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Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Interpretation Criteria for Assessment of Antibiotic Treatment Response in Pyogenic Spine Infection

Silvia A. Riccio, MD[a,*], Angel K. M. Chu, MD[b], Harvey R. Rabin, MD[b], Reinhard Kloiber, MD[a]

[a]*Department of Radiology, University of Calgary, Calgary, Alberta, Canada*
[b]*Department of Medicine, Microbiology and Infectious Diseases, University of Calgary, Calgary, Alberta, Canada*

Abstract

Purpose: The objective of the study was to determine if fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) can assess the response of patients with pyogenic spine infection to antibiotic treatment in a clinically useful time frame.
Methods: Twenty-eight patients with suspected pyogenic spine infection had baseline ^{18}F-FDG PET/CT. Patients with proven or probable infection were divided into good and poor responders to antibiotic therapy based on clinical criteria. These patients had a follow-up ^{18}F-FDG PET/CT 6-8 weeks later.
Results: Six of 28 patients were deemed negative for infection based on ^{18}F-FDG PET/CT. Two patients were excluded because of discrepancies in interpretation. Of the 20 patients deemed positive for infection, 13 had a pathogen isolated and all showed ^{18}F-FDG uptake in bone and/or soft tissue at baseline. Patients with a poor clinical response to treatment had persistent ^{18}F-FDG uptake in bone and/or soft tissue on follow-up. Patients with good clinical response had uptake confined to the margins of the destroyed disc. None of these patients had recurrent infection, even if antibiotics had already been discontinued at the time of the follow-up scan.
Conclusions: ^{18}F-FDG uptake confined to the margins of a destroyed disc after antibiotic therapy of pyogenic spine infection must not be considered indicative of persistent infection and likely represents mechanically induced inflammation. ^{18}F-FDG uptake in bone or soft tissue does indicate active infection. Quantification of activity could not reliably differentiate patients with active infection from those without active infection and those who had had a successful response to therapy. The pattern of activity is critical to accurate interpretation.

Résumé

Objet : L'étude avait pour objectif de déterminer si la tomographie par émission de positrons couplée à la tomodensitométrie avec injection de fluorodésoxyglucose marqué au fluor 18 (TEP-TDM au 18F-FDG) permettait d'évaluer dans un délai raisonnable sur le plan clinique la réponse thérapeutique de patients ayant reçu un traitement par antibiotique en raison d'une infection pyogène de la colonne vertébrale.
Méthodes : Une TEP-TDM au 18F-FDG de référence a été réalisée chez 28 patients qui semblaient présenter une infection pyogène de la colonne vertébrale. À partir de critères cliniques, les patients présentant une infection avérée ou probable ont été répartis en deux catégories, selon qu'ils présentaient des réponses satisfaisantes ou non à l'antibiothérapie. Ces patients ont ensuite subi une TEP-TDM au 18F-FDG de suivi, de six à huit semaines plus tard.
Résultats : Sur les 28 patients examinés, 6 ont été réputés ne pas présenter d'infection à la TEP-TDM au 18F-FDG. Deux patients ont été exclus en raison de résultats d'interprétation divergents. Parmi les 20 patients jugés positifs d'infection, un pathogène a été isolé chez 13 d'entre eux, et une fixation de 18F-FDG a été observée dans les tissus osseux et mous de tous les patients à l'examen de référence. À l'examen de suivi, une fixation persistante de 18F-FDG a été relevée dans les tissus osseux et mous des patients dont la réponse thérapeutique n'était pas satisfaisante sur le plan clinique. Chez les patients dont la réponse était satisfaisante, la fixation du produit était circonscrite aux marges du disque détruit. Aucun des patients n'a présenté d'infection récurrente, même si l'antibiothérapie était déjà terminée au moment de l'examen de suivi.
Conclusions : La fixation de 18F-FDG circonscrite aux marges d'un disque détruit, après une antibiothérapie en raison d'une infection pyogène de la colonne vertébrale, ne doit pas être considérée comme un signe évoquant une infection persistante, mais probablement comme

* Address for correspondence: Silvia A. Riccio, MD, Foothills Medical Centre, 1403 29 St NW, Calgary, Alberta T2N 2T9, Canada.
E-mail address: ricciosilvia@hotmail.com (S. A. Riccio).

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le signe d'une inflammation induite mécaniquement. La fixation de 18F-FDG dans les tissus osseux et mous révèle toutefois une infection active. La mesure quantitative de l'activité n'a pas permis de distinguer efficacement les patients présentant une infection active de ceux qui n'en présentaient pas ni de ceux qui répondaient de façon satisfaisante au traitement. La représentation de cette activité est essentielle à une interprétation juste.

Key Words: FDG PET/CT; Spine infection; Vertebral osteomyelitis; Discitis; Antibiotic treatment response

The clinical presentation of pyogenic spine infection (PSI) is often nonspecific, resulting in a delay in diagnosis [1]. Progressive low back pain is the most common symptom. Fever is present in more than half of patients [2], and elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in greater than 90% [1]. Blood cultures are positive in approximately 50% of cases [3]. Bone biopsy identifies organisms in approximately 40%, but yields are reduced after antibiotic therapy has been started [4]. Despite best efforts, the etiologic pathogen is not identified in approximately one third of cases and antibiotics are selected empirically [2].

There are currently no clinical criteria or recommended imaging modalities to objectively evaluate the effectiveness of antibiotic treatment; rather, it is gauged by the patient's subjective clinical response. This can be problematic because persistent or worsening pain may be the result of residual active infection requiring prolonged or different antibiotic therapy, mechanical causes resulting from progressive bone destruction in the absence of persistent infection, or co-morbid conditions.

Magnetic resonance imaging (MRI) is currently considered the optimum imaging modality for initial diagnosis of vertebral osteomyelitis. It can localize the abnormality through visualization of soft tissue and marrow edema and contrast enhancement. MRI can identify optimal sites for biopsy, distinguish between phlegmon and drainable abscess, and clarify neurological complaints by demonstrating nerve or spinal cord compression [5]. MRI is highly sensitive and specific for detection of spinal infection [6,7]. False positives can result from contrast enhancement in some noninfected degenerated discs [8]. However, MRI is of limited value in reassessing patients who are at the conclusion of their therapy. Noninfectious bone and disc abnormalities may persist or even worsen during the weeks or months after successful antibiotic treatment [9,10] making MRI interpretation invalid for assessing response to therapy.

The sensitivity and specificity of fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) for detection of chronic active osteomyelitis in both the axial and appendicular skeleton in a 2005 meta-analysis was 96% and 91%, respectively, and therefore comparable to MRI [11]. Data on the usefulness of ^{18}F-FDG PET/computed tomography (CT) in assessing treatment response is limited but more promising than for MRI [12−15]. Two previous reports on the use of sequential FDG PET [16,17] concluded that the most reliable criterion to confirm a favorable treatment response was a decrease in maximum standardized uptake values (SUVmax) between the baseline and follow-up studies. In clinical practice, a baseline study is unlikely to have been done. This paper proposes diagnostic criteria that can be applied to a stand-alone ^{18}F-FDG PET/CT done at the end of the usually prescribed course of parenteral antibiotic therapy.

Methods

Ethics approval for this prospective study was obtained from the Conjoint Health Research Ethics Board of the Faculties of Medicine, Nursing, and Kinesiology. Informed written consent approved by the Conjoint Health Research Ethics Board was obtained from all patients prior to enrolment in the study.

Enrollment

Twenty-eight patients with suspected pyogenic infection of the cervical, thoracic, or lumbar spine (osteomyelitis, discitis, or epidural abscess) localized by CT, MRI, or bone scintigraphy who had been referred to the infectious diseases service were enrolled. A baseline ^{18}F-FDG PET/CT was used to confirm or exclude the presence of infection. Patients diagnosed as having active infection on ^{18}F-FDG PET/CT were further categorized as proven infection if blood or biopsy cultures were positive or presumed infection if cultures were negative. A second ^{18}F-FDG PET/CT was performed 6-8 weeks later to see if scan results correlated with clinical symptoms. Patients whose baseline ^{18}F-FDG PET/CT was not indicative of infection and in whom antibiotics were withheld did not have a second ^{18}F-FDG PET/CT. All patients were followed clinically for a minimum of 6 months.

Patients were excluded from the study if they received antibiotics for more than 2 weeks prior to baseline ^{18}F-FDG PET/CT, had spine surgery within 3 months of presentation, or had internal fixation hardware at the site of concern. Others with nonpyogenic infection (eg, tuberculosis or fungus) were also excluded, as they were expected to follow a different clinical course than pyogenic infection.

^{18}F-FDG PET/CT Acquisition

A single intravenous injection of 350 MBq of ^{18}F-FDG was administered to each subject at least 30 minutes prior to scanning. All patients had fasted for a minimum of 6 hours. Those with glucose levels greater than 10 mmol/L were