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Metabolic assessement of spleen infiltration by non-Hodgkin lymphoma using ^{18}F-FDG PET/CT: Preliminary clinical results

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Abstract ^{18}F-FDG PET/CT was used for evaluation of spleen infiltration in patients with B-cell non-Hodgkin lymphoma (NHL). Five patients with histological diagnosed B-cell NHL underwent ^{18}F-FDG PET/CT examination. On integrated PET/CT image, spleen infiltration was considered when PET images revealed a discrete margin of solid splenic masses or diffuse lesion of spleen with higher maximum standardized uptake value (SUV) greater than those of normal liver structures. CT images demonstrating a positive splenic index (>480 mL) or focal hypodensities were classified as positive for spleen infiltration. All the patients underwent systemic chemotherapy. The ^{18}F-FDG PET and CT results were compared with final diagnoses. All patients had spleen infiltration originating from B-cell NHL at final diagnosis. Final diagnoses, which were confirmed by clinical and CT (n=3) or ^{18}F-FDG PET/CT (n=1) follow-up in 4 patients and biopsy of 1 patient. On integrated PET/CT image, ^{18}F-FDG PET was true-positive in all 5 patients with spleen infiltration. CT was true-positive in 4 of the 5 patients with spleen infiltration and false-negative in 1 patients (spleen infiltration without morphology changes). The accuracies of ^{18}F-FDG PET and CT for evaluating the spleen infiltration were 100% and 80% at staging, respectively. Our preliminary results suggested metabolic imaging of ^{18}F-FDG PET/CT may be helpful in the diagnosis of spleen infiltration in B-cell NHL patients. These patients may benefit from ^{18}F-FDG PET/CT in diagnosis, when spleen infiltration without morphology changes, which may not be diagnosed exactly by conventional image.

Key words Non-Hodgkin lymphoma, ^{18}F-fluorodeoxyglucose, Positron emission tomography/computed tomography, Splenic lymphoma, Lymphoma staging

1 Introduction

Less than 50% of newly diagnosed patients with aggressive histology non-Hodgkin's lymphoma (NHL) are cured with standard treatment. Staging has an important role in the treatment of all malignancies and is critically important for patients with lymphoma[1]. Accurate staging allows minimized therapies, such as extended-field irradiation or over aggressive chemotherapy, decreasing the risk of secondary malignancies, which exceeds 10% in several historical series of patients with early-stage Hodgkin's disease (HD)[2,3].

On the other hand, the ability to accurately monitor response to treatment is crucial in selecting patients who need more intensive or salvage treatment[4]. New diagnostic imaging methods have been developed in recent years for patients with NHL in an attempt to improve the detection of spleen involvement within the scope of staging and to discriminate between fibrosis and vital lymphoma after treatment[5]. Whole-body ^{18}F-FDG PET and PET/CT is a promising method in diagnosis and staging and re-staging lymphoma, because it offers the unique capability of visualising metabolic activity and morphology changes throughout the entire body[6–8].

2 Materials and methods

2.1 Patients

From January 2007 to October 2007, five consecutive patients (4 males and 1 female, aged 34–67, in mean

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age of 49.6) with diagnosed B-cell NHL underwent ^{18}F-FDG PET/CT for diagnosis, staging or restaging after treatment. All patients had been proved with B-cell NHL by neck lymph node resection biopsy. Spleen lesions on conventional CT were studied with ^{18}F-FDG PET/CT. ^{18}F-FDG PET and CT results were compared with those at follow-up.

2.2 ^{18}F-FDG PET/CT technique

The patients were asked to fast for at least 4 h before undergoing PET/CT. The blood glucose level should be within the normal range (0.7–1.2 mg/mL) prior to intravenous injection of ^{18}F-FDG. The patients received an intravenous injection of 370–666 MBq of ^{18}F-FDG. Data acquisitions with an integrated PET/CT system (Discovery STE; GE Medical Systems, USA) were performed within 60 min after injection. The procedure was as follows: CT scanning was performed first, from the head to the pelvic floor, at 110 kV, 110 mA, with a tube rotation time of 0.5 s, and a 3.3-mm section thickness, which matches the PET section thickness. Immediately after CT scanning, a PET scan that covered the identical transverse field of view was obtained. Acquisition time was 3 min per table position. PET image data sets were reconstructed iteratively by applying the CT data for attenuation correction, and coregistered images were displayed on a workstation.

2.3 Definitive diagnoses of spleen infiltration originating from B-cell NHL

It is not practical to histologically confirm all ^{18}F-FDG–avid lesions. Diagnoses obtained from sites other than the spleen are based on the fact that in routine clinical practice it is assumed that all pathologic sites of uptake are related to a single pathology. B-cell non-Hodgkin lymphoma was confirmed in all the 5 patients by neck lymph node resection biopsy. The final diagnosis was determined by histology or clinical imageological follow-up of spleen lesion in the 5 patients.

Splenic index is obtained by multiplying spleen thickness, width, and length as visualized on CT. The length is determined by adding all section-thicknesses (and intervals if any) on which the spleen is seen. The width is the longest (straight) organ diameter in the transverse (scanning) plane. The thickness is the distance between the center (inner) and peripheral (outer) surface, measured at the level of the splenic hilum. In our study, we used the criterion of a splenic index exceeding 480 mL as indicative to discriminate between normal and diseased spleens on CT. Furthermore, the spleens were evaluated for the presence of focal hypodensities nodules.

On integrated PET/CT image, spleen infiltration was considered when PET images reveal solid splenic masses with a discrete margin or diffuse spleen lesions in which maximum standardized uptake value (SUV) was greater than that in normal liver structures. On integrated PET/CT image, CT images with a positive splenic index (>480 mL) or focal hypodensities was classified as positive for spleen infiltration. ^{18}F-FDG PET and CT results were compared with final diagnoses. For ^{18}F-FDG–avid splenic masses, the final diagnosis of spleen infiltration was achieved by clinical and imaging follow-up (n = 4), splenic biopsy (n = 1).

All patients were followed-up by clinical and conventional CT (n=3) and ^{18}F-FDG PET/CT (n=1) follow-up in 4 patients. Final positive diagnosis in 1 patient was confirmed by biopsy. Definitive evidence of the NHL spleen infiltration was considered after treatment if SUV was decreased to a level which was lower than that in normal liver structures and shrinkage of the spleen or solid splenic masses on ^{18}F-FDG PET/CT, CT, or MRI after anti-tumor therapy.

3 Results

All the five patients had neck lymph node resection biopsy-proven B-cell NHL. All of them had a final diagnosis of lymphoma with splenic involvement, confirmed by clinical and conventional CT, ^{18}F-FDG PET/CT follow-up in 4 patients and biopsy in 1 patient. On integrated PET/CT image, ^{18}F-FDG PET was true-positive for all 5 patients with spleen infiltration. Both visually and semiquantitatively, splenic uptake of ^{18}F-FDG was higher than hepatic uptake in patients with spleen infiltration. The semiquantitative method yielded spleen/liver (S/L) ratios of 2.1–6.8 in patients with spleen infiltration (Table 1).

Table 1 Imaging data on five patients with spleen infiltration

Patients	CT Findings		FDG PET/CT SUV			Treatment response
	SI/mL	Focal hypodensities	Spleen	Liver	S/L ratio	
1	2126	+	7.4	4.2	1.8	Spleen shrinkage on CT
2	807	+	7.1	3.8	1.9	Spleen shrinkage on CT
3	817	+	23	3.4	6.8	Spleen shrinkage on CT, remained FDG-avid lesion on PET
4	3328	+	5.0	3.2	1.6	Spleen shrinkage
5	450	− Before treatment	7.0	3.3	2.1	No spleen shrinkage, SUV decrease to normal on PET
		After treatment	4.0	4.1	0.9	

Note: SI=Splenic index, SUV= Standardized uptake value.

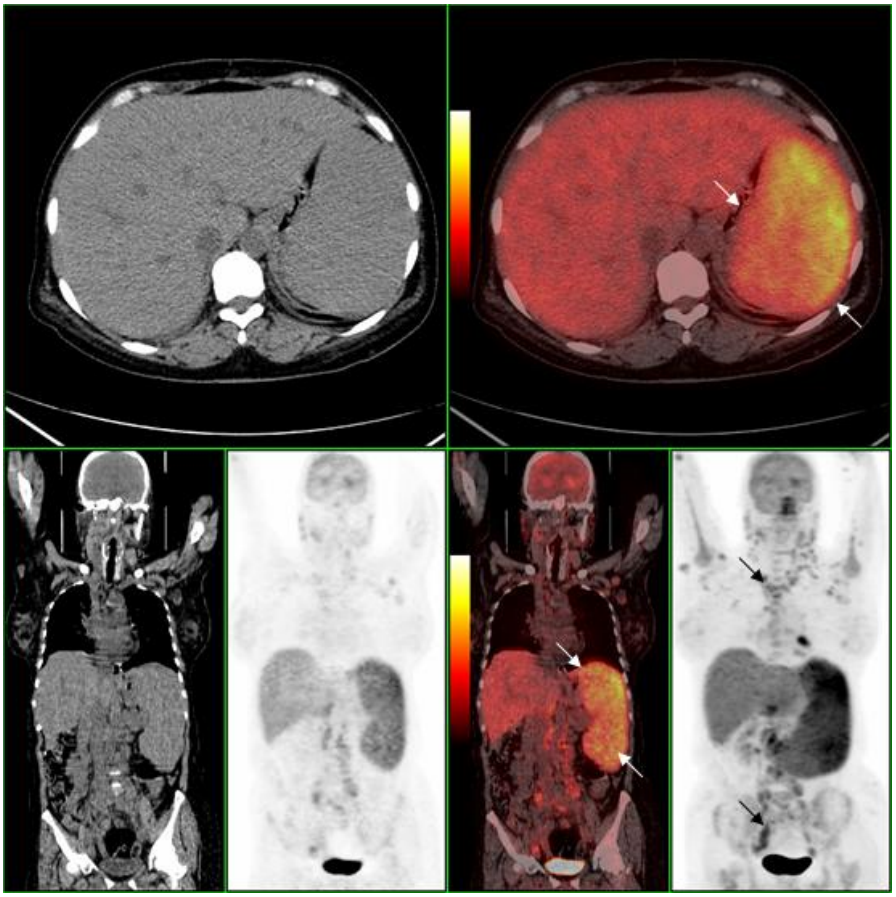

Fig.1 Stage IIIS NHL with splenic involvement in a 54-year-old woman. The axial and coronal ^{18}F-FDG PET image shows diffusely increased splenic uptake of ^{18}F-FDG, which is higher than hepatic uptake (white arrows). The splenic index was 2,126 mL, with S/L ratio of 1.8. Coronal PET/CT and projection images show multiple high metabolism lymph nodes (black arrows) and diffuse splenic hyper-metabolism.

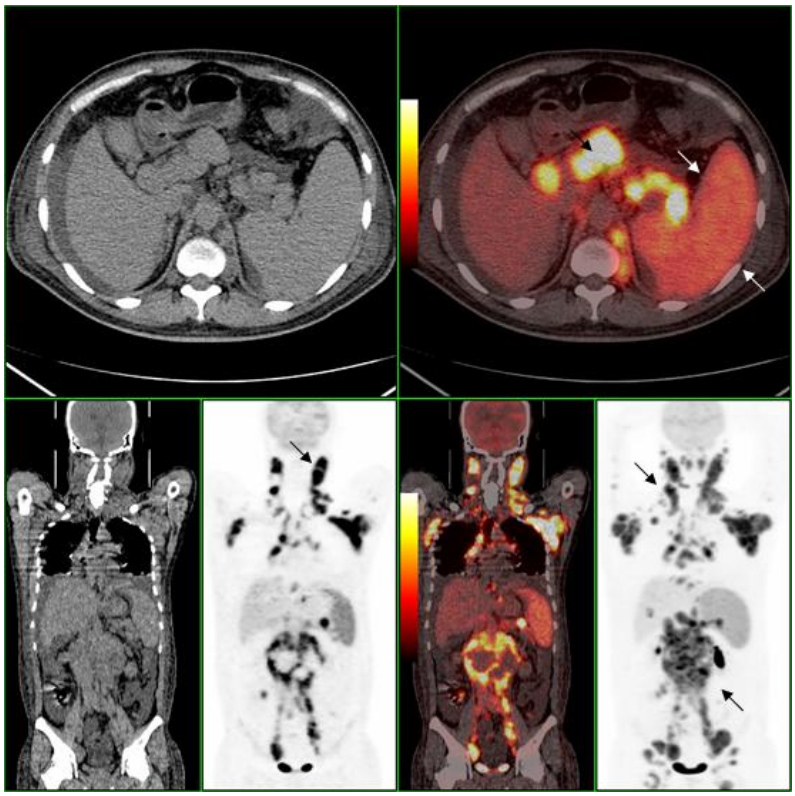

Fig.2 Stage IIIS NHL with splenic involvement in a 35-y-old man with HBV. The axial and coronal ^{18}F-FDG PET/CT image shows diffusely increased splenic uptake of ^{18}F-FDG, which is higher than hepatic uptake and moderate ascites. The splenic index was 807 mL, with S/L ratio of 1.9. Coronal PET/CT and projection images show multiple high metabolism lymph nodes and diffuse splenic hyper-metabolism. The patient had HBV infection with liver function damage, but there is no evident of NHL liver involvement.

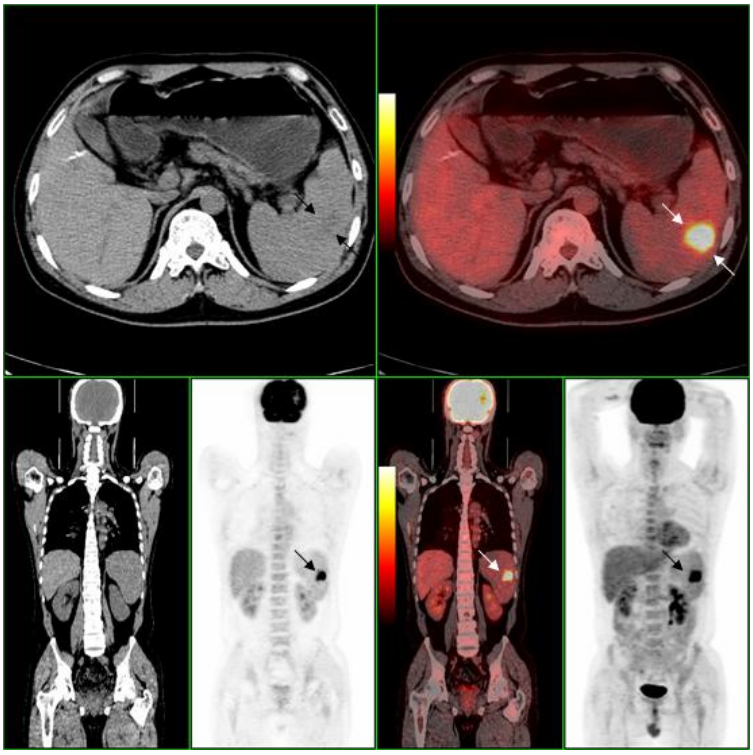

Fig.3 Restage IIIS NHL of a 34-y-old man, who was previously diagnosed as B cell NHL. The axial and coronal PET/CT images show ^{18}F-FDG–avid splenic mass (black and white arrows, S/L ratio = 6.8), proven to be remain NHL on biopsy, with absence of other ^{18}F-FDG–avid disease in the whole body after six cycles of chemotherapy.

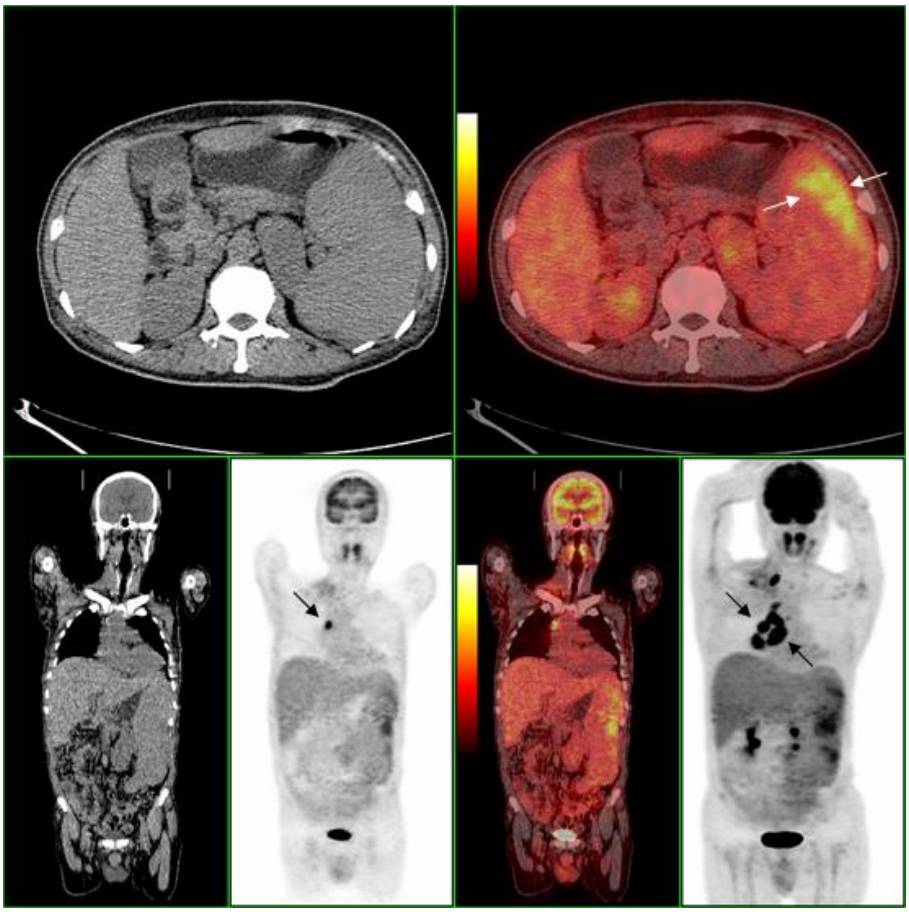

Fig.4 Stage IIIS NHL with splenic involvement in a 67-y-old man. The axial and coronal ^{18}F-FDG PET image shows increased splenic local uptake of ^{18}F-FDG, which is greater than hepatic uptake (white arrows). The spleen index was 3328 mL, with S/L ratio of 1.6. Coronal PET/CT and projection images show multiple high metabolism lymph nodes (black arrows).

On the integrated PET/CT image, CT was true-positive in 4 of 5 patients with splenic disease. Two patients (Figs.1 and 2) had positive splenic indices of 2126 and 807 mL, and the other two in Figs.3 and 4 had positive splenic index of 817 mL and 3328 mL, combined with focal abnormalities. CT was false-negative in Patient 5 with splenic disease, a 58-year-old male patient with a normal splenic index of 450 mL (<480 mL=normal) and homogeneous parenchyma without morphology changes and focal hypodensities.

In the re-staging, conventional CT showed spleen shrinkage or solid splenic masses (Patient 1，2, 3 and 4), but the CT failed in confirming spleen remain active disease through size of the spleen was shrinkage, which only was found by ^{18}F-FDG PET/CT and confirmed by biopsy (Patient 1). Conventional CT also failed in confirmed spleen infiltration release in a patient without morphology changes before and after treatment, who was only found by decreasing of SUV lower than those of normal liver structures after treatment on ^{18}F-FDG PET imaging (Fig.5). ^{18}F-FDG PET/CT confirmed all of the patients in the spleen disease and other sites of disease through the whole body.

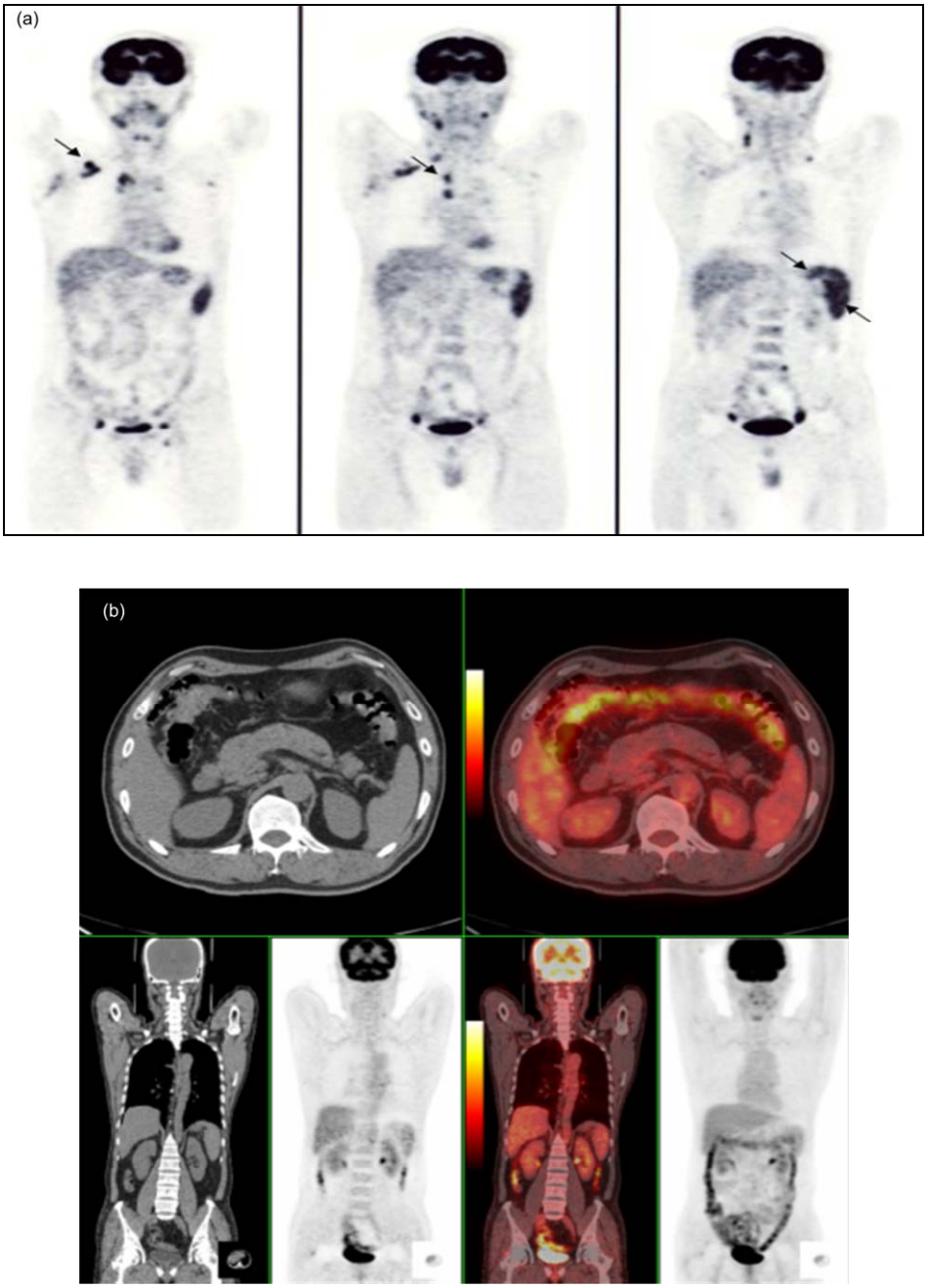

Fig.5 Stage IIIS NHL and splenic involvement in a 58-y-old man before treatment (a) and after six cycles of chemotherapy (b). The coronal PET images demonstrated splenic uptake of ^{18}F-FDG that is more intense than hepatic uptake and multiple high metabolism lymph nodes (black arrows). S/L ratio was 2.1. CT image shows homogeneous appearance of spleen. Splenic index of 450 mL was normal for age (≤480 mL=normal). Splenic uptake of ^{18}F-FDG is lower than hepatic uptake. S/L ratio was 0.9. The CT image showed no obvious morphology change of spleen before and after chemotherapy.

4 Discussion

Spleen is a frequent site of involvement in patients with NHL and may be involved in about 30%–40% of patients with HD. Primary spleen lymphoma is a rare disorder, with an incidence of less than 1% [9-11]. Large B cell lymphoma, presenting with a tumor mass, is associated with a relatively favorable clinical course, and the clinical presentation of a tumor confined to the spleen and the hilar lymph node is associated with lower aggravates[12]. The most common presenting symptoms in malignant lymphoma of the spleen are fever, malaise and weight loss in this study. This is in accordance to previous reports. Several studies have

reported that the prevalence of the hepatitis C virus (HCV) infection is significantly overrepresented in patients affected with NHL[13,14]. In the five patients, one (Fig.2) suffered from HBV infection with serous liver function damaging received entikawei pian treatment, which led to a good virological response and hematological remission as well as the release of clinical symptoms.

Splenic involvement by lymphoma is characterized by one or more tumor nodules, often less than 1 cm in diameter. In imaging data, lymphomatous involvement of the spleen may manifest as either focal lesions or diffuse disease[15,16]. Although marked splenomegaly is almost always indicative of tumor, lymphomatous spleens frequently are normal in size, and modestly enlarged spleens often give no evidence of tumor[17,18]. So, splenomegaly is not a reliable indicator of lymphomatous involvement of the spleen because the organ's size is normal in one third of patients with splenic disease[19,20]. Recent reports have shown that ^{18}F-FDG PET and PET/CT are more accurate than CT for identifying splenic involvement by lymphoma[21–23].

Detecting lymphomatous involvement of the spleen with CT depends on identifying morphologic changes, including enlargement or discrete tumor nodules[24,25]. Splenomegaly, unless massive, is a nonspecific finding, and focal hypodensities, although specific, are rarely seen[26]. Reported accuracies of CT for identifying splenic involvement by HD were different[22,23]. Rueffer et al reported that spleen weight could be estimated with the help of a spleen index. Above an index of 1000 mL the probability of spleen involvement is higher than 90%[24]. Strijk et al defined the splenic index exceeding 480 mL as indicative of splenic involvement by HD and found that CT detected splenic involvement with an accuracy of 91%[25]. These investigators concluded that detection of splenic involvement by HD is improved when a more exact definition of splenic size is used, that is, the splenic index[26–28]. So, a positive splenic index (> 480 mL) or focal hypodensities was classified as positive for spleen infiltration on CT imaging in this study.

Our findings in the present study confirmed the results of these reports. In the five patients, spleen infiltration is characterized by splenomegaly in four patients. One patient with normal spleen size and a homogeneous parenchyma was detected with diffuse increasing metabolism level of his spleen was, which was greater than that of normal liver structures. In the re-staging, ^{18}F-FDG PET/CT is better than conventional CT, which may be limited in confirming spleen still in disease after treatment and patient without morphology changes before and after treatment. It was only confirmed by SUV lower than those of normal liver structures after treatment on ^{18}F-FDG PET imaging. Detecting lymphomatous involvement of the spleen with ^{18}F-FDG PET/CT as opposed to CT depends on identifying increased glucose metabolism of tumor cells[29, 30]. Metabolic changes are evident when there is diffusion or focal tumor infiltration, regardless morphologic changes. This study illustrates the importance of metabolic imaging: ^{18}F-FDG PET/CT identified splenic involvement in all the 5 patients, but CT imaging was correct in only 4 of the 5 patients.

5 Conclusion

The reported increased sensitivity of PET/CT over CT may attribute to the ability of ^{18}F-FDG PET which detects metabolic abnormalities that precede the morphologic changes seen by CT. ^{18}F-FDG PET/CT may helpful in diagnosis of spleen infiltration in B-cell NHL patients. Our preliminary results suggested these patients may be benefit from ^{18}F-FDG PET/CT in diagnosis, when spleen infiltration is demonstrated by other modalities without morphology changes, which may not be diagnosed exactly by conventional image.

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