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ORIGINAL RESEARCH

The Role of 18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) in Management of Nocardiosis: A Retrospective Study and Review of the Literature

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ABSTRACT

Introduction: 18-Fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is a well-established tool for managing metastatic infections. Nocardiosis, a primarily pulmonary infection, disseminates at high rates. Routine imaging includes chest CT and brain imaging. We examined the use of FDG-PET/CT in nocardiosis and assessed its contribution to diagnosis and management.

Methods: A retrospective study in two tertiary medical centers during 2011–2020. Individuals with nocardiosis for whom FDG-PET/CT was implemented for any reason were included and

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their medical records were reviewed. A board-certified nuclear medicine physician independently reviewed all scans. Additionally, a systematic review was conducted according to the PRISMA guidelines, to extract data from publications reporting FDG-PET/CT use for the management of nocardiosis.

Results: FDG-PET/CT contributed to the management of all seven patients who met inclusion criteria. It assisted in ruling out an underlying malignancy (29%, 2/7); establishing a wide infection extent (57%, 4/7); and affecting decisions regarding treatment (57%, 4/7), including drug regimen, oral step-down, and duration of therapy. We identified 20 published case reports on this topic. In 80% (16/20), FDG-PET/CT contributed to the management of nocardiosis similar to our study. In addition, in most of the literature cases, FDG-PET/CT guided the diagnostic biopsy.

Conclusion: FDG-PET/CT is valuable in the diagnosis and management of individuals with nocardiosis. The contribution of incorporating FDG-PET/CT to the management of individuals with nocardiosis and its role in monitoring treatment response and shortening treatment duration should be evaluated in prospective studies.

Keywords: Imaging; *Nocardia* infections; Opportunistic infections

Key Summary Points

Why carry out this study?

Nocardiosis is a rare infection that may be life-threatening; however, the evidence for its management is scarce and mostly based on expert opinion.

Limited data are available to guide initial evaluation of infection extent, as well as duration of treatment.

In this study we evaluated the contribution of PET/CT in the management of individuals with nocardiosis, in two tertiary healthcare centers. In addition, we systematically reviewed the medical literature and gathered the existing evidence on this subject.

What was learned from the study?

Incorporating PET/CT can facilitate the diagnosis of nocardiosis by revealing unknown extrapulmonary dissemination, excluding an underlying malignancy and guiding biopsy.

Incorporating PET/CT can assist in treatment-related decisions, e.g., promote shortening of the total antimicrobial therapy duration, rule out nocardiosis relapse in the setting of breakthrough fever, etc.

INTRODUCTION

Integrated positron emission tomography/computed tomography (PET/CT) with 18-fluorodeoxyglucose (FDG) is a useful modality for managing some infections [1], mostly disseminated infections [2, 3]. FDG-PET/CT can predict extracardiac infective endocarditis (IE) complications [4], and contributes to its treatment approach and decision-making [5, 6]. FDG-PET/CT has therefore become an established tool in the management of IE, and was incorporated into its diagnostic criteria [7].

FDG-PET/CT is also useful in the management of musculoskeletal infections [8], and may be particularly effective in the work-up of opportunistic infections. It has been used as an adjunct diagnostic method for *Pneumocystis jirovecii* [9], and for predicting therapy response in individuals with tuberculosis [10]. Similarly, it seems useful for assessment of both the initial systemic spread and treatment response in cases of invasive fungal infections [11].

Nocardiosis, a pulmonary opportunistic infection which disseminates in up to 43% of cases [12], usually occurs in organ transplant recipients [12], individuals subjected to corticosteroid therapy for any reason [13], and individuals with chronic obstructive pulmonary disease [14] or cancer [15]. Accordingly, FDG-PET/CT may be useful both in diagnosing nocardiosis dissemination as well as revealing an underlying malignancy. Revealing the extent

of the infection may assist in management decisions such as need for invasive percutaneous procedures or surgical interventions. In addition, considering the prolonged antimicrobial course usually administered for nocardiosis [16], FDG-PET/CT can have a role in guiding treatment duration.

The aim of the current study was to describe the uses of FDG-PET/CT in the management of individuals with nocardiosis, and suggest future directions. The core question of this study was whether FDG-PET/CT influenced the management of individuals with nocardiosis.

METHODS

We describe a case series and systematic review.

For the case series, we reviewed the medical charts of all individuals with *Nocardia* infection who had undergone a FDG-PET/CT examination in two large volume tertiary medical centers between January 2011 and December 2020.

Patients with a positive culture for *Nocardia* spp. from any source were identified using the microbiology laboratory computerized database in each hospital. We included consecutive adult patients from whom the isolated *Nocardia* was considered to represent an infection (nocardiosis) rather than asymptomatic colonization [17], and were treated accordingly. The medical records of these individuals were further reviewed to identify patients for whom FDG-PET/CT was implemented as part of their diagnostic work-up and/or follow-up. FDG-PET/CT scans conducted for other purposes were allowed if they occurred within the pre-diagnosis symptomatic period (up to 1 month) or during the 6 months following the diagnosis of nocardiosis. Patients' demographics, comorbidities, and clinical details regarding their *Nocardia* infection, including C-reactive protein level (CRP), imaging and microbiological data, were collected. In order to define the contribution of FDG-PET/CT to the management of our patients, we considered for each case whether the conduction of FDG-PET/CT prompted the diagnosis, ruled out alternative diagnoses and underlying diseases, or guided treatment and management decision-making.

PET/CT Implementation Protocol

After fasting for at least 4 h, all patients underwent a FDG-PET/CT scan, executed by a GE Discovery STE Whole Body PET/CT scanner (GE Medical Systems, Milwaukee, WI, USA) or similar. CT images were acquired at 120 kV and 80 mA, pitch 1.75, 0.8 s per tube rotation, and slice thickness of 3.75 mm. During the CT examination, 80–120 mL of a contrast agent (Ultravist 300, Schering AG, Berlin, Germany) was intravenously administered to ensure fully diagnostic CT data (if there was no contraindication). The PET scan was performed 60–75 min after an ^{18}F-FDG intravenous injection of 7–10 mCi (depending on the individual's weight). The contrast-enhanced CT was used also for attenuation correction of the PET data. The PET scan was performed from the base of the skull to the mid-thigh, 1.5–2 min per bed position, resulting in a total scan time of approximately 15–20 min.

For the purpose of the current study, a board-certified nuclear medicine physician (HB) with 15 years of experience independently reviewed all FDG-PET/CT scans from both centers, confirmed the results, and measured the lesion's size, volume, and standard uptake volume (SUV).

Statistical Analysis

The statistical methods used in this study were mainly descriptive. The correlation between CRP and maximum SUV was implemented using Spearman's rank correlation coefficient.

Ethical Approval

The ethics committees of Rabin Medical Center and Rambam Health Care Campus approved the study protocol. An exemption from informed consent was given by the ethics committees because of the retrospective design of the study. All methods were performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Systematic Review

We reviewed the medical literature for publications reporting the use of FDG-PET/CT for the management of individual with nocardiosis. Two reviewers (IM and DY) independently searched the literature and retrieved all English written study types reporting in detail the use of FDG-PET/CT as part of the diagnosis or management of individuals with nocardiosis. The search was conducted in the MEDLINE database, Cochrane library, and ECCMID library, combining the following search terms: *Nocardia* or Nocardiosis and PET or Positron emission or FDG or Fluorodeoxyglucose or Nuclear medicine or Mimicking malignancy. The contribution of FDG-PET/CT to case management was assessed as above.

RESULTS

Nocardia was isolated from 131 individuals in both centers between January 2011 and December 2020. Of these, 7 (5.3%) met inclusion criteria.

Characteristics, clinical scenario and imaging findings of the seven patients included in the study are presented in Table 1. Of these, 71% (5/7) were male, the average age was 63.7 (range 43–86; standard deviation [SD] 14.2) years, and 71% (5/7) were subjected to immune suppressive conditions (29% [2/7] solid organ transplant recipients; 43% [3/7] hematological malignancies). The *Nocardia* isolated from 86% (6/7) underwent species identification using polymerase chain reaction (PCR). Of these, 83% (5/6) were identified as *Nocardia cyriacigeorgica* and 17% (1/6) were identified as *Nocardia farcinica*. The *Nocardia* isolated from the remaining patient was diagnosed using mass spectrometry, and species level was not appropriately determined.

The contributions of FDG-PET/CT performed around the diagnosis included proof of clinically significant infection in all included cases, demonstration of previously unknown extrapulmonary dissemination (57%, 4/7), exclusion of an underlying malignancy (29%, 2/7) or disease progression (29%, 2/7), and assistance in treatment-related decisions (57%, 4/7) (Table 1).

FDG-PET/CT revealed patchy colonic uptake (Figs. 1 and 2) that was presumed to reflect nocardiosis involvement, although this remained questionable in the absence of microbiological evidence. In one of these patients (patient 3), detecting the colonic involvement (colonic malignancy is unlikely since the patient was cured following appropriate antimicrobial therapy) redefined the disease as disseminated infection, rather than local pulmonary infection (Fig. 1). In another patient (patient 6), lower limb lymphocutaneous involvement, which was not detected on physical examination, was revealed by FDG-PET/CT. In an additional patient (patient 7), FDG-PET/CT revealed a cardiac abscess representing prosthetic aortic valve endocarditis, which was not detected by transthoracic echocardiography, and helped to rule out progression of the underlying hematologic malignancy (Fig. 3).

In one immunocompromised patient (patient 1), resolution of the pulmonary infectious process was demonstrated on FDG-PET/CT performed approximately 6 weeks following the initiation of antimicrobial therapy. This supported antibiotic monotherapy for a period of 6 months, the shortest treatment duration acceptable for stable pulmonary disease in immunocompromised individuals, at that time [18]. This patient was considered cured from nocardiosis as was evident during follow-up visits up to 1 year following treatment completion.

In another patient (patient 2) with breakthrough fever during treatment for nocardiosis, FDG-PET/CT demonstrated progression of the underlying malignancy. Accordingly, nocardiosis relapse was ruled out and the anti-*Nocardia* regimen remained unchanged. In an additional patient (patient 6), FDG-PET/CT demonstrated active pulmonary nodules and cutaneous involvement and proved that the positive blood culture reflected nocardiosis and not contamination, as initially assumed. Consequently, systemic therapy was started. In an additional patient (patient 7), the detection of cardiac abscess which was not revealed by

Table 1 Individuals with nocardiosis who concurrently underwent an FDG-PET/CT: characteristics, PET findings, and contribution

Case number	Admission year	Sex	Age (years)	Culture to PET interval (days)[a]	Patient's immune status and daily dose of current immunosuppressive medications	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
1	2011	F	68	50	Marginal zone lymphoma, receiving R-CHOP protocol Prednisone 5 mg/day	*N. cyriacigeorgica* Pulmonary	Interim PET for assessing treatment response	The pulmonary infectious process has resolved (no FDG uptake)	Supported antibiotic monotherapy for the shortest duration acceptable
2	2012	M	61	50	Multiple myeloma, localized involvement, on radiotherapy alone	*Nocardia* spp. Pulmonary, cutaneous	Breakthrough fever during treatment for nocardiosis	Partially improved disseminated infection (as compared to a recent CT). Increased pathological FDG uptake in an LUL mass extending towards the pleura (SUVmax 6.7), in an LLL pleural nodule (SUVmax 7.1), and in a cutaneous mass adjacent to the sacrum (SUVmax 18.6) Progression of the underlying malignancy	Distinguishing between treatment failure and disease progression
3	2018	F	43	− 4	Kidney transplant recipient Prednisone 10 mg/day, tacrolimus 3 mg/day, mycophenolate mofetil 720 mg/day	*N. cyriacigeorgica* Pulmonary, intestinal	Work-up for weight loss and diarrhea, with non-diagnostic colonoscopy	Increased pathological FDG uptake in an LLL infiltrate adhesive to the diaphragm (SUVmax 8.1), and in a mass lesion in the transverse colon (SUVmax 5.6) (Fig. 1)	Revealing disease extent and dissemination (colonic involvement)

Table 1 continued

Case number	Admission year	Sex	Age (years)	Culture to PET interval (days)[a]	Patient's immune status and daily dose of current immunosuppressive medications	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
4	2020	M	52	− 5	Bilateral lung transplant recipient Prednisone 10 mg/day, tacrolimus 10 mg/day	*N. cyriacigeorgica* Pulmonary, lymphocutaneous, intestinal	Work-up for cervical lymphadenopathy in a patient with immune suppression	Increased pathological FDG uptake in an RLL infiltrate invading to the pleura (SUVmax 19.2), in cervical lymphadenopathy in the anterior (SUVmax 12.6) and left (SUVmax 10.4) neck, and in the left colic flexure (SUVmax 13.2) (Fig. 2)	Revealing disease extent (colonic involvement)
5	2020	M	86	2	Apparently immunocompetent	*N. cyriacigeorgica* Pleuropulmonary, bacteremia, endocarditis	Suspected underlying malignancy (an opportunistic infection in an apparently immunocompetent patient)	Increased pathological FDG uptake in pleural masses, the largest is right sided (SUVmax 4.1), in ground glass opacity in the LUL (SUVmax 2.4), in cervical and mediastinal lymphadenopathy—the largest a right supraclavicular lymph node (SUVmax 4.1), and a slightly increased FDG uptake in the pacemaker bed (SUVmax 2.3)	Revealing disease extent (pacemaker involvement) Ruling out an underlying malignancy
6	2020	M	56	27	Apparently immunocompetent Diabetes mellitus	*N. cyriacigeorgica* Pleuropulmonary, lymphocutaneous, bacteremia (The patient was concomitantly diagnosed with candidemia with an infected nephrostomy as the probable source)	Suspected underlying malignancy (two concomitant opportunistic infections in an apparently immunocompetent patient)	Increased pathological FDG uptake in multiple pulmonary nodules, the largest in the RUL (SUVmax 3.0), in the left ankle (SUVmax 3.7), and in the intercondylar fossa of femur (SUVmax 4.6)	Deciding on treatment for nocardiosis (the isolation was initially addressed as contamination, until the demonstration of pulmonary nodules) Revealing disease extent (lymphocutaneous involvement) Ruling out an underlying malignancy

Table 1 continued

Case number	Admission year	Sex	Age (years)	Culture to PET interval (days)[a]	Patient's immune status and daily dose of current immunosuppressive medications	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
7	2020	M	80	8	Marginal cell lymphoma and therapy related myelodysplastic syndrome Dexamethasone 2 mg/day Azacitidine 140 mg/day, for 7 days, every 28 days. The patient completed 3 cycles	*N. farcinica* Pulmonary, cutaneous, endocarditis (in a prosthetic aortic valve, 4 months following a transcatheter aortic valve replacement)	Assessment of the disease extension. Suspected progression of the underlying malignancy	Increased pathological FDG uptake in the cardiac interventricular space (SUVmax 9.2), in multiple bilateral pulmonary nodules, the largest within the LLL (SUVmax 5.7), and in the cutaneous and subcutaneous tissue in the right ankle and distal shin (SUVmax 4.1). In addition, mildly increased FDG uptake was observed in multiple splenic infarctions (Fig. 3)	Revealing disease extent (detection of endocarditis, which was not detected by trans-thoracic echocardiography) Progression of the underlying lymphoma was ruled out

[a] Indicates the time period that elapsed between sampling the culture from which *Nocardia* was isolated and the conduction of PET scan (negative values signify that the PET scan was conducted before sampling)

F female, *M* male, *CT* computerized tomography, *CNS* central nervous system, *FDG* ^{18}fluorodeoxyglucose, *MRI* magnetic resonance imaging, *PET* positron emission tomography, *SUVmax* maximum standard uptake value, *LLL* pulmonary left lower lobe, *LUL* pulmonary left upper lobe, *R-CHOP* rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone, *RLL* pulmonary right lower lobe, *RUL* pulmonary right upper lobe

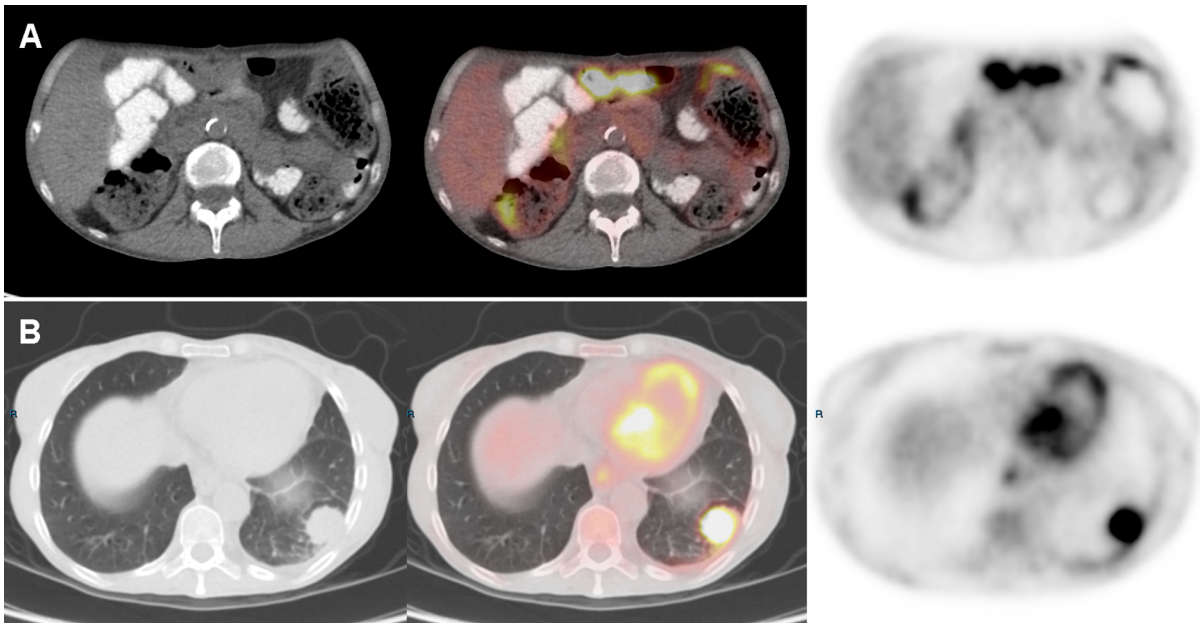

Fig. 1 Patient 3. Axial view CT, FDG-PET/CT fusion and maximum intensity projection images: **a** Increased pathological FDG uptake in a mass lesion in the transverse colon, SUVmax 5.6. **b** Increased pathological FDG uptake in an LLL infiltrate adhesive to the pleura, SUVmax 8.1

transthoracic echocardiography could potentially guide cardiac surgery; however, the patient was frail and was therefore treated conservatively.

For the six patients for whom the FDG-PET/CT revealed an increased pathological FDG uptake compatible with infection, the CRP level was obtained at an average time interval of 1.2 days (SD 2.2 days; range 0–6) from the performance of FDG-PET/CT. The maximum SUV of the leading infectious lesion positively correlated with the CRP level ($\rho = 0.77$); however, this finding was not statistically significant ($p = 0.072$), likely because of the small sample size (Fig. 4).

Systematic Literature Review

As of October 15, 2020, the literature search yielded 105 references. These were evaluated, and a total of 19 relevant publications were identified, reporting 19 individuals with nocardiosis for whom FDG-PET/CT was used for diagnostic work-up or follow-up. An additional reference was identified through the references list of another paper. All publications were case reports of individual patients. Nine were published between 2004 and 2014 [19–27], five were published in 2015 [28–32] and six were published between 2016 and 2020 [33–38]. These 20 case reports are summarized in Table 2.

The indication for performing FDG-PET/CT was mentioned in 19/20 of the cases. The most common indication was suspected malignancy (74%, 14/19), most frequently pulmonary malignancy (79% 11/14). For the remaining five cases, the indication for performing FDG-PET/CT was either assessment of the infection's extent (16%, 3/19) or work-up for an unresolved pleural effusion, i.e., searching for an underlying inflammatory or malignant disease (11%, 2/19).

In most of these cases the performance of FDG-PET/CT contributed to the management of nocardiosis (80%, 16/20). In the majority of cases (55%, 11/20), the use of FDG-PET/CT guided biopsy or aspiration. FDG-PET/CT also contributed in revealing disease involvement in additional body sites, which was sometimes asymptomatic (20%, 4/20), and in ruling out an underlying malignancy (15%, 3/20). Contribution to treatment-related issues beyond

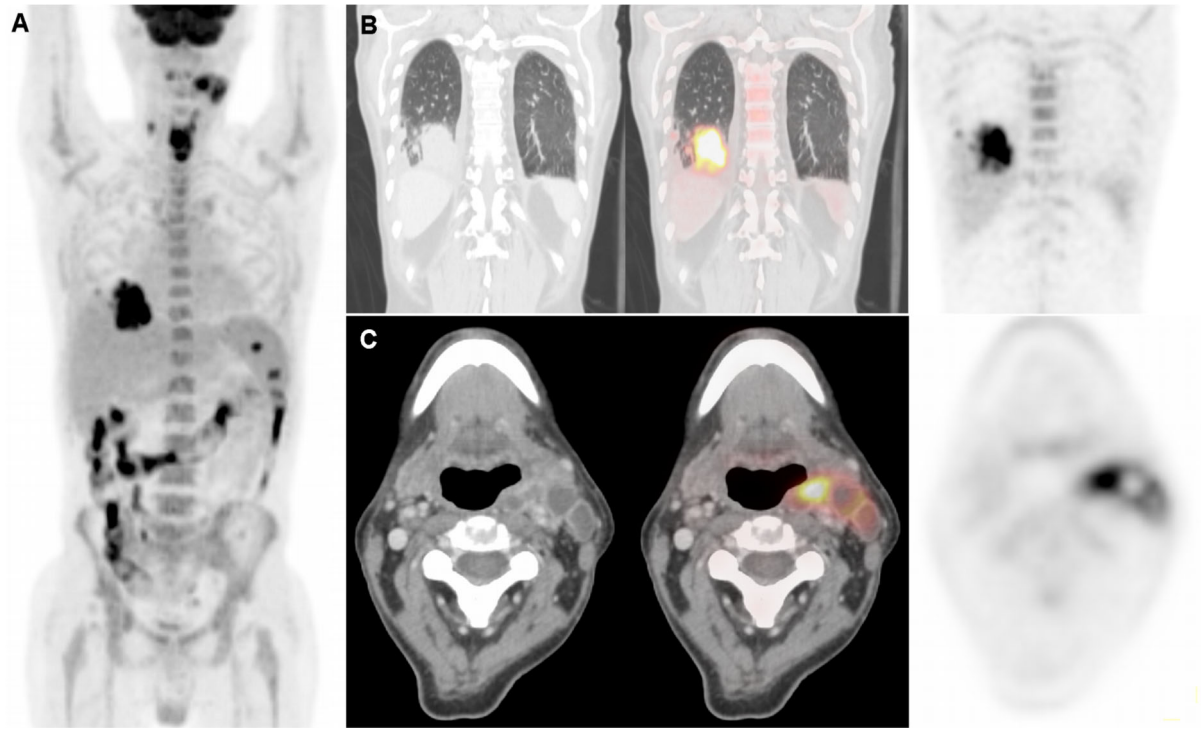

Fig. 2 Patient 4. **a** Anterior view maximum intensity projection showing increased pathological FDG uptake in the right lung, left neck, anterior neck, and colon. **b** Coronal view CT, FDG-PET/CT fusion, and maximum intensity projection images of increased pathological FDG uptake in an RLL infiltrate invading to the pleura, SUVmax 19.2. **c** Axial view CT, FDG-PET/CT fusion, and maximum intensity projection images of increased pathological FDG uptake in left neck lymph nodes, SUVmax 10.4

diagnosing a disseminated disease was not documented; however, in all reported cases FDG-PET/CT was conducted for initial work-up, usually before the diagnosis was made. In 20% (4/20) of the cases, no contribution could be attributed to the FDG-PET/CT.

DISCUSSION

By summarizing our experience and reviewing the medical literature, we demonstrated that FDG-PET/CT may play an important role in the diagnosis and management of individuals with nocardiosis. Yet, despite its potential contribution, FDG-PET/CT is only seldom used for this purpose.

In the majority of literature cases we reviewed, FDG-PET/CT guided the location for biopsy of a suspected lesion, leading to the diagnosis of nocardiosis. In addition, FDG-PET/CT was used as a diagnostic tool to rule out an undiagnosed underlying malignancy, a common underlying disease in nocardiosis [39].

Diagnosis of nocardiosis relies on microbiological evidence of the pathogen. Although the lungs are the most frequently affected organ [40], sputum cultures may be negative despite the existence of pulmonary infection [41]. This is particularly relevant for peripheral pulmonary or pleural infections [42]. In such cases, FDG-PET/CT can possibly guide biopsy, revealing the lesion that will most likely yield the diagnosis.

FDG-PET/CT was also frequently used for assessing extrapulmonary involvement of nocardiosis and often detected unexpected disease dissemination. We found that FDG-PET/CT identified soft tissue involvement, for which it has been reported as a more sensitive modality

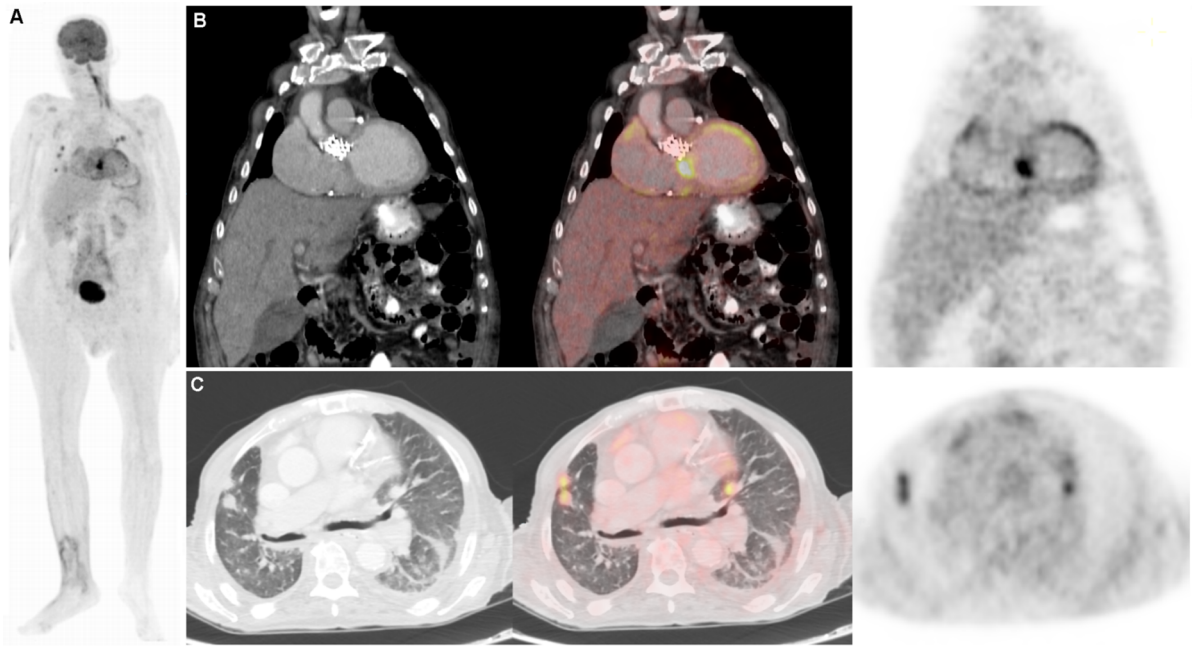

Fig. 3 Patient 7. **a** Anterior view maximum intensity projection showing increased pathological FDG uptake in the mediastinum, lungs, and in cutaneous and subcutaneous tissue in the right ankle and distal shin, SUVmax 4.1. In addition, increased FDG uptake of low intensity was observed in multiple splenic infarctions, SUVmax 3.3. **b** Coronal view CT, FDG-PET/CT fusion, and maximum intensity projection images showing increased pathological FDG uptake in the cardiac interventricular space, adjacent and below the transaortic inserted prosthetic valve, SUVmax 9.2. **c** Axial view CT, FDG-PET/CT fusion, and maximum intensity projection images showing increased pathological FDG uptake in bilateral multiple pulmonary nodules, the largest within the LLL, SUVmax 5.7; others in the LUL, SUVmax 4.8, and in the RML, SUVmax 4.7

compared to CT [43]; cardiac prosthetic material involvement that was not detected by echocardiography as reported previously [44]; and presumed abdominal involvement, not identified in the routine chest CT performed. Since most clinicians will prefer combination antibiotic therapy with longer duration for disseminated disease [18], by detecting extrapulmonary involvement, FDG-PET/CT can indirectly influence the therapeutic regimen. Nonetheless, non-specific FDG uptake does not necessarily reflect dissemination and should be interpreted with caution. This is particularly relevant for sites such as the gastrointestinal tract, an infrequent site for nocardiosis, in which incidental foci of FDG uptake were described [45]. Additionally, it should be noted that central nervous system involvement is common in nocardiosis and reported in approximately 20% of cases, usually representing disseminated disease [46]. Hence, other imaging modalities, such as magnetic resonance, are needed in addition to FDG-PET/CT. Nevertheless, our findings imply that using FDG-PET/CT routinely in cases of nocardiosis may redefine dissemination patterns of the disease and reveal a higher prevalence of dissemination than has been so far known.

Traditionally, individuals with nocardiosis are treated for long periods, usually for at least 6–12 months. Recent data suggest that much shorter durations may achieve similar cure rates [47]. Since antibiotic therapy accelerates the emergence of resistant pathogens [48] and is associated with high rates of adverse effects [49], it is imperative to shorten treatment duration whenever possible. Although none of the cases reported in the literature used FDG-PET/CT for

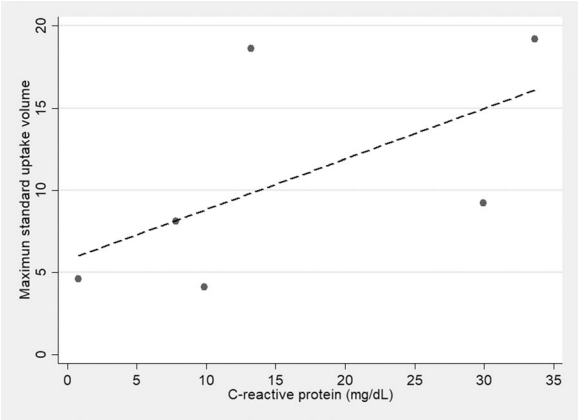

Fig. 4 A scatter plot (each dot represents an individual with nocardiosis) with fit regression line showing a possible correlation between C-reactive protein and maximum standard uptake volume of the leading lesion ($\rho = 0.77$, $p = 0.072$)

therapy decision-making, it is possible that if used as an auxiliary follow-up tool it can facilitate decisions on treatment duration [50]. Similarly, FDG-PET/CT conducted shortly after the diagnosis of *Staphylococcus aureus* bacteremia guided treatment duration and improved survival [3]. Furthermore, FDG-PET/CT facilitated monitoring of the initial response to antibiotic therapy in infectious spondylodiscitis [51] and in predicting relapse of pulmonary tuberculosis when conducted at the time of treatment completion [52]. It is therefore possible that incorporating FDG-PET/CT at an accepted interval (e.g., 3 months from diagnosis) into the follow-up of individuals with nocardiosis may guide ongoing duration-related treatment decisions (i.e., if no pathologic FDG uptake is observed, the infection could be deemed controlled and the patient can benefit from a shorter therapeutic course).

Furthermore, our experience suggests that FDG-PET/CT can assist clinicians in other therapeutic dilemmas. We demonstrated that in the context of breakthrough fever in an individual with malignancy and nocardiosis, in which FDG-PET/CT assisted in distinguishing between antibiotic treatment failure and malignancy progression. However, although the morphology and patterns seen in CT can suggest that the FDG uptake is compatible with either malignancy or infection, the ability to differentiate between these conditions without tissue sampling is limited.

Our finding of a possible trend between CRP levels and maximum SUV is supported by a previous study on aortic graft infections, where the repertoire of pathogens does not typically include *Nocardia* [53]. However it seems that CRP alone cannot ultimately substitute the role of FDG-PET/CT, as treatment-related decisions are often being made according to FDG-PET/CT findings even when CRP levels are normal [53].

The current study is limited by its observational design. Accordingly, the contribution of FDG-PET/CT to the management was retrospectively appraised and is therefore subject to bias.

As for the systematic review, a publication bias is possible, i.e., cases in which FDG-PET/CT had no contribution to the management of nocardiosis were not published. Additionally, when performed, FDG-PET/CT was conducted as part of the initial management, and almost none of the included FDG-PET/CT tests were performed during follow-up. We therefore had to hypothesize about what could be the benefit of an additional FDG-PET/CT at an accepted interval.

It can be concluded that FDG-PET/CT is a potentially useful tool in the management of individuals with nocardiosis. We argue that the integration of FDG-PET/CT at baseline could add information regarding disease extent and underlying malignancies, which cannot be gained by CT alone. In addition, it may assist in treatment-related decisions at time of therapy initiation and during follow-up, including choice of initial and subsequent treatment regimens and duration of treatment. Further cohort study with historical control group is warranted in order to appraise the outcomes of FDG-PET/CT-guided therapy duration for individuals with nocardiosis and for determining the optimal timeframe for conducting a follow-up FDG-PET/CT.

Table 2 Summary of cases reporting the use of FDG-PET/CT in the management of nocardiosis, previously published in the medical literature

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Thomas et al. [19]	2004	F	73	N/A	*Nocardia* spp. Pleuropulmonary	Suspected malignancy (mesothelioma or pleural metastases)	Markedly increased FDG uptake in the pleural space, correlating with the pleural-based nodules noted on the CT scan	Guiding biopsy that led to the diagnosis
Mascarenhas et al. [20]	2006	M	69	Apparently immunocompetent	*Nocardia* spp. Pulmonary, CNS	Suspected lung cancer with brain metastasis	Increased FDG uptake (SUVmax 11.1) in the pulmonary LUL mass (without lymphadenopathy), and in a right frontal cerebral ring-enhancing lesion (SUVmax 11.0) seen on MRI	None The brain lesion was biopsied and led to the diagnosis (the pulmonary mass resolved with therapy)
Darwiche et al. [21]	2007	M	76	Apparently immunocompetent	*N. abscessus* Pulmonary	Suspected lung cancer	Increased FDG uptake (SUVmax 13.4) in a pulmonary RUL mass	None The mass was surgically excised. Tissue analysis ruled out malignancy and revealed the diagnosis
Iannotti et al. [22]	2009	M	53	Apparently immunocompetent (previous smoker)	*N. farcinica* Pulmonary, CNS	Suspected lung cancer	A hypermetabolic pulmonary RLL nodule, without a systemic involvement (although MRI revealed a 2.0-cm temporoparietal ring-enhancing lesion)	None The brain abscess was surgically excised and led to the diagnosis (the pulmonary mass resolved with therapy)

Table 2 continued

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Parikh et al. [23]	2010	M	59	Chronic lymphocytic leukemia (on intermittent rituximab with or without fludarabine and cyclophosphamide)	*N. pseudobrasiliensis* Pulmonary, cutaneous	Suspected chronic lymphocytic leukemia transformation	Increased uptake in a band-like opacity in the pulmonary RUL (SUVmax 13.1), in a right axillary mass (SUVmax 6.7), and in a left iliac mass (SUVmax 13.4). These lesions had evidence of central necrosis, suggesting an infectious etiology	Guiding fine needle aspirations of the lymphocutaneous masses Tissue evaluation ruled out malignant transformation and led to the diagnosis
Zhao et al. [24]	2012	M	55	Uveitis (high-dose corticosteroid therapy 6 months prior to diagnosis with nocardiosis)	*Nocardia* spp. Pleuropulmonary	Suspected malignancy (unresolved pulmonary infection with multiple pulmonary and pleural nodules)	Increased FDG uptake in pleural based nodules, the largest in the RLL (SUVmax 11.15). The pleural thickening with an encapsulated effusion did not have an increased uptake	Guiding pleural aspiration biopsy that ruled out malignancy and revealed the diagnosis
Tsunezuka et al. [25]	2012	M	65	Apparently immunocompetent	*N. beijingenesis* Pleuropulmonary	Suspected lung cancer	Increased FDG uptake (SUVmax 8.40) in a pulmonary RUL nodule with pleural indentation	Guiding needle biopsy which was not diagnostic. Eventually surgical biopsy ruled out malignancy and led to the diagnosis

Table 2 continued

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Yi et al. [26]	2014	M	77	Apparently immunocompetent	*N. cyriacigeorgica* Pleuropulmonary	Work-up for bilateral pleural effusions, with no cytological or microbiological findings	Diffuse hypermetabolism of both pleural surfaces	Revealing pleural involvement suggestive of inflammatory lesion Repeated pleurocentesis led to the diagnosis
Crozier et al. [27]	2014	M	48	Apparently immunocompetent	*N. beijingensis* Pulmonary, lymph nodes	Suspected malignancy in an individual with paramediastinal mass and hilar lymphadenopathy	Increased FDG uptake (SUVmax 29.6) in a left paramediastinal mass extending to the left superhilar region, in a suprasternal lymph node, with a diffusely hyperstimulated bone marrow	Revealing a new nodal involvement and guiding an open biopsy. Tissue evaluation and sputum cultures led to the diagnosis
Bertero et al. [28]	2015	M	68	Gliomatosis cerebri On temozolomide, no current corticosteroid use	*Nocardia* spp. Pulmonary, CNS	Suspected lung cancer with brain metastasis	An increased FDG uptake in the cerebellar and lung lesions	None Surgical resection of the cerebellar lesion led to the diagnosis
Yasar et al. [29]	2015	M	35	N/A	*Nocardia* spp. Pulmonary	N/A	Increased FDG uptake (SUVmax 5.9–7.1) in a pulmonary RLL cavitation	Guiding a fine needle aspiration which was not diagnostic Eventually the patient underwent a surgical resection that led to the diagnosis

Table 2 continued

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Poisnel et al. [30]	2015	M	51	Glioblastoma multiforme On chemotherapy (lamustine, vincristine, and procarbazine) and methylprednisolone 32 mg/day	*N. veterana* Pleuropulmonary, urinary tract (including prostatitis)	Work-up for suspected "deep infection"	Increased FDG uptake in the prostate (pulmonary findings were not reported)	Revealing disease extent (involvement of the prostate gland)
Erdemir et al. [31]	2015	M	39	Behçet's disease (recent immunosuppressive therapy)	*Nocardia* spp. Pulmonary, musculocutaneous	Suspected malignancy (non-resolving pulmonary infection and multiple pulmonary nodules)	Increased FDG uptake in a pleural based mass in the RUL (SUVmax 12.0), in multiple parenchymal nodules in both lungs (SUVmax 6.5), and in diffuse musculocutaneous lesions (SUVmax 10.7)	Revealing disease extent (musculocutaneous involvement) Guiding biopsies that led to the diagnosis
Peeters et al. [32]	2015	F	81	N/A	*Nocardia* spp. CNS	Work-up for an unidentified CNS infection	Increased uptake in supraclavicular nodules (biopsy revealed benign lymphatic tissue) and the hepatic curve of the colon (biopsy revealed an adenoma)	Ruled out systemic involvement. A surgical biopsy of the brain abscess led to the diagnosis

Table 2 continued

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Xu et al. [33]	2016	M	35	Adrenocorticotropic hormone-secreting paraganglioma	*Nocardia* spp. Pulmonary	Determine whether bilateral multiple pulmonary lesions are metastatic or infectious foci	Increased FDG uptake in a tumor focus in the anterior mediastinum and in some of the multiple clear-boundary pulmonary nodules (SUVmax 10)	Suggesting that the nodular pulmonary lesions are infectious, leading to the collection of sputum cultures that led to the diagnosis
Canouï et al. [34]	2017	M	30	Diffuse large B cell lymphoma with recent autologous stem cell transplantation	*N. farcinica* (with *Ureaplasma urealyticum* coinfection) Pleuropulmonary	Non-resolving pleural effusion in an individual with immune suppression	Increased FDG uptake in bilateral pleural and pulmonary sites (SUVmax 5). Hypermetabolism was not noted at the initial lymphoma sites	Suggesting that the pleural lesions reflect an infection rather than lymphoma recurrence. Pleural open biopsy led to the diagnosis
Biswas Roy et al. [35]	2018	F	63	Lung transplant recipient On prednisone, tacrolimus, and mycophenolate mofetil	*N. paucivorans* Renal	Renal mass suspicious for renal cell carcinoma (per MRI)	Increased FDG uptake in the right renal mass (SUVmax 14.3)	Guiding surgical excision. Tissue evaluation led to the diagnosis

Table 2 continued

Publication	Year	Sex	Age	Patient's immune status	*Nocardia* species and systems involved	Indication for PET scan	PET findings	PET contribution to nocardiosis management
Playe et al. [36]	2020	M	63	Asthma, on oral low-dose corticosteroid therapy	*N. brasiliensis* CNS, musculocutaneous	Assessment of the extent of the infection in an individual with multiple CNS abscesses and dermal lesions	Increased FDG uptake in right hilar lymphadenopathy and in multiple cutaneous, subcutaneous, and muscle abscesses: left buttock subcutaneous (SUVmax 6.0), left extensor digitorum longus (SUVmax 8.4), and right leg posterior compartment muscles (SUV = 8.0). Hypermetabolism was not noted in the CNS lesions	Revealing disease extent (diffuse musculocutaneous involvement) Guiding skin biopsies that led to the diagnosis
Tramèr et al. [37]	2020	M	81	Diffuse large B cell lymphoma, in remission. The patient received no immunosuppressive therapy	*N. paucivorans* A retroperitoneal abscess	Suspected lymphoma recurrence	Increased FDG uptake in a right adrenal mass with central necrosis	Revealing a single focus disease Guiding biopsy that led to the diagnosis
Kodaganur Gopinath S et al. [38]	2020	M	34	Apparently immunocompetent	*Nocardia* spp. Pulmonary, lymphocutaneous, vertebral	Suspected lung cancer	Increased FDG uptake in the lung apexes with extension into the vertebra	Revealing disease extent (lymphocutaneous and vertebral involvement) Guiding biopsy that led to the diagnosis

F female, *M* male, *N/A* not applicable, *CT* computerized tomography, *CNS* central nervous system, *FDG* 18-fluorodeoxyglucose, *MRI* magnetic resonance imaging, *PET* positron emission tomography, *SUVmax* maximum standard uptake value, *LUL* pulmonary left upper lobe, *RLL* pulmonary right lower lobe, *RUL* pulmonary right upper lobe

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REFERENCES

1. Vaidyanathan S, Patel CN, Scarsbrook AF, Chowdhury FU. FDG PET/CT in infection and inflammation—current and emerging clinical applications. Clin Radiol. 2015;70:787–800.

2. Hess S. FDG-PET/CT in fever of unknown origin, bacteremia, and febrile neutropenia. PET Clin. 2020;15:175–85.

3. Ghanem-Zoubi N, Kagna O, Abu-Elhija J, et al. Integration of FDG-PET/CT in the diagnostic workup for staphylococcus aureus bacteremia: a prospective interventional matched-cohort study. Clin Infect Dis. 2020. https://doi.org/10.1093/cid/ciaa929.

4. Orvin K, Goldberg E, Bernstine H, et al. The role of FDG-PET/CT imaging in early detection of extracardiac complications of infective endocarditis. Clin Microbiol Infect. 2015;21:69–76.

5. San S, Ravis E, Tessonier L, et al. Prognostic value of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in infective endocarditis. J Am Coll Cardiol. 2019;74:1031–40.

6. Erba PA, Lancellotti P, Vilacosta I, et al. Recommendations on nuclear and multimodality imaging in IE and CIED infections. Eur J Nucl Med Mol Imaging. 2018;45:1795–815.

7. Habib G, Erba PA, Iung B, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. Eur Heart J. 2019;40:3222–32.

8. Love C, Palestro CJ. Nuclear medicine imaging of bone infections. Clin Radiol. 2016;71:632–46.

9. Reid AB, Chen SC-A, Worth LJ. Pneumocystis jirovecii pneumonia in non-HIV-infected patients. Curr Opin Infect Dis. 2011;24:534–44.

10. Sánchez-Montalvá A, Barios M, Salvador F, et al. Usefulness of FDG PET/CT in the management of tuberculosis. PLoS One. 2019;14:e0221516.

11. Leroy-Freschini B, Treglia G, Argemi X, et al. 18F-FDG PET/CT for invasive fungal infection in immunocompromised patients. QJM An Int J Med. 2018;111:613–22.

12. Coussement J, Lebeaux D, van Delden C, et al. *Nocardia* infection in solid organ transplant recipients: a multicenter European case-control study. Clin Infect Dis. 2016;63:338–45.

13. Margalit I, Goldberg E, Ben Ari Y, et al. Clinical correlates of nocardiosis. Sci Rep Nat Res. 2020;10:14272.

14. Garcia-Bellmunt L, Sibila O, Solanes I, Sanchez-Reus F, Plaza V. Nocardiosis pulmonar en pacientes con EPOC: características y factores pronósticos. Arch Bronconeumol. 2012;48:280–5.

15. Wang HL, Seo YH, LaSala PR, Tarrand JJ, Han XY. Nocardiosis in 132 patients with cancer. Am J Clin Pathol. 2014;142:513–23.

16. Fatahi-Bafghi M. Nocardiosis from 1888 to 2017. Microb Pathog. 2018;114:369–84.

17. Margalit I, Muhsen K, Ben Ari Y, et al. *Nocardia* colonization in contrast to nocardiosis: a comparison of patients' clinical characteristics. Eur J Clin Microbiol Infect Dis. 2020;39:759–63.

18. Restrepo A, Clark NM. Infectious Diseases Community of Practice of the American Society of Transplantation. *Nocardia* infections in solid organ transplantation: Guidelines from the Infectious Diseases Community of Practice of the American Society of Transplantation. Clin Transpl. 2019;1:e13509.

19. Thomas A, Singh A, Greenspan B. Localization of F-18 FDG in *Nocardia* lung infection. Clin Nucl Med. 2004;29:834–5.

20. Mascarenhas NB, Lam D, Lynch GR, Fisher RE. PET imaging of cerebral and pulmonary *Nocardia* infection. Clin Nucl Med. 2006;31:131–3.

21. Darwiche K, Totzeck B, Gatermann S, Bollow M, Ewig S. Nocardiosis as a differential diagnosis of a PET-positive pulmonary nodule. Pneumologie. 2007;61:176–80.

22. Iannotti CA, Hall GS, Procop GW, Tuohy MJ, Staugaitis SM, Weil RJ. Solitary *Nocardia farcinica* brain abscess in an immunocompetent adult mimicking metastatic brain tumor: rapid diagnosis by pyrosequencing and successful treatment. Surg Neurol. 2009;72:74–9.

23. Parikh SA, Bhusal Y, Faderl SH, et al. The great imitator: systemic nocardiosis mimicking Richter's transformation in relapsed chronic lymphocytic leukemia. J Clin Oncol. 2010;28:e732–4.

24. Zhao K, Dong M-J, Sheng Z-K, et al. Elevated uptake of 18F-FDG in PET/CT imaging of a *Nocardial* pleural nodule. Clin Imaging. 2012;36:383–5.

25. Tsunezuka Y, Furusawa T, Fujimori H, Kurumaya H. Pulmonary nocardiosis with a tumor-like solitary nodule caused by *Nocardia beijingenesis*: first report of human surgical infection. Surg Infect (Larchmt). 2012;13:418–9.

26. Yi C, Kwon MJ, Ki CS, et al. Necrotizing pneumonia and empyema in an immunocompetent patient caused by *Nocardia cyriacigeorgica* and identified by 16S rRNA and secA1 sequencing. Ann Lab Med. 2014;34:71.

27. Crozier JA, Andhavarapu S, Brumble LM, Sher T. First report of *Nocardia beijingensis* infection in an immunocompetent host in the United States. J Clin Microbiol. 2014;52:2730–2.

28. Bertero L, Cassoni P, Rudà R. *Nocardia* abscesses mimicking tumor progression in gliomatosis cerebri responding to temozolomide. J Neurooncol. 2015;121:225–7.

29. Yasar Z, Acat M, Onaran H, et al. False-positive 18-fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET/CT) scans mimicking malignancies. Med Glas (Zenica). 2015;12:40–6.

30. Poisnel E, Roseau JB, Landais C, Rodriguez-Nava V, Bussy E, Gaillard T. *Nocardia veterana*: disseminated infection with urinary tract infection. Braz J Infect Dis. 2015;19:216–9.

31. Erdemir RU, Elri T, Sahin H, Sami Salihoglu Y, Aras M, Cabuk M. Disseminated *Nocardia* infection mimicking malignancy on FDG PET/CT. Rev Esp Med Nucl Imagen Mol. 2015;34:268–9.

32. Peeters I, Casselman JW, Vandecasteele SJ, et al. Multiple *Nocardial* abscesses of the brainstem and spinal cord diagnosed after an open biopsy through a cervical partial central corpectomy: case report. J Neurosurg Spine. 2015;23:290–3.

33. Xu L, Xu Q, Yang M, Gao H, Xu M, Ma W. Nocardiosis in ectopic ACTH syndrome: a case report and review of 11 cases from the literature. Exp Ther Med. 2016;12:3626–32.

34. Canouï E, Blanc K, Loubinoux J, et al. The value of molecular techniques to diagnose *Ureaplasma urealyticum* and *Nocardia farcinica* pleuropneumonia in a patient with diffuse large B-cell lymphoma. Int J Infect Dis. 2017;64:93–5.

35. Biswas Roy S, Ross MD, Patil PD, Trepeta R, Bremner RM, Panchabhai TS. Primary *Nocardia* infection causing a fluorodeoxyglucose-avid right renal mass in a redo lung transplant recipient. Case Rep Transpl. 2018;2018:1–5.

36. Playe M, Einfalt M, Toch SR, Froissart A, Bodardel G. 18F-FDG imaging of a case of disseminated nocardiosis. Clin Nucl Med. 2020;45:55–6.

37. Tramèr L, Mertz K, Huegli R, et al. Intra-abdominal nocardiosis—case report and review of the literature. J Clin Med. 2020;9:2141.

38. Kodaganur Gopinath S, Pulle MV, Dhamija A, Puri H, Bin Asaf B, Kumar A. A rare disease mimicking lung cancer. Indian J Tuberc Tuberculosis Association of India. 2020;67:430–2.

39. Robin P, van Es N, Le Roux PY, et al. Performance of 18F-fluorodesoxyglucose positron-emission tomography/computed tomography for cancer screening in patients with unprovoked venous thromboembolism: results from an individual patient data meta-analysis. Thromb Res Elsevier Ltd. 2020;194:153–7.

40. Minero MV, Marín M, Cercenado E, Rabadán PM, Bouza E, Muñoz P. Nocardiosis at the turn of the century. Medicine (Baltimore). 2009;88:250–61.

41. Li S, Song X, Zhao Y, et al. Clinical analysis of pulmonary nocardiosis in patients with autoimmune disease. Medicine (Baltimore). 2015;94:e1561.

42. Sukahri S, Zainudin LD, Hadi MF, Mohd Firdaus MAB, Abdul Hafidz MI. Recurrent empyema thoracic secondary to pulmonary nocardiosis in immunocompetent patients. Case Rep Pulmonol. 2020;2020:8840920. https://doi.org/10.1155/2020/8840920.

43. Palestro CJ. FDG-PET in musculoskeletal infections. Semin Nucl Med. 2013;43:367–76.

44. Chen W, Kim J, Molchanova-Cook OP, Dilsizian V. The potential of FDG PET/CT for early diagnosis of cardiac device and prosthetic valve infection before morphologic damages ensue. Curr Cardiol Rep. 2014;1:16.

45. Israel O, Yefremov N, Bar-Shalom R, et al. PET/CT detection of unexpected gastrointestinal foci of 18F-FDG uptake: incidence, localization patterns, and clinical significance. J Nucl Med. 2005;46:758–62.

46. Beaman BL, Beaman L. *Nocardia* species: host-parasite relationships. Clin Microbiol Rev. 1994;7:213–64.

47. Lebeaux D, Freund R, van Delden C, et al. Outcome and treatment of nocardiosis after solid organ transplantation: new insights from a European study. Clin Infect Dis. 2017;64:1396–405.

48. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010;74:417–33.

49. Tamma PD, Avdic E, Li DX, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. JAMA Int Med. 2017;177:1308–15.

50. Stern Shavit S, Bernstine H, Sopov V, Nageris B, Hilly O. FDG-PET/CT for diagnosis and follow-up of necrotizing (malignant) external otitis. Laryngoscope. 2019;129:961–6.

51. Righi E, Carnelutti A, Muser D, et al. Incremental value of FDG-PET/CT to monitor treatment response in infectious spondylodiscitis. Skeletal Radiol. 2020;49:903–12.

52. Lawal IO, Fourie BP, Mathebula M, et al. 18F-FDG PET/CT as a noninvasive biomarker for assessing adequacy of treatment and predicting relapse in patients treated for pulmonary tuberculosis. J Nucl Med. 2020;61:412–7.

53. Husmann L, Ledergerber B, Anagnostopoulos A, et al. The role of FDG PET/CT in therapy control of aortic graft infection. Eur J Nucl Med Mol Imaging. 2018;45:1987–97.

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