ELSEVIER

European Journal of Radiology 66 (2008) 325–331

EJR
EUROPEAN JOURNAL OF RADIOLOGY

www.elsevier.com/locate/ejrad

Prospective study of bone marrow infiltration in aggressive lymphoma by three independent methods: Whole-body MRI, PET/CT and bone marrow biopsy

Vincent Ribrag [a,*], Daniel Vanel [b], Sophie Leboulleux [b], Jean Lumbroso [b], Dominique Couanet [b], Guillaume Bonniaud [c], Anne Aupérin [d], Florence Masson [b], Jacques Bosq [e], Véronique Edeline [b], Christophe Fermé [a], Frédéric Pigneur [b], Martin Schlumberger [b]

[a] *Department of Medicine, Institut Gustave Roussy, Villejuif, France*
[b] *Department of Medical Imaging, Institut Gustave Roussy, Villejuif, France*
[c] *Department of Medical Physics, Institut Gustave Roussy, Villejuif, France*
[d] *Department of Biostatistics and Epidemiology, Institut Gustave Roussy, Villejuif, France*
[e] *Department of Pathology, Institut Gustave Roussy, Villejuif, France*

Received 3 January 2006; received in revised form 2 April 2007; accepted 15 June 2007

Abstract

Purpose: Initial lymphoma staging requires bone marrow assessment in aggressive lymphomas. Bone marrow lymphoma infiltration is routinely assessed by bone marrow biopsy (BMB), considered as the "gold standard". The aim of this study was to compare the performance of BMB, whole-body MRI and PET/CT for evaluation of BM infiltration.
Methods: Patients with newly diagnosed aggressive lymphoma were evaluated by BMB, MRI and PET/CT. Two radiologists, two nuclear medicine physicians and one pathologist independently assessed the results of the three modalities. Bone was considered as involved if BM was positive or if PET/CT or MRI was positive and if there was a resolution of the abnormal image shown on PET/CT or MRI halfway or at the end of therapy.
Results: Both MRI and PET/CT detected bone marrow lesions in the 9/43 patients, but two patients with multiple lesions had more lesions detected by PET/CT compared to MRI. Among these nine patients, two with an iliac crest lesion detected by both MRI and PET/CT had bone marrow involvement with large-cell lymphoma on histological examination. The other seven patients had focal MRI and PET/CT lesions in areas other than the iliac crest, where the blind BMB was done. The other patients had bone marrow without large-cell lymphoma involvement. In all cases, after lymphoma therapy bone marrow involvement regressed on histological examination, PET and MRI.
Conclusion: These preliminary results suggest that non-invasive morphological procedures could be superior to BMB for bone marrow assessment in aggressive lymphomas. Ongoing study is underway to validate these results.

Keywords: Lymphomas; Bone marrow biopsy; PET; MRI

1. Introduction

Computed tomography (CT) and histopathological examination of bone marrow remain the current approaches for initial staging of aggressive lymphomas [1]. This staging is necessary for choosing therapy that can include high-dose therapy with hematopoietic stem cell rescue in young patients when poor prognostic factors are present (such as bone marrow involvement). However, for bone marrow staging, their effectiveness is limited because CT scan threshold for detection of lymphoma involvement is low and depends on the lesion size, and the reliability of blind bone marrow biopsy (BMB) is limited because bone marrow involvement is frequently heterogeneous in aggressive lymphomas [1–5]. In fact, bilateral iliac crest BMB increases the detection rate of bone marrow involvement by 10–20%, as compared to a single BMB [2–6]. Bone marrow involvement with small lymphocytes encompasses cases with clonally related but with clinically occult small-cell component, as well as unrelated B-cell neoplasms present at different

* Corresponding author at: Département de Médecine, Institut Gustave-Roussy, 39 Rue C Desmoulins, 94805 Villejuif, France. Tel.: +33 1 42 11 43 21; fax: +33 1 42 11 52 71.
E-mail address: ribrag@igr.fr (V. Ribrag).

0720-048X/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2007.06.014

locations [6]. The presence of large lymphoma cells in the bone marrow is associated with a poor outcome, and for this reason is screened in the staging of aggressive lymphoma.

Recent studies with new imaging techniques have shown that lymphoma bone marrow involvement can be focal and located outside the iliac crest areas [7–13]. These studies usually compared BMB results with MRI or PET scan, but no studies have prospectively assessed whole-body MRI, PET/CT and histopathologic results in the same patients with aggressive lymphomas.

We report here a prospective study planned to compare the performance of BMB, whole-body MRI and PET/CT for evaluation of BM infiltration in aggressive lymphomas.

2. Material and methods

2.1. Patients and bone marrow analysis

2.1.1. Eligible patients

All patients with newly diagnosed aggressive lymphoma between June 2003 and October 2004 were eligible for this prospective study. In all patients, histological diagnosis was established by excision of a node or biopsy. Histological samples were classified according to the WHO recommendations [20].

Pre-treatment evaluation included physical examination, performance status evaluation, complete blood count, renal and hepatic function tests, serum lactate dehydrogenase (LDH) levels, pelvic, abdominal and thoracic CT scans. Patients' characteristics are presented in Table 1.

Table 1
Characteristics of the 47 patients included in the study

Characteristics	No. of patients (%)
Median age (range)	50 years (24–75 years)
Gender (M/F)	23/24
Pathology (WHO)	
Diffuse large B-cell (DLBCL)	43
Anaplastic T-cell lymphoma	1
Peripheral T-cell	3
Performance status	
0	38
1	6
2	3
Serum LDH level	
N	29
>*N*	18
Clinical stage	
I–II	26
III–IV	21
IPI	
0	10
1	24
2	9
3	3
4	1

All patients were treated with CHOP or reinforced CHOP chemotherapy (ACVBP according to the Groupe d'Etude des Lymphomes Agressifs (GELA) protocols) [14]. Rituximab was combined with CHOP or reinforced CHOP in B-cell lymphomas according to the ongoing GELA protocols.

The search for bone marrow involvement consisted of a bone marrow biopsy of the iliac crest, a whole-body MRI and a FDG PET/CT. All patients gave an informed consent.

2.2. Bone marrow assessment

Marrow aspirates were stained with May–Grünwald–Giemsa. Trephine biopsy samples were decalcified and stained with hematoxylin and eosin. Immunophenotyping on bone marrow was also performed.

2.3. PET scan

Positron emission tomography (PET) was carried out using a hybrid PET-CT imager (Biograph LSO, Siemens Medical Solutions, Erlangen, Germany) after injection of 18-fluorodesoxyglucose (FDG). The injected activity ranged from 367 to 866 MBq (median 539 MBq); the patients have fasted for 6–16 h before injection (median 13 h) and had a glucose blood level ranging from 4 to 7.9 mmol/L (median 5.55 mmol/L). The delay between FDG injection and PET images acquisition (3D mode) ranged from 46 to 184 min (median 78 min). The PET examination consisted of seven to eight bed-steps of 4–5 min each, from the top of the skull to the mild femoral region and of 2 min additional bed-steps for the lower limbs. CT images were recorded for attenuation correction and image fusion using a low-dose CT protocol (helical acquisition, 110 kV, 60–80 mA s). PET Images reconstruction was performed using a FORE rebinning and attenuation weighted OSEM algorithm (eight subsets, four iterations, gaussian post-filtering with a 5 mm FWHM). Fused images were visually interpreted together with standardized uptake value (SUV) recording for each abnormal uptake focus.

2.4. Whole-body MRI

MR imaging examination was performed in the supine position on a 1.5 T unit (Signa version 4,8; GE Medical Systems, Milwaukee) with a body coil. To cover the axial and appendicular skeleton, four contiguous coronal acquisitions with two different MR imaging sequences were used: short tau inversion recovery (inversion time at 150 ms, a repetition time (TR) of 4775 ms, an echo time (TE) of 42 ms) and spin echo T1 (TR at 575 ms, TE at 12.3 ms). The slice center was started at the inferior border of the mandible, scanned with a slice thickness of 8 mm, an interslice of 2 mm and a field of view of 48 cm. The matrix was 384×384. No respiratory gating was performed during the acquisition. No intravenous contrast agent was administered. The entire total body MR imaging with eight sequences was performed within 20 min, including patient positioning.