18-F FDG-PET in the staging of lymphocyte-predominant Hodgkin's disease

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ABSTRACT

This bicentric study assessed retrospectively the usefulness of 18 F-FDG-PET in the staging of 31 patients with lymphocyte-predominant Hodgkin's disease (LPHD). FDG-PET and conventional explorations (CE) were performed for initial disease (n=25) or recurrence (n= 6). All the 68 involved sites were detected by PET including 5 extra-nodal lesions. Only 43 nodal sites (68%) and one splenic focus were detected by CE. PET changed staging in 9 patients (7 upstaged, 2 downstaged) and radiation fields in 3 patients. These results showed the potential role of PET in the staging of LPHD.

Key words: 18F FDG-PET, FDG-PET/CT, lymphocyte-predominant Hodgkin's disease, staging

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Introduction

Lymphocyte predominant Hodgkin's disease (LPHD) is a rare and specific subtype of Hodgkin's lymphoma (HL)[1,2] in most cases involving the lymph nodes, with limited extension (Ann Arbor stage I or II) and an indolent outcome.[3,4] This disease requires regular follow up due to the tendency toward frequent relapses.[4,5]

No consensus has been yet established on the management of LPHD, as chemotherapy,[6] radiotherapy,[7] immunotherapy,[8] and watch and wait attitude are possible options.[9]

Positron emission tomography using 2-[18F]fluoro-2-deoxy-D-glucose (FDG-PET) plays an important role in evaluation of HL and non Hodgkin's lymphoma (NHL), for staging and therapy assessment.[10,11]

This study was conducted to assess the role of FDG-PET in the management of LPHD.

Design and Methods

Patients

Among the 39 LPHD patients explored between July 2002 and May 2006, 31 (79%) were retrospectively included (25 men, 6 women, median age: 35 years, range 16-75) from the hematology departments of Nantes and Rennes University Hospitals. The diagnosis of LPHD was proven pathologically by two independent pathologists according to REAL classification[1] either at the onset of the disease (n=25) or at relapse (n=6). Five patients had previously been treated with ABVD followed by involved field radiotherapy (IFRT) and one by surgery followed by IFRT.

Conventional explorations

Conventional explorations (CE) included medical history, physical examination (lymph node >1 cm was suspected to be pathological), laboratory screening, chest X-Ray, computed tomography (CT) of neck, thorax, abdomen, pelvis with intravenous contrast enhancement, and neck (n=5) or abdomen (n=9) ultrasound. A bone marrow biopsy was performed in 13 patients.

CT was analyzed independently by two radiologists according to classical criteria. CT size criteria for pathological lymph nodes was a diameter >1.5 cm in cervical, axillary, mesenteric and inguinal regions and >1.0 cm elsewhere.

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FDG-PET imaging

Ten whole-body FDG-PET, prior to May 2004 in Rennes, were performed with a GE Advance and 21 whole-body FDG-PET/CT with either a Discovery LS in Nantes or a Discovery ST in Rennes (GE Medical Systems, Milwaukee, WI, USA). PET was conducted 60 minutes after intravenous injection of 5 MBq/kg of ^{18}F-FDG. Patients fasted at least 6 hours and normoglycaemia was established. The emission scan was acquired after registration of CT or transmission scan with Germanium 68 external ring source. The CT was used for PET attenuation correction and for localization of the foci. No contrast agent was administered.

FDG-PET interpretation

FDG-PET images were reviewed by two experienced nuclear medicine specialists, blinded to CE results. Discrepancies in interpretation between observers were resolved by consensus. Abnormal focal uptake was defined as greater than background activity in bordering tissue and not related to physiologic sites of tracer uptake and abnormal splenic uptake as greater than in the liver. Semi-quantitative analysis was performed using the maximum standard uptake values (SUV*max*) normalized to body weight, of all abnormal foci.

Imaging performance analysis and Gold standard

For both ethical and practical reasons, every suspected involved lesions have not been evaluated by histology. Gold standard was therefore determined on the basis of histology and follow-up according to International Workshop Criteria (IWC).[12] When confirmation of involvement was not possible by histology or follow-up, a lesion detected only by one modality of CE or only by FDG-PET was considered uncertain and not valuable to modify the staging. True-positive (TP) corresponded to an abnormal image on CE or FDG-PET confirmed by histopathology or by follow-up as progression or response after treatment according to IWC. A negative finding on CE or FDG-PET was considered to be false-negative (FN) if positive by histopathology or by 1 imaging method plus follow-up. A false-positive (FP) was a positive finding on CE and/or FDG-PET and negative findings on histopathology or other imaging modalities and follow-up (no progression or no response to treatment). Sensitivity of CE or FDG-PET was determined on an anatomic sites basis analysis.

Results and Discussion

Patients and clinical outcome

A total number of 75 sites were involved and 7 peripheral nodal sites were fully removed before imaging. Sixty eight sites were considered as involved according to gold standard, allowing staging of 16 patients as Ann Arbor stage I (5 patients with no residual lesion after surgery), 11 patients as stage II, 2 patients as stage III and 2 as stage IV.

A watch and wait attitude was adopted for 14 patients (45%). Seventeen patients (55%) received treatment: chemotherapy (ABVD, n=2), rituximab (n=5), IFRT (n=5), chemotherapy and radiotherapy (n=4) or chemotherapy and rituximab (n=1).

Conventional exams

CE concluded to 44 involved sites, 43 peripheral lymph nodes and one extra-nodal lesion (spleen) CE showed 3 FP in 3 patients: a differentiated thyroid carcinoma pathologically proven, an inguinal node and a splenic nodule confirmed as unspecific by follow-up. Sensitivity of CE was 65%.

FDG-PET results

FDG-PET concluded to 68 involved sites , 63 nodal sites and 5 extra-nodal sites. Six FP were displayed: bilateral axillary and inguinal foci in a 16 year-old patient with viral inflammation confirmed pathologically, 1 thyroid carcinoma pathologically proven and 1 splenic focus not detected by US, MRI, CT and confirmed as unspecific by follow-up. FDG-PET and CE results were concordant for 44 sites. FDG-PET revealed 20 additional nodal sites, confirmed by follow-up and 4 additional extra-nodal sites, in stomach and guts pathologically confirmed and in spleen and bones confirmed by follow-up. Sensitivity of FDG-PET was 100%.

SUV*max* of LPHD foci ranged from 1.2 to 20.1 (median= 6.1). In the 6 patients at relapse, SUV*max* ranged from 1.2 to 17.6 (median= 6.1). Mean SUV*max* per patient was equal to 9.5±4. Ten patients (32%) had at least one lesion with a SUV*max* > 10 (16 sites).

Impact of FDG PET on Ann Arbor staging and treatment

Impact on Ann Arbor staging is summarized in Table 1. As compared with CE, FDG-PET allowed upstaging in 7 patients (23%). For 2 patients with neck lesions, FDG-PET revealed axillary and supraclavicular lesions, changing the stage I to stage II. In 2 patients with upper-diaphragmatic relapse, FDG-PET led modification of stage II to stage III showing small mesenteric nodes and abnormal foci in the liver hilar region. Two patients showed upstaging from stage III to stage IV with bone (Figure 1) or stomach-intestine involvement detected by FDG-PET.

Compared with CE, FDG-PET led to downstage 2 patients (6%). One patient was downstaged from stage III to stage II: an inguinal node discovered by CT did not show any uptake and remained unchanged after immunotherapy and 2 year-follow up whilst other upperdiaphragmatic nodes responded completely to treatment according to IWC. The second one was downstaged from stage III to stage I, in absence of abnormal uptake on a 13 mm splenic lesion, stable 22 months after initial US whilst IFRT was decided on the left cervical lesion visualized by CT and FDG-PET.

Table 1. Impact of FDG-PET on final staging according to Ann Arbor classification.

		FDG-PET			
		Stage I	*Stage II*	*Stage III*	*Stage IV*
CE	Stage I	15	3	0	0
	Stage II	0	7	2	0
	Stage III	1	1	0	2
	Stage IV	0	0	0	0

CE: conventional explorations.

The treatment strategy was changed for 3 patients (10%) based on FDG-PET findings, leading in extending the radiotherapy fields for 2 patients, and in reducing them for 1.

Over the last decade, FDG-PET has been considered as an useful tool in the staging, therapeutic evaluation and characterization of residual masses of HL[13,14] and aggressive NHL.[15-16] FDG-PET has proven superior to CE in detecting involved regions leading to changes in treatment strategy in 15-25% of cases. A few cases of LPHD have recently been reported in series exploring the role of FDG-PET in the staging of HL.[14,17] We report on a large series of 31 LPHD patients explored by FDG-PET.

FDG uptake appeared to be relatively intense since the median SUV*max* per sites was 6.1 with a wide intra and inter-individual variation. Recently, Hutchings *et al.* demonstrated a significant difference in FDG uptake between the histological subtypes of HL,17 finding a mean SUV*max* of 8.3 in the 7 LPHD patients compared with 11.2 for nodular sclerosis and 14.6 for mixed cellularity patients. In the series of NHL of Schoder *et al.*, SUV*max* >10 excluded indolent lymphoma with 81% specificity.[18] Ten of our patients had a SUV*max* >10. None of them showed aggressive transformation to date.

In our study, the staging using FDG-PET led to 22 confirmations (71%) and 9 modifications in the Ann Arbor stage, with 7 upstaging (23%) and 2 downstaging (6%). FDG-PET appeared to be superior to CE (in order) to stage accurately LPHD at initial assessment. Several studies in HL patients have shown upstaging in 11-41% and downstaging in 0-28% usingFDG-PET.[13,14, 19,20]

In our series, 3 modifications (10%) in the treatment strategy according to FDG-PET results affected the extent of radiotherapy fields. A recent report indicates a change in therapeutic strategy in 9% of HL patients after considering the results of PET/CT.[14]

In conclusion, this retrospective study showed in a large series of 31 patients that FDG-PET may be helpful in the initial staging of LPHD. However, enhanced staging quality provided by FDG-PET will be valuable if accompanied by a change in therapeutic strategy towards less toxic and more individually tailored therapy in this indolent disease.

Authorship and Disclosures

CA, TH, FKB, TL: conception and design of the study; collection, analysis and interpretation of data; manuscript writing; final approval of manuscript. SdG, TG, SLG, TL: contribution and management of patients; CA, TH, AD, EG, FKB: analysis and interpretation of FDG-PET; AM: histopathological review. All the authors approved the content of manuscript, order of authorship.

The authors declined any conflict of interest.

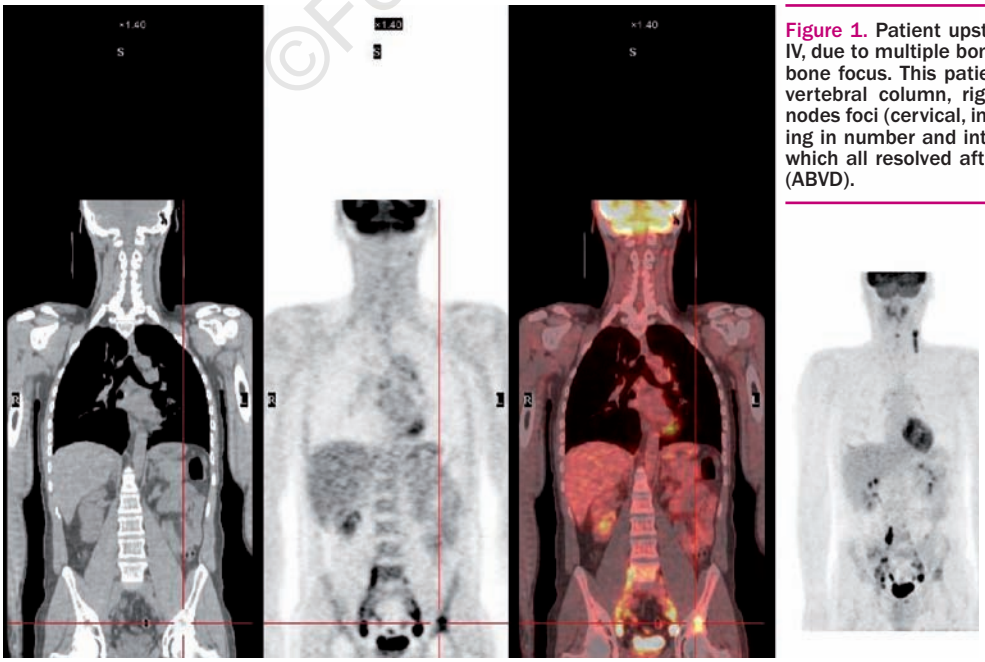

Figure 1. Patient upstaged from stage III to stage IV, due to multiple bone uptake. Abnormal left iliac bone focus. This patient had other bony foci (ribs, vertebral column, right iliac bone…) and lymph nodes foci (cervical, inguinal, iliac regions), increasing in number and intensity on a second FDG-PET, which all resolved after 2 cycles of chemotherapy (ABVD).

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