the lower left ribs (arrows).

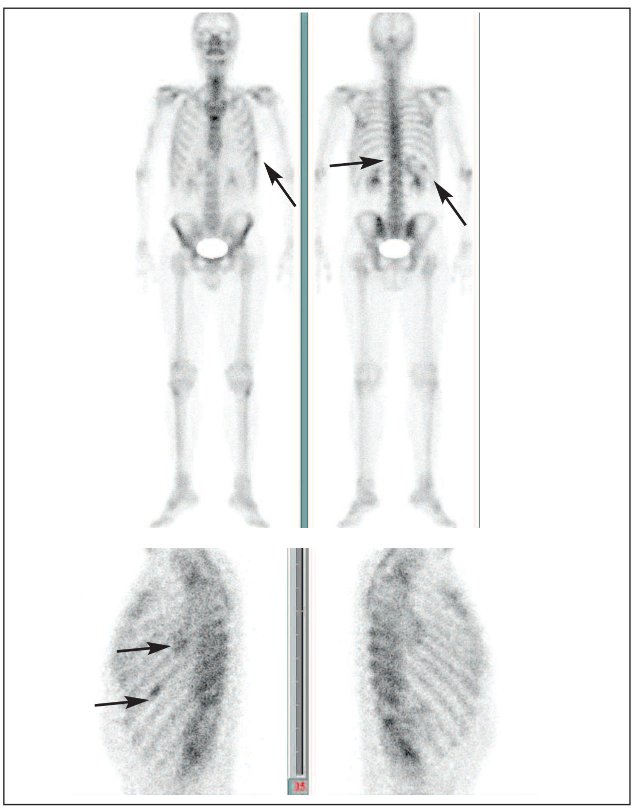

Figure 2. The ^{99m}Tc-MDP bone scan showed increased uptake in the 5th left, 6th left and the 11th right ribs and in the T11 vertebra (arrows).

The ^{18}F-FDG PET/CT tomographic scan showed increased uptake in a pathological tissue, at the anatomic region of the right adrenal gland, compatible with local recurrence that extended to the segment I of the liver, in two thoracic vertebrae (T7 and T11), in lateral area of the 5th and 6th left ribs and additionally in an aortocaval lymph node (Fig. 3). Thus, the ^{18}F-FDG PET/CT scan not only localized accumulatively the lesions found with the other two methods but additionally detected a small abdominal lymph node metastasis, that had not been recognized before. The ^{18}F-FDG PET/CT has the advantage of using a low dose CT, for better localizing the lesions. The ^{99m}Tc-MDP bone scan showed a false positive lesion in an old rib fracture in the 11th right rib. This lesion was not detected by the other imaging methods and according to the patient's history it was due to an old fracture.

As there is no established treatment for neuroblastoma in adults, treatment of recurrence followed the guidelines for pediatric neuroblastoma, and treatment was given according to the pediatric protocol HRNBL1.5/SIOPEN [1, 7]. Surgery was performed two years before the detection of the recurrence and the treatment that we refer to. The patient received high dose chemotherapy with 3 cycles of cyclophosphamide-adriamycin-vincristine and 2 cycles of cisplatin-etoposide followed by one cycle of high dose busulfan-melphalan with peripheral stem cell transplantation support. Two months after the completion of this treatment, imaging with ^{123}I-MIBG and ^{18}F-FDG PET/CT showed

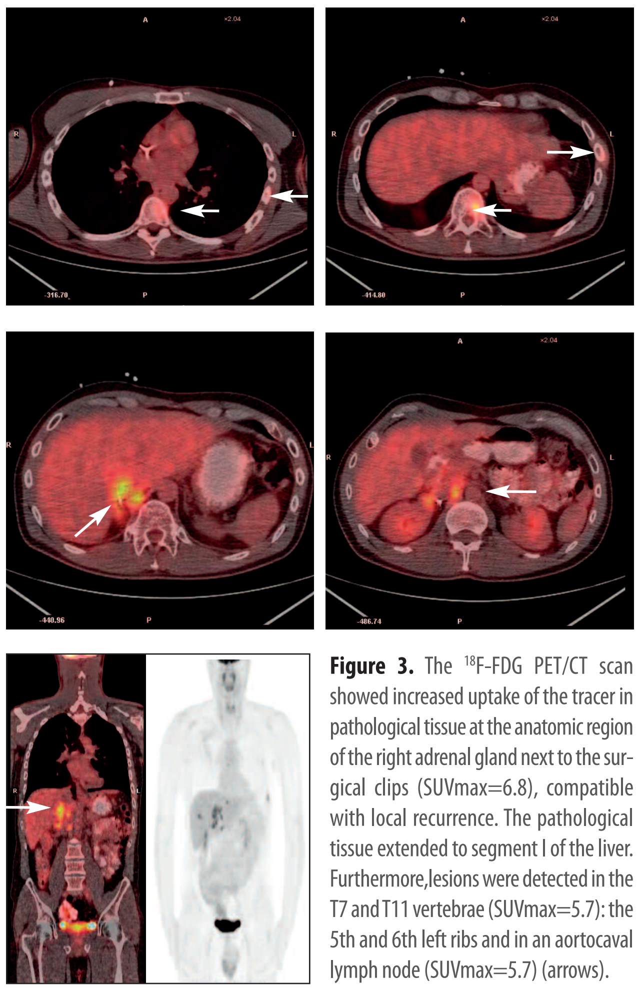

Figure 3. The ^{18}F-FDG PET/CT scan showed increased uptake of the tracer in pathological tissue at the anatomic region of the right adrenal gland next to the surgical clips (SUVmax=6.8), compatible with local recurrence. The pathological tissue extended to segment I of the liver. Furthermore,lesions were detected in the T7 and T11 vertebrae (SUVmax=5.7): the 5th and 6th left ribs and in an aortocaval lymph node (SUVmax=5.7) (arrows).

complete response, with no pathological uptake of the radiopharmaceuticals (Fig. 4, 5). Since there was no residual disease, the patient underwent 3-D conformal radiotherapy to the liver and on the sites of previous bone metastases (TD: 20Gy, 10fr.200cGy/fr).

Discussion

Imaging with ^{123}I-MIBG is an established imaging method for diagnosis, staging, and treatment response assessment of neuroblastoma [8-13]. On the other hand, initial reports showed neuroblastoma avidity for ^{18}F-FDG, and in one study it was proposed to be the only imaging modality to assess

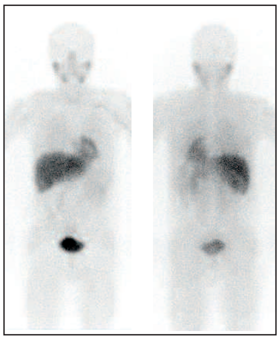

Figure 4. The ^{123}I-MIBG scan after treatment showed no increased uptake.

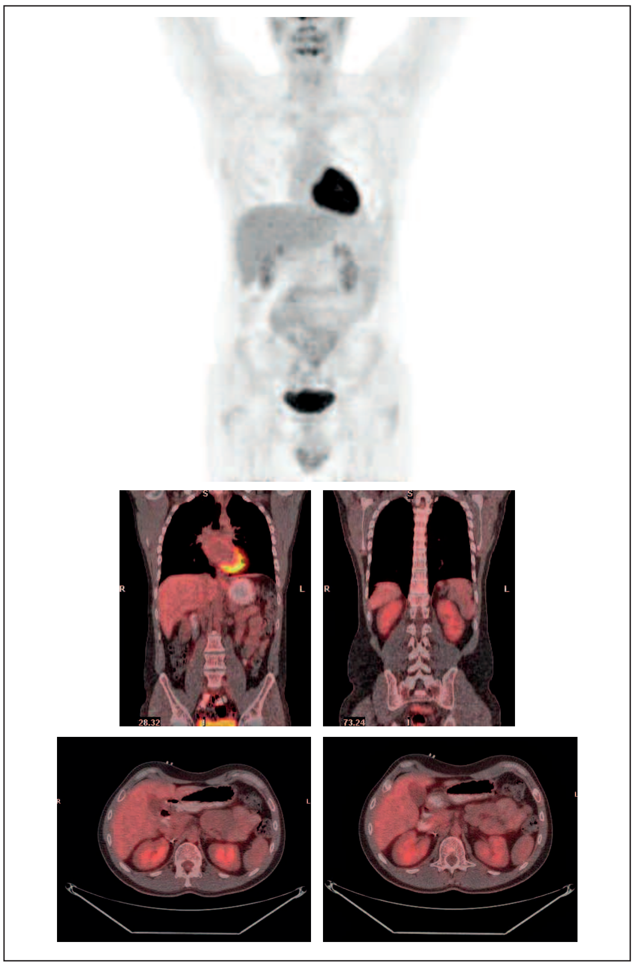

Figure 5. The ^{18}F-FDG PET/CT scan after treatment showed no pathological uptake of the tracer.

disease progression in both children and adults while this study included mostly children and few adults [14, 15]. However, the exact diagnostic accuracy of this technique remains to be defined.

In a recent study in children, ^{123}I-MIBG and ^{18}F-FDG PET uptake patterns showed noticeable differences [16]. The findings of this study suggested that, in children, ^{18}F-FDG PET/CT could not replace ^{123}I-MIBG in the initial staging of the disease [16]. Nevertheless, in a small percentage of neuroblastoma patients, who do not accumulate ^{123}I-MIBG and in children when disease extent is suspected to be larger than that depicted by ^{123}I-MIBG, the ^{18}F-FDG PET/CT scan is indicated [9, 14, 16, 17].

During follow-up for the detection of recurrence, in a lesion-based analysis study, the ^{18}F-FDG PET scan seems to be superior to ^{123}I-MIBG, with a sensitivity of 64% versus 48% and a specificity of 91% versus 82%, respectively [16]. Nevertheless, another study showed that ^{123}I-MIBG imaging has better per-patient sensitivity than ^{18}F-FDG PET/CT in mapping the extend of the disease (100% versus 86%) [18]. Beyond disease detection, ^{18}F-FDG PET/CT seems to give significant prognostic information in patients with neuroblastoma in both children and adults studied [18]. Intense ^{18}F-FDG uptake, high standardized uptake value (SUV) and large extent of bone and bone marrow disease seems to correlate with decreased survival and poor prognosis [18]. Preclinical and clinical studies in both children and adults showed that ^{18}F-FDG uptake correlates with high proliferative activity, cellular dedifferentiation, and aggressiveness of neuroendocrine tumors [18-20].

As mentioned before, in childhood ^{123}I-MIBG scan is the principal functional imaging modality for the detection and monitoring of neuroblastoma while ^{18}F-FDG PET/CT is used as an alternative, mostly in neuroblastomas that do not accumulate ^{123}I-MIBG [21]. In adults there are only few available data concerning imaging of neuroblastoma, because of the low incidence of the disease [1-4, 7]. There are only few available studies concerning neuroblastoma in adults because of the low incidence of the disease in adults.

In conclusion, in a case of an adult with adrenal neuroblastoma, ^{18}F-FDG PET/CT scan seems to be able to localize more lesions and had better detection accuracy than jointly accumulatively the ^{123}I-MIBI and the ^{99m}Tc-MDP whole-body scans. This may be due to the aggressiveness, the dedifferentiation and different biologic characteristics of neuroblastoma in adults. More cases and larger studies are needed to provide further information.

The authors declare that they have no conflicts of interest.

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