

Diagnostic role of ^{18}F -FDG-PET in gastric MALT lymphoma

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ABSTRACT

BACKGROUND: The aim of the study was to evaluate the usefulness of ^{18}F -FDG-PET in patients with gastric lymphoma, in particular those affected by mucosa-associated lymphoid tissue (MALT) type and aggressive gastric non-Hodgkin's lymphoma (NHL).

MATERIAL AND METHODS: The study group consists of 15 patients with a previous diagnosis of gastric NHL referred to our PET centres in Bologna Hospital and Rovigo Hospital, Italy, in the period 2003–2004. In 9/15 patients the subsequent histological evaluation was consistent with a gastric MALT lymphoma, while aggressive gastric NHL was diagnosed in the other 6/15. PET scan was carried out in patients with known active disease in order to stage or re-stage disease prior to treatment or in patients in complete clinical remission to monitor disease during follow up. Patients were considered in complete clinical remission if free from disease for at least 8 months after chemotherapy or surgery. ^{18}F -FDG PET was performed following standard procedures.

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RESULTS: Overall ^{18}F -FDG-PET was true positive in all cases of gastric MALT and non-MALT aggressive NHL with known active disease, while no pathological ^{18}F -FDG uptake was evident in the subjects who were in complete clinical remission. The degree of ^{18}F -FDG uptake (mean SUVmax values) in MALT lymphoma was much less intense in comparison to aggressive gastric NHL, suggesting a prognostic role of SUV calculation in gastric lymphomas.

CONCLUSION: Our data demonstrate the significant accuracy of ^{18}F -FDG-PET in detecting active disease in gastric lymphoma of both MALT and non-MALT NHL type. A higher SUV value appears to be related to a more aggressive disease.

Key words: ^{18}F -FDG-PET, aggressive non-Hodgkin's lymphoma, mucosa-associated lymphoid tissue

Introduction

In recent years, ^{18}F -FDG-PET has become widely used to study lymphoid malignancies in both adult and pediatric patients [1], providing relevant information to clinicians, with a direct impact on management decisions [2]. ^{18}F -FDG-PET has various indications in malignant lymphoma (ML) since it is useful for staging the extent of disease, for evaluating early response to therapy, for radiotherapy planning and for monitoring disease during follow up [2–7].

The histologic subgroup of low-grade lymphoma referred to as extranodal marginal zone lymphoma (MZL) mimics the cytomorphological features of the mucosa-associated lymphoid tissue (MALT). Usually these lymphomas arise from sites where lymphoid tissue is normally absent, and lymphocyte accumulation frequently follows a chronic inflammatory event or autoimmune disorder [8]. Although MALT lymphoma can be found in various non-gastrointestinal sites (salivary glands, thyroid, skin, lungs, conjunctiva, orbit, breast, liver, kidneys, intracranial dura), the stomach is the most commonly involved site [8]. At presentation, MALT lymphoma is generally localised (stage IE or IIE), differing from the behaviour of most low-grade B-cell lymphomas. It often shows a relatively indolent behaviour. A correct imaging staging is very important in these patients, both in order to establish a baseline to compare with future diagnostic examinations, and to choose the most appropriate therapeutic approach, either using local or systemic treatment [9]. The detection of patients with residual disease after therapy and of early disease relapse may have a relevant impact on patient management. Furthermore, accurate

assessment of complete responders is extremely vital for appropriate follow up.

Positron emission tomography has been reported to be reliable in detecting ML in patients with large-B-cell non-Hodgkin's lymphoma [10]. Nevertheless, some authors describe a lower PET sensitivity in detecting marginal zone lymphoma (MZL) [11], particularly in cases of extranodal MZL of the mucosa-associated lymphatic tissue (MALT) type [12]. More recently, however, a sensitivity of ^{18}F -FDG PET of 81% in extranodal MZL has been reported in a series of 42 patients [13].

The aim of the present study was to evaluate the accuracy of ^{18}F -FDG PET in patients with gastric MALT and aggressive NHL.

Material and methods

We retrospectively evaluated all ^{18}F -FDG-PET scans carried out in ML patients at Policlinico S.Orsola-Malpighi Hospital (Bologna), and S. Maria della Misericordia Hospital (Rovigo), in the period 2003 to 2004, and all cases with a histological diagnosis of gastric extra nodal MZL or non-MALT aggressive NHL were included in the study. The histological diagnosis was based on the WHO classification [14].

Patients with known active disease underwent ^{18}F -FDG-PET in order to stage or re-stage disease prior to treatment, while for cases in complete remission the exam was carried out to monitor disease during follow up. Each patient was intravenously injected with 5.3 MBq/kg of ^{18}F -FDG and images were recorded 60–90 minutes after tracer administration. ^{18}F -FDG was produced locally using standard synthesis techniques. PET scans were carried out using a dedicated PET scanner (Advance scanner, GE Medical System, Waukesha, WI, USA) in both hospitals. PET scan emission images were recorded for 4 minutes per bed position while non-uniform attenuation correction was performed with a 2-minute transmission scan. None of our patients had a history

of diabetes. To optimise ^{18}F -FDG uptake in normal and neoplastic tissue, patients were asked to fast for at least 6 hours before undergoing PET examination. Before PET scanning, patients were encouraged to void in order to minimize activity in the bladder. Positron emission tomography images were visually evaluated by three experienced readers, aware of all clinical and histological data. In all cases, an agreement among readers was obtained for final report. A scan was considered negative when no pathological uptake was detectable. SUVmax was measured in all sites of known active disease or in the site of the previously treated disease (i.e. for a gastric MZL in complete remission the SUVmax was measured in the stomach).

Results

A total of 15 patients (6 males, 9 females; median age 53 years, range 33–72 years) with a histological diagnosis of extra nodal MZL (9 patients) or gastric non-MALT high grade NHL (6 patients) met the criteria for inclusion in the study. Patient characteristics and PET scan results are reported in Table 1.

Among the patients with gastric MALT lymphoma, six with known active disease underwent ^{18}F - ^{18}F -FDG PET scan in order to stage or re-stage disease prior to treatment, while in the remaining 3 cases PET was carried out in complete clinical remission to monitor disease during follow up. In five patients, the PET scan was repeated in follow-up (patients 1, 3, 4, 6, 7). In all subjects with known active gastric MALT, PET revealed pathologic ^{18}F -FDG uptake at the gastric level (Figure 1) while it was negative in all cases studied in complete remission. In all cases presenting with known active disease, mean SUVmax value was higher than in the cases in complete clinical remission (mean 6.43 vs. 2.25). In one case (patient 6) with active gastric MALT lymphoma, ^{18}F - ^{18}F -FDG uptake was detected not only in the stomach, but also in the cervical and axillary lymph nodes.

Table 1. Gastric MALT and gastric non-MALT NHL patients clinical data and PET scan results

Haematological disease	Case number	Gender/Age (years)	FDG-PET 1 st scan			FDG-PET 2 nd scan			FDG-PET 3 rd scan		
			Disease State	FDG-PET	SUVmax	Disease State	FDG-PET	SUVmax	Disease State	FDG-PET	SUVmax
MALT	1	M/68	AC	Pos	06:05	AC	Pos	07:05	AC	Pos	06:04
MALT	2	F/33	AC	Pos	06:01	–					
MALT	3	F/72	AC	Pos	06:05	AC	Pos	05:02		–	
MALT	4	F/72	AC	Pos	12:04	CR	Neg	02:09	CR	Neg	02:07
MALT	5	M/41	AC	Pos	05:01	–					
MALT	6	M/65	AC	Pos	05:07	AC	Pos	10:00	–		
MALT	7	M/61	CR	Neg	02:09	CR	Neg	02:06	–		
MALT	8	F/43	CR	Neg	03:02	–					
MALT	9	F/65	CR	Neg	02:06	–					
NHL B	10	M/52	AC	Pos	08:04	–					
NHL T	11	F/51	AC	Pos	14:02	–					
NHL B	12	F/63	AC	Pos	20:03	AC	pos	08:07	–		
NHL B	13	M/48	AC	Pos	22:03	–					
NHL T	14	F/53	AC	Pos	19:04	–					
NHL B	15	F/35	AC	Pos	11:07	CR	neg	02:05	–		

MALT — mucosa associated lymphoid tissue; NHL — non-Hodgkin lymphoma; M — male; F — female; SUV — standardized uptake value; AC — active disease; CR — complete remission; Pos — positive; Neg — negative

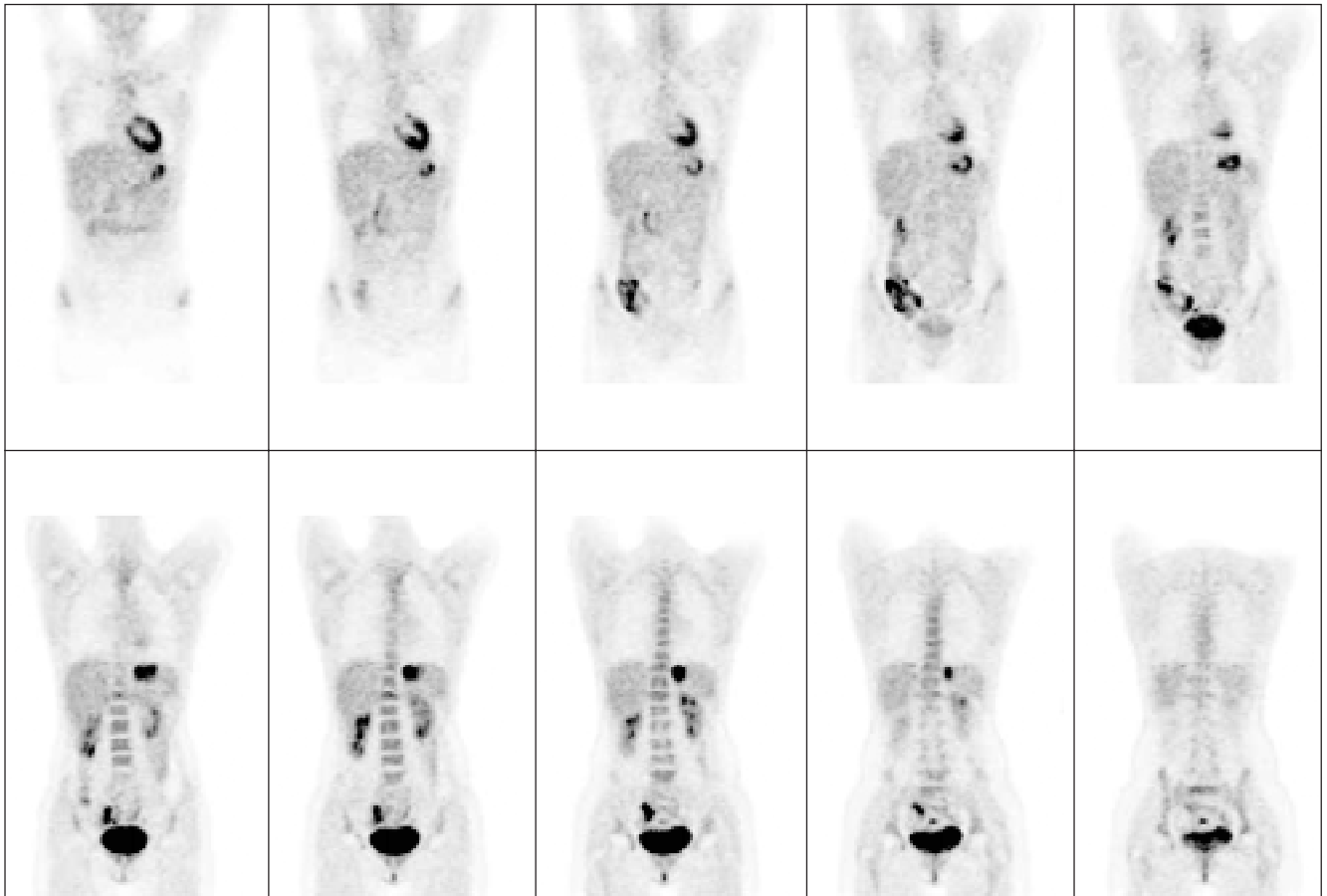


Figure 1. Coronal sections of ¹⁸F-FDG-PET scan of a patient with gastric MALT showing a focal area of increased metabolic activity in the stomach.

¹⁸F-FDG-PET was positive (Figure 2) in all cases of gastric non-MALT aggressive non-Hodgkin lymphoma with known active disease (4 cases were studied at presentation, 2 at first relapse). In three patients, PET showed pathological ¹⁸F-FDG uptake in the gastric lymph nodes, revealing metastatic sites not detected by other diagnostic procedures (US and CT) (patients 12, 14, 15). PET was repeated in two of those patients for follow-up (patients 12, 15).

Overall, considering the patients scanned while disease was active, the mean SUVmax value was higher in the aggressive NHL vs. MALT lymphoma patients (15.4 vs. 7.0).

Discussion

¹⁸F-FDG-PET has recently acquired an important role in the evaluation of patients with malignant lymphoma, providing valuable information for clinical management [1–3]. The opportunity to accurately stage disease extent prior to treatment as well as to evaluate early therapeutic response; appear to offer significant advantages in patients' management [4–7].

Among all NHLs, MALT lymphomas are the third most common histological entity (8%), following diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma [15].

Generally characterized by very indolent behaviour, MALT lymphomas tend to remain localized for long periods. The possibility

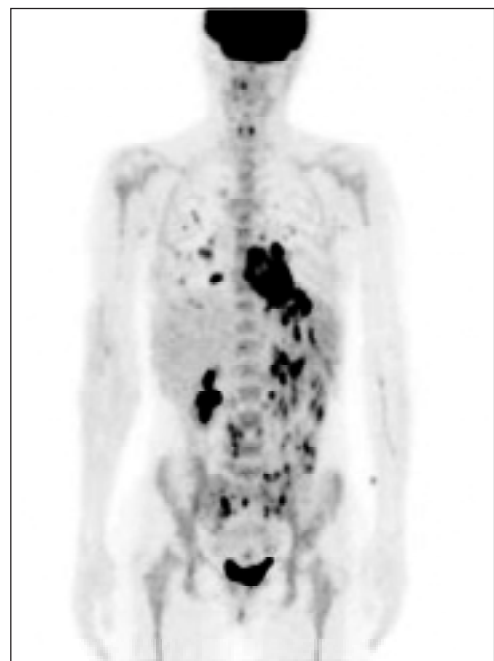


Figure 2. Three-dimensional projection image of ¹⁸F-FDG-PET scan of a patient with non-MALT gastric NHL. Areas of pathologic uptake are evident in the stomach, left lung and pelvis, and are consistent with disseminated disease.

of identifying disease at an early stage and providing definitive local treatment emphasizes the need to accurately stage the disease at diagnosis. This not only provides a baseline study for comparison with future scans, but also assists in the choice of the most appropriate approach to therapeutic intervention (surgery, chemotherapy, *H. Pylori* eradication therapy alone) [9]. Although most MALT lymphomas are localized at diagnosis (stage IE), disseminated disease may occur [15–17]. Moreover, it is not infrequent (10–20%) to find involvement of the regional lymph nodes at diagnosis [17] and ^{18}F -FDG-PET is accurate in demonstrating involved nodes that were undetectable with conventional imaging techniques alone (HRCT, US).

In this series we demonstrate excellent sensitivity and specificity of ^{18}F -FDG-PET in gastric MALT and gastric non-MALT aggressive NHL. Abnormal ^{18}F -FDG uptake was evident at the gastric level in both groups of patients with active disease while it was negative in all cases except in one while in clinical remission. In the single case in which the follow up PET scan was inconclusive, the SUVmax value of the region of interest was significantly increased from the first acquisition. These findings suggest the importance of evaluating the activity of the ROI for accurate PET interpretation. Our results are in agreement with the data reported by Beal et al. [13] and by Rodriguez et al. [18] supporting and important diagnostic and prognostic role of ^{18}F -FDG-PET in both gastric MALT and non-MALT NHL.

Overall, the mean SUVmax value between MALT and non-MALT NHL differed significantly, with aggressive NHL cases presenting higher values. In a much larger population of 97 cases, Schoder et al. demonstrated that the SUVmax value in aggressive lymphoma is higher than in indolent disease, and that PET results correlate with histology [19].

With the limits of a relatively small population, the present paper supports the hypothesis that extranodal MALT lymphoma has the same glucose avidity as other, more aggressive malignant lymphomas. Moreover, ^{18}F -FDG-PET has a high sensitivity for studying gastric aggressive NHL.

Conclusion

^{18}F -FDG-PET appears to be a useful diagnostic and prognostic tool for staging, re-staging and follow up patients with extranodal MALT lymphoma and aggressive gastric NHL.

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