

# The Role of Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Management of Brucellosis: An Observational Cohort Study

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**Background.** Diagnosis of focal infection in brucellosis is important to direct optimal treatment. Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) may be helpful in this aspect.

**Methods.** The clinical and imaging data of all patients with brucellosis, who underwent FDG PET/CT as part of the investigation in Rambam Health Care Campus, where FDG PET/CT became the recommended imaging modality for suspected focal infection in brucellosis since 2016, were analyzed retrospectively. The detection of focal infection as well as management modification before and after FDG PET/CT were recorded.

**Results.** FDG PET/CT was performed in 30 episodes of brucellosis occurring in 27 patients: 20 primary episodes and 10 suspected relapse episodes. The mean age of the patients was  $50 \pm 15.07$  years. Focal disease was diagnosed in 18 of 30 (60%) episodes, of which 8 (26.6%) were diagnosed for the first time by FDG PET/CT, all of whom had spinal infection, with a concomitant additional focus in 5. Overall, multifocal disease was diagnosed in 10 of 18 (55.5%) of patients with focal disease. Management modification following FDG PET/CT was recorded in 17 of 30 (56.6%) episodes, mainly by treatment extension in spinal infection and withholding treatment in patients with suspected relapse but no evidence of active disease by FDG PET/CT.

**Conclusions.** FDG PET/CT was found to be helpful in the diagnosis of focal infection in brucellosis. Multifocal disease seems more prevalent than previously described. The clinical impact of adding FDG PET/CT to the diagnostic workup of brucellosis should be evaluated in future studies.

**Keywords.** brucellosis; FDG PET/CT; focal infection.

Brucellosis is one of the important zoonotic diseases and is still common in many countries worldwide [1]. Focal infection in human brucellosis is reported to occur in 20%–50% of cases. The most common are skeletal infections including vertebral osteomyelitis, sacroiliitis, and septic arthritis [2].

Identifying focal disease in brucellosis is crucial as the duration of treatment as well as type and number of antimicrobial agents should be adjusted accordingly. For example, in spondylitis a duration of at least 8–12 weeks of treatment is recommended instead of the standard 6 weeks' duration for noncomplicated brucellosis [3, 4]. The addition of ceftriaxone is recommended in

neurobrucellosis [3, 5]. In some focal infections, triple therapy seems to be preferred over the standard dual therapy, as in the case of infective endocarditis [3], neurobrucellosis [5], and selected cases of complicated spinal infections [4].

Detecting focal infection in brucellosis may be challenging clinically since the disease typically presents with prolonged, nonspecific symptoms, with patients reporting on multiple painful sites (eg, back pain, general weakness). There are no current recommendations for imaging investigation in brucellosis. Physicians use different modalities for investigation of focal disease such as bone scintigraphy, computed tomography (CT), and magnetic resonance imaging (MRI), which depends on the suspected site of infection and access to imaging tests [6]. In many cases, the requirement for multiple imaging modalities may lead to delay in diagnosis and appropriate management.

Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) has demonstrated a high diagnostic yield in several infectious processes including skeletal and deep-seated infections [7]. Few case reports reported the contribution of FDG PET/CT in diagnosing atypical brucellosis [8–14]. These included pulmonary [8] and hepatic brucellosis [10, 12], infected aortic aneurysm [14], a case of neurobrucellosis with massive

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intraspinal FDG uptake [13], and 2 cases of spinal brucellosis [9, 11]. In addition, a small case series of patients with spinal brucellosis was reported [15].

The current study aimed to assess the benefit of FDG PET/CT in the management of patients with brucellosis and suspected focal infection, focusing on its clinical impact on management.

## METHODS

### Study Design and Setting

This was an observational retrospective study. Patients who underwent FDG PET/CT as a part of their diagnostic workup of brucellosis were identified at Rambam Health Care Campus (RHCC), a 1000-bed primary and tertiary care university-affiliated hospital. We included hospitalized patients, as well as outpatients referred to the RHCC Infectious Diseases (ID) clinic, between the years 2000 and 2021. Patients who were diagnosed with primary infection (first episode) as well as patients diagnosed with suspected relapse were included.

Since April 2016, patients were prospectively identified and actively investigated. A daily automated electronic laboratory report of microbiological results positive for brucellosis was sent to the ID staff (Rose Bengal test, serum agglutination serology [ $>1:40$ ], isolation of *Brucella* spp in any body fluid sample, or positive polymerase chain reaction [PCR] for *Brucella* spp). All patients with positive results were contacted actively and consulted by an ID physician. When focal disease was suspected, FDG PET/CT was recommended and patient management was directed by FDG PET/CT findings following hospital local guidelines. These guidelines, in brief, recommended treatment with 7 days of gentamicin and 6 or 12 weeks of doxycycline as first-line regimen for uncomplicated and complicated brucellosis, respectively. All patients were advised ID follow-up after discharge. Patients diagnosed since July 2017 were offered follow-up at the hospital ID outpatient clinic every 3 months up to 12 months. Clinical data, serology, and additional imaging results, if available, were recorded in every visit and were used for further analysis.

### Outcomes

*New focal infection* was considered a new focus compatible with infection by FDG PET/CT, not previously diagnosed by other means.

*Management modification* was considered any change in type of antimicrobial drug (initiation or discontinuation), route of administration, dosing, and duration triggered by the FDG PET/CT results. In addition, any surgical procedure performed or directed by FDG PET/CT findings was considered a management modification.

### Data Collection

For the purpose of this study, we identified patients using the electronic medical records by diagnosis of brucellosis, according

to *International Classification of Diseases, Ninth Revision* classification and/or by microbiology laboratory results consistent with probable or confirmed brucellosis (see definitions below), who underwent FDG PET/CT.

FDG PET/CT results were documented. In the case of focal infection shown on PET/CT, it was classified as either new or previously diagnosed. In addition, any management modification that was done following PET/CT findings was also recorded.

### Definitions

A confirmed case of brucellosis was defined as a clinically compatible illness with a definitive laboratory evidence of *Brucella* infection (identification of *Brucella* spp based on culture of a clinical specimen).

A probable case was defined as clinically compatible disease with presumptive laboratory evidence, that is, a total *Brucella* antibody titer of  $\geq 1:160$  by a standard tube agglutination test or detection of *Brucella* DNA in a clinical specimen by a PCR test.

Relapse was diagnosed on basis of recurrence of symptoms compatible with brucellosis with presumptive laboratory evidence (suspected or probable) or definitive laboratory evidence (confirmed relapse).

Primary episodes were defined when brucellosis was diagnosed for the first time or after  $>2$  years of a previous episode.

### FDG PET/CT Acquisition, Interpretation, and Analysis

Patients underwent FDG PET/CT after 4 hours of fasting. The scan was performed 60 minutes after the injection of [ $^{18}$ F] FDG. In cases with suspected cardiac infection, a longer fasting time of 12 hours preceded by a low-carbohydrate, fat- and protein-enriched diet was recommended in order to suppress myocardial physiological FDG uptake. Patients underwent eye- to midhigh PET/CT, with head and lower limb scanning added when clinically indicated.

All FDG PET/CT studies were interpreted by an experienced nuclear medicine physician with access to clinical information and previous imaging reports. Sites of nonphysiological increased radiotracer activity were recorded. The final diagnosis of infection was made in consultation with the referring clinical team.

### Microbiological Diagnosis

Blood cultures were performed using BD BACTEC 9240 and BD BACTEC FX (Becton Dickinson, New Jersey) systems. Isolates were cultured on 5% blood agar (Hy Laboratories, Rehovot, Israel). Serological detection included the Rose Bengal test (Bio-Rad, Hercules, California), followed by serological testing with the Brucellacapt serum agglutination test (Vircell, Granada, Spain). Molecular identification was performed using *Brucella* sp-specific primers (F4: 5'-TCG AGC GCC CGC AAG GGG-3' and R2: 5'-AAC CAT AGT GTC TCC ACT AA-3') [16].

**Table 1. Baseline Characteristics and Clinical Presentation of Patients With Brucellosis Who Underwent Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (N = 27)<sup>a</sup>**

Characteristic	No. (%)
Age, y, mean ± SD	50 ± 15.07
Ethnicity (Arab)	23 (85.1)
Sex (female)	14 (51.8)
Exposure mode <sup>b</sup>	
Livestock animal contact	11 (40.7)
Unpasteurized dairy product consumption	19 (70.3)
Unknown	7 (26)
Charlson Comorbidity Index, median (IQR)	0 (1–3)
Duration of symptoms to diagnosis, d, median (IQR)	30 (7–52.5)
Acute disease (<14 d)	13 (48)
Fever on presentation	21 (77.7)
Days of fever to admission	
Mean ± SD	11.6 ± 24.6
Median (IQR)	7 (0–10)
Night sweats	15 (55.5)
Chills	6 (22.2)
Weight loss	10 (37)
Headache	10 (37)
Malaise	14 (51.8)
Loss of appetite	5 (18.5)
Back pain	14 (51.8)
Arthralgia	8 (29.6)
Gastrointestinal symptoms	6 (22.2)
Abdominal pain	5 (18.5)
Respiratory symptoms	4 (14.8)
Hepatosplenomegaly on physical examination	4 (14.4)
Lymphadenopathy on physical examination	3 (11)
Limping	3 (11)
Arthritis	4 (14.8)
WBC, ×10 <sup>3</sup> /μL, mean ± SD	8.56 ± 3.99
Hemoglobin, g/dL, mean ± SD	11.72 ± 1.42
Platelets, ×10 <sup>9</sup> /L, mean ± SD	284.3 ± 173.03
ALT (GPT), U/L, mean ± SD	54 ± 11
Elevated ALT (>55 U/L)	12 (44)
AST (GOT), U/L, mean ± SD	44 ± 25
Elevated AST (>35 U/L)	11 (40.7)
ALP, U/L, mean ± SD	149 ± 114
Elevated ALP (>150 U/L)	8 (29.6)
GGT, U/L, mean ± SD	211 ± 233
Elevated GGT (>36 U/L)	17 (63)
Bilirubin, mg/dL, mean ± SD	0.46 ± 0.23
Elevated bilirubin (>1.2 mg/dL)	0
Albumin, g/dL, mean ± SD	3.5 ± 0.3
Creatinine, mg/dL, mean ± SD	0.81 ± 0.17
C-reactive protein, mg/L, mean ± SD	60 ± 50
Elevated CRP (>5 mg/L) (n = 24)	21 (87)
Patients with <i>Brucella</i> bacteremia	19 (70)
Days of documented bacteremia <sup>c</sup> , mean ± SD	2.1 ± 3.2
<i>Brucella</i> antibodies (n = 25), median (IQR)	1280 (320–1280)
Titer ≥1:160	25 (100)
Titer ≥1:320	24 (96)

### Statistical Analysis

Characteristics of included cases were described through categorical and continuous variables as appropriate. Categorical

**Table 1. Continued**

Characteristic	No. (%)
First diagnosis	
Confirmed	20 (74)
Probable	7 (26)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; GOT, glutamic oxaloacetic transaminase; GPT, glutamic-pyruvic transaminase; IQR, interquartile range; SD, standard deviation; WBC, white blood cell.

<sup>a</sup>Clinical presentation of the first episode presented. The n values indicate number of patients with available data.

<sup>b</sup>Some patients had >1 possible exposure mode.

<sup>c</sup>Follow-up blood cultures were taken in a minority of cases.

data were summarized as percentages and continuous data were summarized as means with standard deviation or median with interquartile range (IQR). We calculated the rate of focal disease, FDG PET/CT findings, and treatment modifications in the study cohort.

The ethics committee of RHCC approved the study.

## RESULTS

We identified 27 patients with 30 episodes of brucellosis who underwent FDG PET/CT for investigation of suspected focal infection: 20 episodes of primary infection (15 confirmed brucellosis, 5 probable brucellosis) and 10 episodes of relapse/chronic infection (2 confirmed brucellosis, 8 probable brucellosis). The vast majority of the cohort (27 episodes) belonged to the period after April 2016. During this time period there were overall 99 episodes of brucellosis diagnosed at RHCC.

Characteristics of included patients are presented in Table 1. All were adults (>18 years old) with a mean age of 50 ± 15.07 years. The cohort included 23 (85%) Arab patients. Median duration of symptoms until the diagnosis of the first episode was 30 days (IQR, 7–52.5 days). Back pain was documented in 14 cases (51.8%), limping in 3 (11%), and arthritis on physical examination in 4 cases (14.8%). C-reactive protein was elevated during the first episode in 21 of 24 (87%) cases, with a mean of 60 ± 50 mg/L.

### Focal Disease and FDG PET/CT

FDG PET/CT was performed within a median of 17 days (IQR, 12–71 days) from start of symptoms. Median time from first diagnosis of brucellosis to performance of FDG PET/CT was 13 days (IQR, 6–65.25 days). Overall, focal disease was diagnosed in 18 of 30 (60%) investigated episodes. Details of the 30 cases including FDG PET/CT findings are available in Supplementary Table 1. Multiple complaints suggestive of focal disease were present in the majority of cases. In addition, some patients underwent FDG PET/CT due to persistent bacteremia and/or suspected concomitant inflammatory or malignant

disease. Focal disease was diagnosed in 10 episodes before PET/CT, either by other imaging modalities (3 by MRI and 1 by CT for spinal infection and 1 by CT for suspected hip arthritis) or by invasive procedures (2 cases with neurobrucellosis by lumbar puncture and 3 cases of arthritis by arthrocentesis).

In 8 episodes, a new focus was diagnosed by FDG PET/CT; all with spinal infection, of whom 5 had concomitantly an additional focus. The types of infectious foci detected by FDG PET/CT are presented in Table 2. Multifocal disease was diagnosed in 10 cases, comprising 55.5% of all patients with focal disease, the majority of which were skeletal infections (Supplementary Table 1). An example of multifocal disease detected by FDG PET/CT is presented in Supplementary Figure 1.

### Modification of Treatment Following FDG PET/CT

Modifications of treatment in accordance with FDG PET/CT findings are summarized in Table 3. In 17 episodes (56.6%), a modification of treatment following FDG PET/CT findings was recorded. The most common modification was extension of treatment duration recorded in 10 (33%) cases, 8 due to a diagnosis of spinal infection, 1 due to suspected prosthetic joint infection, and 1 due to extensive spinal and extraspinal infection. Withholding treatment was recorded in 6 cases (20%), all among patients with suspected relapse or chronic infection, in whom FDG PET/CT showed no evidence of an active disease. None of the 6 patients had evidence of complications during a mean follow-up of  $10 \pm 8.8$  months (range, 3–24 months).

**Table 2. Contribution of Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography to the Final Diagnosis<sup>a</sup>**

Infection	Final Diagnosis (n = 30)	First Diagnosed by PET/CT (n = 30)
Spinal infection	12 (40)	8 (26)
Septic arthritis/PJI	8 (26)	6 (20)
Prostatic infection	4 (13)	4 (13)
Lymphadenopathy $\pm$ increased uptake	15 (50)	12 (40)
Hepato-splenomegaly $\pm$ increased uptake	6 (20)	4 (13)
Others		
Cholecystitis	1 (3)	1 (3)
Empyema	1 (3)	1 (3)
Muscular collection	1 (3)	1 (3)
Noninfectious		
Vasculitis	1 (3)	1 (3)
SOL of kidney	1 (3)	1 (3)
Multifocal infection	10 (33)	10 (33)
No evidence of focal infection	12 (40)	14 (46) <sup>b</sup>

Data are presented as No. (%).

Abbreviations: PET/CT, positron emission tomography/computed tomography; PJI, prosthetic joint infection; SOL, space-occupying lesion.

<sup>a</sup>Patients' final diagnoses are presented (>1 diagnosis per episode possible), with the number of patients in whom the diagnosis was made by fluorodeoxyglucose PET/CT.

<sup>b</sup>Two patients with neurobrucellosis (meningoencephalitis) showed no evidence of focal infection in PET/CT.

**Table 3. Modification of Treatment Following Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Findings**

Type of Modification <sup>a</sup>	Total (N = 30)	Primary Episode (n = 20)	Suspected Relapse/Chronic Infection (n = 10)
Extension of overall treatment duration	10 (33)	8 (40)	2 (20)
Extension of gentamicin duration	3 (10)	3 (15)	0 (0)
Withholding treatment	6 (20)	0 (0)	6 (60)
Addition of antimicrobial agent	2 (6)	2 (10)	0 (0)
Conservative treatment for cholecystitis	1 (3)	1 (5)	0 (0)
None	13 (43)	11 (55)	2 (20)

Data are presented as No. (%).

<sup>a</sup>More than 1 modification occurred in some cases.

Variable periods of follow-up were documented in accordance with variable treatment durations and compliance with follow-up (Supplementary Table 1). Two patients died, 1 of them related to neurobrucellosis.

### FDG PET/CT Follow-up

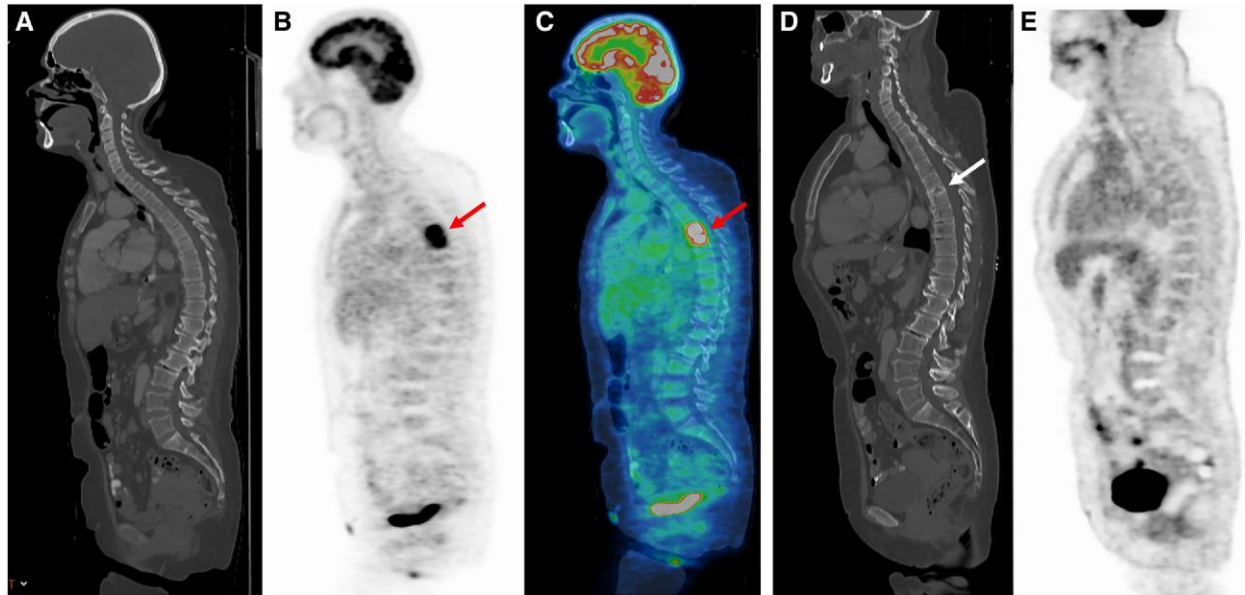
Two patients had repeated FDG PET/CT for follow-up within 6 months of the first episode (both were diagnosed with spinal infection). In both, complete resolution of the pathological uptake was observed. The FDG PET/CT imaging at diagnosis and after 6 months of 1 of these patients is presented in Figure 1.

## DISCUSSION

In the current study, FDG PET/CT detected a high rate of focal infections in a cohort of patients with clinically suspected focal brucellosis. Skeletal infections, particularly those involving the spine, were the most common. In addition, multifocal disease was demonstrated in 10 patients, comprising 55% of patients with focal brucellosis. Investigation by FDG PET/CT was associated with management modifications in more than half of cases (57% of the cohort). These modifications included treatment duration extension with or without addition of antimicrobial drugs when focal disease was detected or, on the contrary, withholding treatment in the context of suspected relapse but no active focal disease on PET/CT. Overall, FDG PET/CT was helpful in differentiating between patients with or without skeletal brucellosis (accordingly adjusting treatment duration) and excluding relapse among patients with primary focal disease (subsequently withholding unnecessary treatment).

The challenges in diagnosing complicated brucellosis based on clinical suspicion were highlighted in our study. Long duration of symptoms until diagnosis has been recognized as a risk factor for complicated brucellosis [17]. The multiple painful sites that were reported in most cases and the long time it took to make the first diagnosis (a median time of 30 days) is





**Figure 1.** Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) in a brucellosis patient before (A–C) and after (D and E) treatment. Images demonstrate pathological FDG uptake consistent with spondylodiscitis at the level of T6–T7 vertebra (A–C, arrows). After treatment (D and E) no activity is shown at this level, indicating complete resolution of the infectious process. On CT, postinfection degenerative changes are seen in the involved vertebral plates (D, arrow).

not unique to our cohort. Symptoms such as arthralgia, myalgia, and back pain were reported in about half of the patients in previous studies [6]. Migratory pain during the disease course is common, making it difficult to localize focal infections and direct imaging. In addition, coexistence of degenerative changes in spine and joints in adults further complicates diagnosis [18]. This was observed in our cohort among the few patients who underwent MRI that did not include the involved part of the spine detected later by FDG PET/CT or infectious foci that were misdiagnosed by spine CT as degenerative changes. The recommended gold-standard imaging for vertebral osteomyelitis/spondylodiscitis is MRI that provides optimal anatomic imaging, including detection of paravertebral and epidural extension of infection [19]. FDG PET/CT had high sensitivity (92%–100%) and specificity (83%–100%) for diagnosis of vertebral osteomyelitis/spondylodiscitis compared to MRI as reference standard in several studies [20–23]. The advantages of FDG PET/CT over MRI include imaging of the whole spine for detection of other spinal involvement and diagnosis of extraspinal infections, and to direct MRI in cases where the location of the infection along the spine is unclear. In addition, the inflammatory process that can be seen on FDG PET/CT before anatomic changes can be seen on MRI may offer an additional advantage [20].

The high proportion of multifocal disease in our cohort is unique. Previous studies reported multifocal noncontiguous brucellosis as a rare event [24–28]. This unique finding is a result of the improved combined anatomic and functional whole-body imaging provided by FDG PET/CT. In a previous small

cohort of 10 cases of patients with spinal brucellosis, 3 patients had been diagnosed with multifocal noncontiguous spinal infection by PET/CT; all were misdiagnosed by MRI as single focal spondylitis [15]. In our study, multifocal disease included mainly spondylitis and peripheral joint arthritis. In addition, nonskeletal concomitant involvement was observed in suspected prostate, gallbladder, and pleural infections. Although microbiological diagnosis was not confirmed, *Brucella* infection was likely the etiology as imaging and clinical findings improved or resolved in follow-up imaging and/or clinical assessments with anti-*Brucella* treatment alone. If this finding is confirmed by additional studies, it may give a new perspective on the pathogenesis of brucellosis. Yet, the clinical importance of discovering additional foci by PET/CT that otherwise would have been undetected warrants further evaluation.

The fact that the optimal duration of treatment in complicated brucellosis is unknown highlights the need for follow-up tools. Persistent or slowly improving back pain and paucity of objective parameters to follow make it difficult to assess treatment response in spinal brucellosis. FDG PET/CT could have a benefit in individualizing treatment durations and in monitoring treatment response. In a previous study that included 147 FDG PET/CT performed to follow treatment response in spinal infection, pattern-based interpretation criteria of the FDG PET/CT achieved a specificity of 100% for assessment of treatment response [29]. Furthermore, a study describing the real-life use of FDG PET/CT in a cohort of 133 patients with proven vertebral osteomyelitis showed that follow-up FDG PET/CT was independently associated

with clinical cure at the end of therapy (odds ratio, 0.45 [95% confidence interval .31–.78] for clinical failure) [30]. In the previously mentioned cohort of 10 patients with spinal brucellosis who underwent FDG PET at initial diagnosis and during follow-up, a good correlation was found between maximal standardized uptake values and good clinical outcome without documentation of relapse [15]. Similarly, we described in our cohort full resolution of the pathological uptake of spinal infection after 6 months on PET/CT in 2 patients.

Diagnosing relapsing infection in brucellosis is another challenge. The continuation of complaints for a long time after treatment of the primary infection has been completed and absence of definite microbiological evidence of active infection is not a rare situation. In some cases, serological follow-up may be helpful showing re-increase in serum antibodies titers [3]. However, serology may be difficult to interpret, especially in individuals repeatedly exposed to *Brucella* organisms [31]. In such cases there is a dilemma whether to re-treat patients on clinical basis only. In a small study that included 30 patients with suspected relapse of spinal infection, FDG PET/CT had better sensitivity and specificity compared to MRI in the diagnosis of relapsing infection with a negative predictive value of 95%. These differences did not reach statistical significance, most probably due to the small size of the cohort [32]. The role of FDG PET/CT for exclusion of active relapsing disease in brucellosis is highly important and should be further evaluated. Of note is the high rate of detection of lymphadenopathy and hepatosplenomegaly by FDG PET/CT that was observed in primary episodes and active relapse episodes. This finding appears to be related to one of the principal pathogenic features of *Brucella* bacterium and its tropism to the reticuloendothelial system and seems to be more frequent than what has been reported in literature [2]. This finding was absent in patients who had suspected relapse but whose final diagnosis excluded active infection.

This study has limitations. The real impact on patients' clinical outcome could not be evaluated in the current cohort study. An earlier diagnosis of focal infection has the potential to reduce the consequent disabilities, which are a major concern of brucellosis, but this could not be evaluated. Other limitations include the small sample size, possibly underestimating rare focal infections, and selection bias where FDG PET/CT was performed in selected patients with suspected focal disease. Patients underwent PET/CT on variable timing after symptom onset. *Brucella* infection in the detected foci was not confirmed pathologically in the majority of cases, but the clinical and radiological courses were compatible with brucellosis. Finally, a study from a single center may reflect pathogenesis related to specific serovars or pathogen–host interaction in specific population. The Arab predominance in our cohort reflects the epidemiology of brucellosis in Israel [33].

In conclusion, we suggest a promising role for FDG PET-CT in the diagnostic pathway of brucellosis. Its contribution is in

detecting foci of the disease necessitating prolongation of treatment for the primary infection and precluding relapse of infection. Our findings should be evaluated in a larger cohort, which will necessitate a global effort of endemic locations. The impact of FDG PET-CT on patients' morbidity and its cost-effectiveness should be evaluated in prospective studies.

### Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

### Notes

**Patient consent.** The ethics committee of Rambam Health Care Campus approved this retrospective study and waived the need for signed informed consent.

**Potential conflicts of interest.** All authors: No reported conflicts of interest.

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