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CASE REPORT

Absence of residual Hodgkin's disease demonstrated by PET/CT in a deceased organ donor

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Summary

With the current limited availability of organs for transplantation, it is important to consider marginal donor candidates, including survivors of potentially curable malignancies such as lymphoma. The absence of refractory/recurrent residual disease at the time of brain death can be difficult to establish. Therefore, it is critical to have objective data to decide whether to proceed or not with organ procurement and transplantation. We report a unique situation in which ^{18}F-fluorodeoxyglucose positron emission tomography (PET) was used to rule out Hodgkin's lymphoma recurrence in a 33-year-old, heart-beating, brain-dead, potential donor with a past history of Hodgkin's disease and a persistent mediastinal mass. PET showed no significant uptake in the mass, allowing organ donation and transplantation to occur. We present a new means of evaluating potential brain-dead donors with a past history of some lymphoma, whereby PET may help transplant physicians by optimizing donation safety while rationalizing the inclusion of marginal donors.

Introduction

Solid organ transplantation is a successful therapy for end-stage organ diseases, but it is currently limited by a severe shortage of available donor organs. Therefore, it is increasingly important to consider marginal candidates as potential donors, including long-term survivors of some neoplastic diseases such as lymphomas. The absence of recurrence or residual disease at the time of donation can be difficult to establish from past history or impossible because of poor or lacking follow-up, especially in the short time interval usually available for deceased-donor evaluation. The absence of residual malignant disease in a potential donor at the time of organ procurement is an important consideration for transplant coordinators and physicians when determining admissibility for solid organ donation [1–3]. Positron emission tomography (PET) with ^{18}F-fluorodeoxyglusose (^{18}F-FDG) has been used for many years in the diagnosis and follow-up of various types of lymphomas and has a very high negative predictive value for the absence of active disease [4]. Thus, PET/CT is potentially useful to guide decisions in some specific deceased-donor situations. To our knowledge, we report in this study the first application of ^{18}F-FDG-PET to demonstrate the absence of residual Hodgkin's disease in a brain-dead donor.

Case presentation

A 33-year-old woman suffered cardiorespiratory arrest secondary to a diving accident. Sinus rhythm was re-established after 40 min of cardiopulmonary resuscitation,

but she did not recover from severe anoxic encephalopathy and brain death was diagnosed 2 days later. She was considered as a potential heart-beating, solid organ donor and underwent predonation screening, including a thoraco-abdominal CT showing a mediastinal mass. Her past medical history included previous Hodgkin's lymphoma (nodular sclerosis type, Ann-Arbor stage IIA, involving mediastinal and left supraclavicular lymph nodes) diagnosed 10 years earlier, and then treated with six courses of chemotherapy [bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP)], followed by radiation therapy to the left supraclavicular area, the mediastinum, and the left pulmonary hilum for a total delivered dose of 30.6 Gy. There was no history of recurrent lymphoma; however, her last follow-up evaluation had been performed 8 years earlier, when she was deemed to be in complete remission, but with the presence of a residual mediastinal mass on CT. Heart or lung organ donation was not considered because of the possible late toxicity of her previous radiation therapy and anthracycline-based chemotherapy. However, she remained a potential candidate for abdominal solid organ donation. As a result of the lack of oncologic follow-up during the last 8 years and the persistence of a mediastinal mass on the initial screening CT (Fig. 1), a doubt persisted about organ donation suitability.

Given the uncertainty regarding the patient's remission status, we used integrated PET/CT as a cancer-screening tool to help guide our organ procurement decision. The PET/CT imaging study was performed 14 h after brain death by injecting 285 MBq of ^{18}F-FDG using standard protocols (Discovery LS scanner, GEMS). The PET/CT images revealed no increase in ^{18}F-FDG uptake in the mediastinal mass (Fig. 2), making a diagnosis of residual Hodgkin's disease very unlikely. The PET/CT also confirmed aspiration pneumonia of the right lung, predominantly in the inferior lobe, already seen on the initial chest X-rays and CT survey performed 48 h before. As expected, no brain ^{18}F-FDG uptake was detected, confirming the clinical diagnosis of brain death. On the basis of the PET/CT, the patient was deemed to be free of residual Hodgkin's disease and procurement of both kidneys for transplantation was performed 20 h after brain death. The pancreas and the liver (hepatic laceration) were not procured. At the time of procurement, the donor had an excellent renal function (serum creatinine of 83 μmol/l and no proteinuria), while on low-dose noradrenalin. A routine medico-legal autopsy performed following the organ procurement did not reveal any morphological signs of Hodgkin's disease in the residual mediastinal mass or any enlarged lymph nodes, while confirming bronchopneumonia in the right lung. The cause of death was brain anoxia resulting from drowning in the context of a diving accident and, except for the bronchopneumonia, no other significant organ-associated pathology was found.

The first kidney recipient was a 60-year-old woman (wait-listed for 2.5 years), while the second recipient was a 70-year-old man (wait-listed for 1.5 years). Currently,

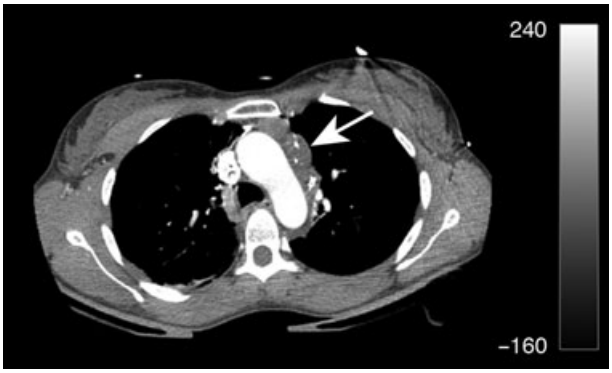

Figure 1 Axial view of the initial CT survey showing a residual mediastinal mass (arrow) that is partly calcified. The pulmonary parenchyma exhibited apical bilateral paramediastinal fibrosis resulting from radiation therapy (not shown).

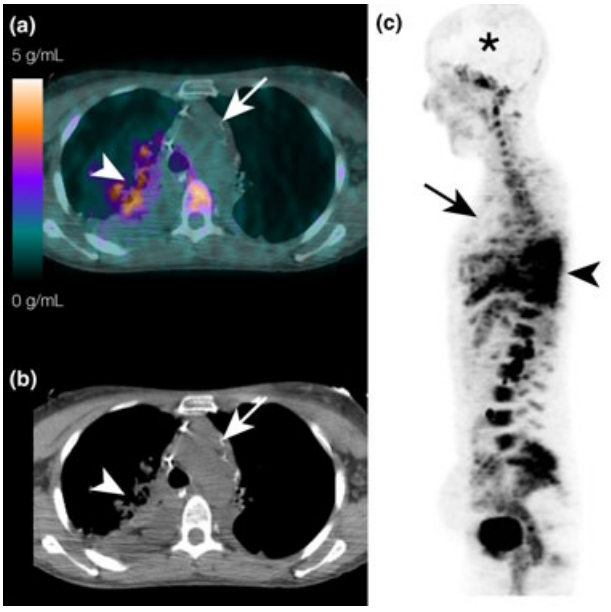

Figure 2 (a) Fused PET/CT axial view and (b) corresponding CT view showing the residual mediastinal mass (arrow) with no significant ^{18}F-FDG uptake (standardized uptake value = 1.1 g/ml). An active right basal pneumonia that had developed within 48 h since initial CT survey was evidenced with an increased ^{18}F-FDG uptake affecting mainly the right lower lobe (arrowhead). (c) PET maximum intensity projection view failed to evidence any increased mediastinal uptake (arrow). Note the absence of ^{18}F-FDG uptake in the anoxic brain (*), but the presence of increased ^{18}F-FDG uptake in the right inferior lobar infection (arrowhead) and in the axial skeleton in relation to bone marrow stimulation.

with 26 months of follow-up, the two kidney transplant recipients are doing well, with good allograft function (respective serum creatinine levels of 118 and 131 μmol/l) and no evidence of post-transplant malignancy, in particular no lymphoma.

Discussion

We report a new application of ^{18}F-FDG-PET, which may be used to guide transplant coordinators and physicians in determining brain-dead, heart-beating donor admissibility in some clinical situations. In our case, potential residual Hodgkin's disease was ruled out by PET/CT, allowing for successful organ procurement. If the PET/CT would have been positive in the mediastinal mass, we most likely would not have proceeded with the organ procurement.

Optimal screening of deceased organ donors to identify conditions that may disqualify the donor (e.g., risk of infection or tumor transmission to the recipient) is a critical process in solid organ transplantation: such process has continuously evolved along the last three decades, aiming to maximize organ donation while ensuring its safety [5]. Current screening guidelines and recommendations, of which several have been published, are largely aimed at detecting known pathogens [5]. Transplant-related transmission of cancer from organ donor to recipient has been rarely reported but can have devastating consequences if it occurs [3,6]. A few cases of lymphoma transmission from donor to recipient have been reported in the literature [3,7–9], even when the donor had no known past history of lymphoma [7–9].

The Council of Europe has recommended that donors with a history of cancer should be excluded from solid organ transplantation, except for donors with a history of low-grade skin tumors, *in situ* cervical cancer, or selected low-grade brain gliomas, or with more than 10 years of documented complete remission [2]. However, these recommendations are based on incomplete and possibly biased registries, where transmission of donor-related malignancies was demonstrated in about 40% of the cases [1]. The real risk remains largely unknown because of the lack of population-based studies [10,11]. Thus, formally establishing absolute contraindications to solid organ transplantation for donors with a past history of cancer remains difficult.

Transplant-related transmission of cancer from donors with a past history of cancer was examined by Kaufmann *et al.* [12], who suggested that the transmission risk might be acceptable if the recurrence-free interval at organ procurement was sufficiently long. Although no donor-derived lymphoma was observed in nine donors with lymphoma out of 257 donors with a history of cancer, the authors still expressed concerns. In a subsequent study, in 51 donors with a previous history of lymphoma or leukemia out of 2508 organ transplants from donors with a history of cancer with a recurrence-free interval of ≥10 years, they observed no death from donor-transmitted lymphoma [13]. Many centers will accept organs from donors if the patient history of cured cancer is >5 years.

Maximizing donation safety while rationalizing the use of marginal donors is a topic of increasing interest, given the widespread organ shortage problem. Patients with a previous history of mediastinal lymphoma have a variable recurrence rate, and conventional CT examination is known to have poor specificity for neoplastic residual tissue contraindicating transplantation. PET has been used successfully for staging and for the follow-up of patients with Hodgkin's disease and some types of non-Hodgkin's lymphomas, including high-grade post-transplant lympho-proliferative disorders [14]. Its high negative predictive value (close to 100%) in Hodgkin's disease allows recurrence to be reliably excluded in patients with ^{18}F-FDG-negative lesions, as in the case reported in this study [4]. However, preoperative biopsies remain important to rule out microscopic disease. In the presence of ^{18}F-FDG-avid lesions, it is recommended that the uptake foci should always be biopsied for histopathologic confirmation, as benign conditions such as fibrosis or granulomatosis can mimic lymphoma recurrence on PET [15].

In a number of large hospitals worldwide, PET/CT imaging can be performed within a few hours to a day, which remains an acceptable time frame for deceased-donor evaluation. It is true that PET/CT is not easily accessible to small, remote hospitals that contribute nevertheless to the donor pool. However, PET/CT use in oncology is expanding, and the number of centers with this technology is increasing rapidly, and most centers can accommodate patients under respiratory assistance. Thus, PET/CT could help transplant coordinators and physicians in evaluating potential solid organ donors with a previous history of neoplastic disease, especially in similar cases of residual mediastinal masses in patients previously treated for lymphoma. To our knowledge, this is the first report describing the use of PET/CT as a complementary tool in the pretransplant screening of a brain-dead donor. Although a single case report cannot determine the safety of use in a population of donors with previous lymphoma, this strategy may help in evaluating the cancer-transmission risk in selected situations. Accumulation of additional experience such as this one may allow for a broader consideration of potential donors with a past history of mediastinal lymphoma.

Authorship

JOP: nuclear medicine data collection, paper design, and editing. SS: diagnostic radiology data collection and paper

editing. PT and RC: clinical inpatient data collection and paper editing. NP: pre-/post-transplant data collection and paper editing. MAD and MP: pre-/post-transplant data collection, and paper design and editing.

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