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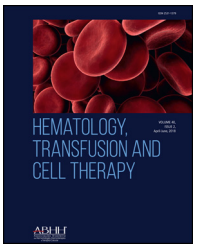

Original article

Fluorodeoxyglucose-positron emission tomography staging can replace bone marrow biopsy in Hodgkin's lymphoma. Results from Brazilian Hodgkin's Lymphoma Study Group

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ABSTRACT

Objective: To investigate, in a large prospective multicenter study, whether 2-[18F]-fluoro-2-deoxy-D-glucose-positron emission tomography is sufficiently accurate to identify clinically important bone marrow involvement by Hodgkin's lymphoma to replace routine bone marrow biopsy in a developing tropical country.

Methods: Patients newly diagnosed with Hodgkin's lymphoma were recruited from six cancer centers in Brazil. All were staged by the results of positron emission tomography/computed tomography that were centrally reviewed and by iliac crest bone marrow biopsy. Patients were classified as having marrow disease if they had lymphoma identified by marrow biopsy histology or had focal 2-[18F]-fluoro-2-deoxy-D-glucose marrow uptake that resolved following chemotherapy.

Results: A total of 246 participants were recruited from six different centers and 62 (25.2%) were judged to have Hodgkin's lymphoma in the bone marrow. Positron emission tomography and biopsies were concordant in 206 patients (83%). Positron emission tomography correctly identified marrow disease in 59/62 patients (95.1%) and marrow biopsy in 25/62 patients (40.3%). In 22/62 (35.4%) patients, the two techniques were concordant in the diagnosis of marrow involvement. Of the forty discordant results, positron emission tomography

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found bone marrow involvement in 37 patients, upstaging 22 to stage IV and having an impact on therapeutic decision in nine cases given their reallocation from early to advanced stage. Three false negative positron emission tomography results were obtained with bone marrow biopsy giving positive findings. All three cases were classified as stage IV regardless of bone marrow findings implying no modification in the clinical management. The sensitivity, specificity and accuracy of positron emission tomography for detecting bone marrow disease were 95%, 100% and 98% and for bone marrow biopsy they were 40%, 100% and 84%, respectively.

CONCLUSION

We conclude that positron emission tomography can replace marrow biopsy in Brazilian patients with Hodgkin's lymphoma without compromising clinical management.

Introduction

In the last decades, positron emission tomography (PET) with 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) has become the established modality for staging Hodgkin's lymphoma (HL), and international guidelines for its use in lymphomas were harmonized in recent years.[1–4]

Defining prognosis has been a cornerstone of patient management and trial design in HL. In addition, bone marrow biopsy (BMB) has been standard in HL staging, although it is often performed even when the likelihood of involvement is low. Patients with early-stage disease rarely have bone marrow involvement in the absence of a suggestive FDG-PET finding, and those with advanced-stage disease rarely have bone marrow involvement in the absence of disease-related symptoms or other evidence of advanced-stage disease. Different studies have suggested that if a PET/computed tomography (CT) is performed, the need for BMB is questionable in the evaluation of patients with HL.[5–7] However, substantial data is not found in the literature about this issue in patients from developing countries, where disease presentation tends to be more advanced at diagnosis,[8] potentially increasing the incidence of marrow involvement. Furthermore, those countries generally have an elevated prevalence of chronic infectious diseases that could theoretically increase the rate of false positive PET results.[9–11]

This study is part of a Brazilian collaborative project, supported by the Brazilian Society of Nuclear Medicine (SBMN) and the Brazilian Association of Hematology, Hemotherapy and Cellular Therapy (ABHH), to investigate applications of PET/CT in the evaluation of HL patients. Here we evaluate the utility of FDG-PET to detect bone marrow involvement in comparison with BMB as part of initial diagnostic staging of patients with HL in six centers.

Methods

Patients were recruited from six major Brazilian cancer centers: Quanta Diagnóstico e Terapia, Instituto do Câncer do Estado de São Paulo (ICESP), Hospital Sírio Libanês, Hospital Samaritano, Universidade Federal de São Paulo (UNIFESP) and Universidade Estadual de Campinas (Unicamp). The study received Research Ethics Committee approval in all participating institutions and written informed consent was obtained from study participants.

Diagnosis and staging

Diagnosis of de novo HL was made by biopsy of sites of primary lymph node or extranodal disease. Under 18-year-old and pregnant patients were excluded. All patients were staged by unilateral BMB and by FDG-PET/CT scans. Bone marrow from the iliac crest was biopsied and assessed by a local senior hematopathologist.

Whole-body FDG-PET/CT imaging was acquired following standard protocols regarding uptake time (60–90 min) after the intravenous administration of 296–444 MBq (8–12 mCi) of FDG with a maximum interval of 14 days between BMB and PET scanning. Scanners were calibrated and images scaled for reading according to local protocols. Staging scans were performed prior to treatment.

FDG-PET/CT was classified as negative for bone marrow involvement in the absence of any focal area of increased bone marrow uptake or in the presence of diffuse bone marrow uptake. FDG-PET/CT was considered positive in the presence of focal FDG uptake regardless of diffuse uptake.

Quality control

PET scans were centrally reviewed by two nuclear medicine physicians (JJC, CACPN). For the purpose of this study, all scans having abnormal FDG-uptake in bone marrow recorded in the database were examined to confirm and classify the pattern of marrow involvement.

Categorizing marrow disease and data analysis

Since histological examination of all sites is not possible, FDG-PET/CT and BMB results were combined in a reference standard in order to establish the diagnostic accuracy of the methods. Positive concordant findings at FDG-PET and BMB were interpreted as true positives. Concordant negative findings were interpreted as true absence of disease. In discordant cases with focal FDG uptake in marrow, resolution of the

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