Hong Kong J Radiol. 2011;14:108-12

CASE REPORT

Primary Cutaneous Gamma-delta T-cell Lymphoma: Predominant Subcutaneous Uptake Detected by ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomographic Scan in a Rapidly Deteriorating Patient

B Lo[1], CM Lok[2], KM Kwok[1], WP Chu[1], WS Mak[1], NY Sin[1]

[1]Department of Radiology and [2]Nuclear Medicine Unit, Department of Radiology, Princess Margaret Hospital, Hong Kong

ABSTRACT

Primary cutaneous gamma-delta T-cell lymphoma is a rare subtype of primary cutaneous peripheral T-cell lymphoma. In the latest World Health Organization / European Organisation for Research and Treatment of Cancer classification and World Health Organization classification (4th edition, 2008), the entity previously called "subcutaneous panniculitis-like T-cell lymphoma with gamma-delta T-cell phenotype" has been reclassified as a form of primary cutaneous gamma-delta T-cell lymphoma. Most literature reported low positive rates of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomographic scans in patients with cutaneous lesions. To our knowledge, the pattern of diffuse predominant subcutaneous uptake in cutaneous gamma-delta T-cell lymphoma using positron emission tomography/computed tomographic scans has rarely been described. In this report, we describe the clinical presentation, pathological findings, and the predominant subcutaneous uptake pattern revealed by positron emission tomography/computed tomographic scanning in a patient with a subcutaneous fat biopsy proven peripheral T-cell lymphoma of the gamma-delta phenotype.

Key Words: *Lymphoma, T-cell, cutaneous; Lymphoma, T-cell, peripheral; Positron-emission tomography*

中文摘要

原發性皮膚γδT細胞淋巴瘤：^{18}F-氟脫氧葡萄糖正電子電腦斷層顯像（^{18}F-FDG PET/CT）於一迅速惡化病例中呈顯著皮下攝取

羅彪、駱昭明、郭勁明、朱惠邦、麥詠詩、單雅怡

原發性皮膚γδT細胞淋巴瘤屬於原發性皮膚外周T細胞淋巴瘤的一個罕見類型。根據世界衛生組織（WHO）／歐洲癌腫研究治療機構（EORTC）的最新分類表（2008年第四版），之前的「皮下似脂膜炎γδT細胞淋巴瘤T細胞表型」經已被重新分類，成為原發性皮膚γδT細胞淋巴瘤的其中一種。大多數文獻記載著^{18}F-FDG PET/CT對於皮膚病灶患者的陽性檢測率偏低。據我們所知，文獻少有記載^{18}F-FDG PET/CT檢出皮膚γδT細胞淋巴瘤瀰漫性皮下FDG攝取的顯著表現。本文描述一名經活檢證實

Correspondence: *Dr Bill Lo, Department of Radiology, Princess Margaret Hospital, Laichikok, Kowloon, Hong Kong. Tel: (852) 2990 1340 ; Fax: (852) 2990 3276 ; Email: ablo1996@lscoba.com*

Submitted: 4 Jan 2011; Accepted: 1 Apr 2011.

患有皮下似脂膜炎γδT細胞淋巴瘤T細胞表型的病人，其臨床症狀、病理學結果及^{18}F-FDG PET/CT顯示皮下FDG攝取的模式。

INTRODUCTION

In the new World Health Organization–European Organisation for Research and Treatment of Cancer (WHO-EORTC) classification and the WHO classification (4th ed, 2008), the term subcutaneous panniculitis-like T-cell lymphoma (SPTL) has been restricted to cases with alpha-beta T-cell phenotype (SPTL-AB). Cases of SPTL with gamma-delta T-cell phenotype (SPTL-GD) have been reclassified as being a cutaneous gamma-delta T-cell lymphoma (CGD-TCL), a provisional entity within the broader category of primary cutaneous peripheral T-cell lymphomas (PTCLs), unspecified.[1,2] Cases with SPTL-GD are more commonly associated with haemophagocytic syndrome (HPS) and usually confer a poor prognosis.[1-3]

The utility of ^{18}fluoro-2-deoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for staging and assessing therapeutic responses in management of Hodgkin's disease and B-cell neoplasms is well supported in the literature.[4] However, most reports have shown low positivity rates for PET/CT scans with cutaneous lesions of T-cell and natural killer-cell (T/NK-cell) neoplasms.[5,6] To our knowledge, the pattern of diffuse predominant subcutaneous uptake in CGD-TCL on PET/CT scans has rarely been described.

CASE REPORT

A 58-year-old woman with good past health was initially admitted to the surgical unit of a public hospital in March 2008 for epigastric pain, vomiting, and constipation. On physical examination, the abdomen was soft with localised epigastric tenderness, and there was a tinge of jaundice. Complete blood picture showed a haemoglobin concentration of 110 g/l, white cell count of 6.1 x 10^9 /l, and platelet count of 280 x 10^9 /l. Liver function tests revealed a total bilirubin of 31 μmol/l (normal range, 5-21 μmol/l), alkaline phosphatase (ALP) of 167 IU/l (normal range, 40-129 IU/l), alanine transaminase (ALT) of 46 IU/l (normal range, 13-53 IU/l). Hepatitis serology for hepatitis B virus and hepatitis C virus were negative. Renal function tests, serum amylase, and the clotting profile were normal. Ultrasound abdomen showed a fatty liver and a distended gallbladder with sludge. Subsequent endoscopic retrograde pancreaticoduodenography showed no biliary stone or ductal dilatation. In hospital, her epigastric pain gradually subsided. She was then discharged and underwent an outpatient colonoscopy appointment and further blood tests, including: gamma-glutamyltransferase, direct / indirect bilirubin, and various autoimmune markers.

She was readmitted to the medical unit one month later, with symptoms of malaise, weakness, and significant weight loss (13.6 kg since her hospital admission), but was afebrile. Serial laboratory tests showed deterioration in her complete blood picture: the haemoglobin concentration dropped from 90 g/l to 66 g/l, the white cell count changed from 4.7 x 10^9 /l to 2.1 x 10^9 /l, and the platelet count fell from 148 x 10^9 /l to the worst of 18 x 10^9 /l. The lactate dehydrogenase level was 312 IU/l. Liver function tests at a later stage were: total bilirubin of 207 μmol/l, ALP of 156 IU/l, ALT of 63 IU/l, total protein of 54 g/l and serum albumin of 22 g/l. The activated partial thromboplastin time was prolonged to >120 s. Blood tests performed earlier were positive for anti-smooth muscle antibodies, perinuclear antineutrophil cytoplasmic antibodies and antinuclear antibodies. Her colonoscopy with biopsy at the terminal ileum and ileocaecal valve yielded no abnormality. An FDG-PET/CT scan was subsequently arranged, owing to the clinical suspicion of underlying malignancy. The patient developed fever and respiratory failure about two weeks after admission and underwent intensive care unit (ICU) care. The PET/CT study was performed three days prior to ICU admission.

The FDG-PET/CT was performed with a General Electric Discovery LS 4-slice PET/CT scanner; 10.4 mCi ^{18}F-FDG was injected intravenously, and the PET imaging from head to upper thighs was acquired 60 minutes afterwards. A plain CT scan was then performed for attenuation correction and localisation. The PET/CT images showed disseminated hypermetabolic soft tissue densities infiltrating the subcutaneous fat over the whole imaging field from vertex to upper thighs, and especially over the anterior thoracic and abdominal walls (maximum standardised uptake value [SUVmax] 5.5). The fat in the gluteal regions, ischiorectal fossae, and axillary fossae was quite symmetrically involved (SUVmax 4.4). Such fatty and subcutaneous uptakes were so extensive that the normal physiological uptake in the brain and liver

were overridden (Figure 1). Hepatosplenomegaly was evident, and an abnormal high FDG uptake compared to liver (SUVmax 2.0) was evident in the enlarged spleen (SUVmax 4.7). Only a few small hypermetabolic lymph nodes were noted in the anterior mediastinum (SUVmax 4.4) and the paraaortic regions in abdomen (SUVmax 3.2) [Figure 2]. No hypermetabolic lesion was demonstrated in the lungs or pleurae. Apart from the increased subcutaneous uptake in scalp, there was no abnormal FDG uptake focus in the head and neck region. Small hypermetabolic foci suspicious of marrow infiltration were noted in T6 and L3 vertebral bodies (SUVmax 5.1).

Subcutaneous fat biopsy targeted at the anterior abdominal wall (where there was higher FDG uptake) was performed. Histology revealed adipose tissue with lobular panniculitis containing mixed small and large lymphoid cells, without apparent haemophagocytosis or apoptosis. Skin was not included in the specimen. The atypical cells were positive for CD2, CD3, CD4, CD5, CD8 (less than CD4), and T-cell intracellular antigen revealed by immunohistological stains. The CD56 stain was largely negative and Epstein-Barr virus RNA stain was negative. The polymerase chain reaction assay showed positive clonal T-cell receptor (TCR) gamma gene rearrangement and negative TCR-beta gene rearrangement. The pathological diagnosis was PTCL.

In view of the aggressive disease and multi-organ failure including the renal, hepatic and respiratory systems, the risk from chemotherapy was exceedingly high. The patient understood this but wished for a trial. Modified CHOP therapy (cyclophosphamide, doxorubicin, vincristine and prednisolone) was given after the patient was discharged from the ICU. However, she ran a downhill course, complicated by chest and urinary tract infections, gastrointestinal bleeding and pulmonary haemorrhage, and eventually succumbed.

DISCUSSION

PTCL comprises a relatively small proportion of non-Hodgkin's lymphomas. Its frequency shows significant geographical and racial variation. Studies in Korea reported that PTCL accounts for approximately 25% of all non-Hodgkin's lymphomas, while there was a lower frequency of 10 to 15% in Europe[3,7-9] and 18% in Hong Kong.[10] Cutaneous T-cell lymphoma (CTCL) accounts for 65% of all primary cutaneous lymphomas.[2,11]

SPTL accounts for 1% of all cutaneous lymphomas. Demonstration of the expression of beta F1 (TCR α/β) by immunohistochemistry is a diagnostic marker for this entity, which accounts for 75% of all subcutaneous forms of T-cell lymphomas.[2] SPTL can run an indolent course and may be preceded by a seemingly benign panniculitis for years.[12] Infiltration of the superficial dermis, epidermis, or dissemination of tumour to extracutaneous sites are rare.[1,2,12] The prognosis for this group of patients is good, especially in the 83% or so not complicated by the HPS. The 5-year overall survival, and the 5-year survival with and without HPS were reported as 82%, 41% and 91%, respectively.[1]

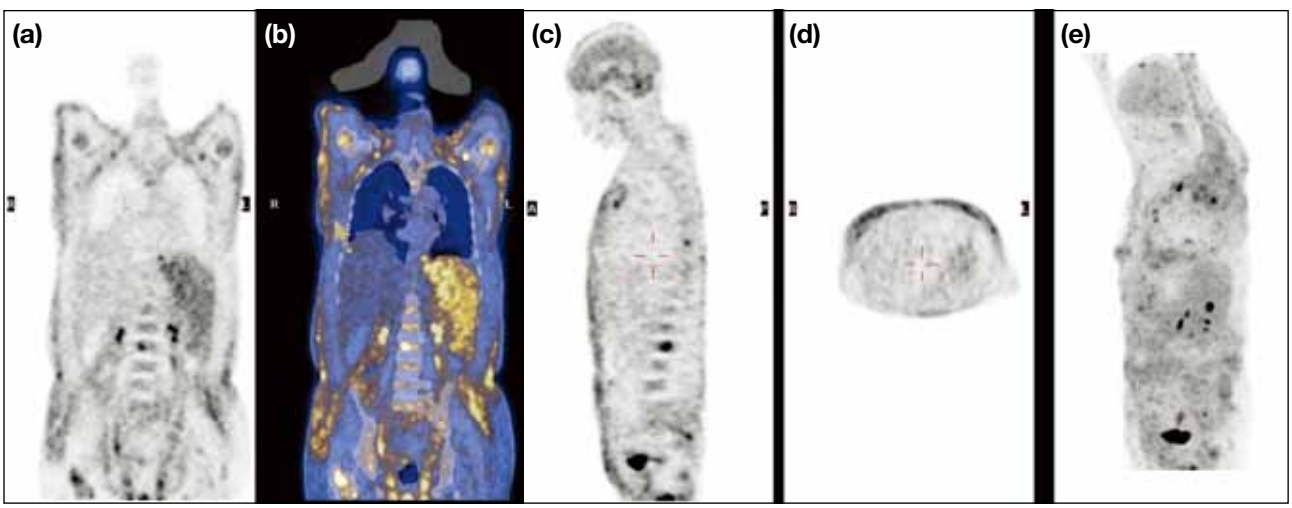

Figure 1. Coronal (a) positron emission tomography (PET) and (b) fusion images showing hepatosplenomegaly and predominantly high uptake over the subcutaneous fat and the enlarged spleen. (c, d) Sagittal and axial PET images and (e) maximum-intensity-projection image showing disseminated hypermetabolic soft tissue densities infiltrating the subcutaneous fat over the whole imaging field, especially over the anterior thoracic and abdominal walls. The normal physiological uptake in brain and liver were overridden.

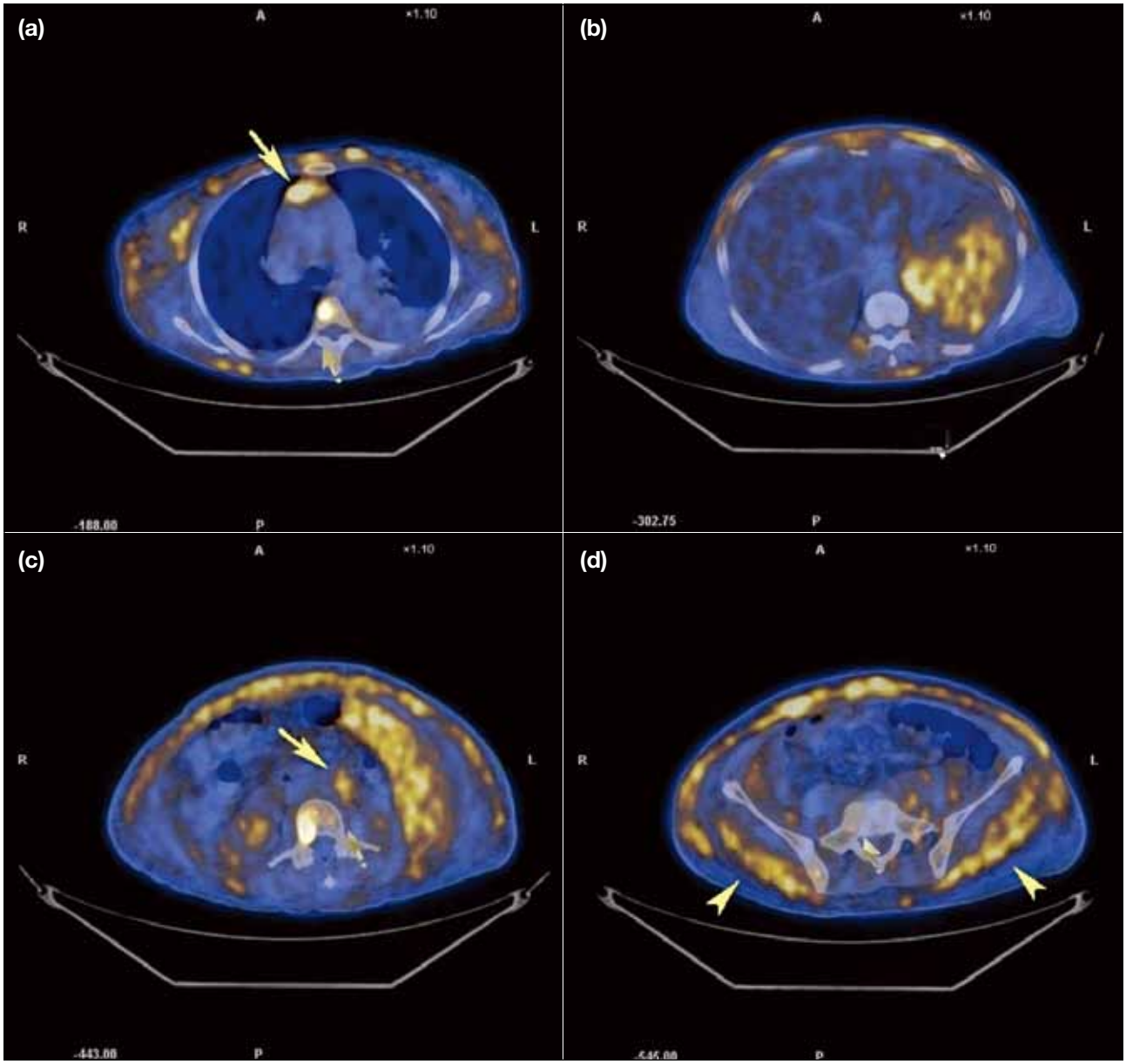

Figure 2. Axial positron emission tomography/computed tomography (PET/CT) fusion images showing small hypermetabolic lymph nodes (large arrows) in the (a) anterior mediastinum and (c) paraaortic regions in abdomen. (b) The spleen shows abnormally high ^{18}fluoro-2-deoxyglucose uptake compared to the liver. (d) Involvement of fat bilaterally in the gluteal regions (arrowheads).

Regarding the subcutaneous form of CGD-TCL phenotype, approximately 25% of all cases typically display monotonous and diffuse subcutaneous infiltrates. Infiltration of the upper dermis and epidermis is common. Angioinvasion and angiodestruction are frequently demonstrated. Apoptosis and necrosis are common and may be extensive. Its association with HPS was reported to be up to 50%. Many cases are highly resistant to multiagent chemotherapy. New targeted therapies or even allogeneic bone marrow stem cell transplantation may be required. The prognosis is poor irrespective of the presence of HPS or co-expression of CD56. The 5-year overall survival was reported to be about 11%.[1,2]

Most reports indicate that the ^{18}F-FDG PET/CT scans have a limited role in detecting primary or secondary skin lesions of T/NK-cell neoplasms, especially for patches, plaques and erythrodermic lesions.[5,6] Tumorous (mass-like) cutaneous lesions may be FDG-avid.[5] Valencak et al[13] evaluated the clinical usefulness of ^{18}F-FDG PET in 13 consecutive patients with

histologically verified CTCL and showed clear-cut negative results for stage Ia disease (limited skin lesion <10% body surface area) and clear-cut positive results for stage IV disease (extracutaneous involvement). Kako et al[5] retrospectively evaluated FDG-PET scans from 41 patients with T/NK-cell lymphomas and reported similar results. Kuo et al[14] described the ability of PET/CT to delineate various cutaneous lesions from thin plaques to thick tumours, as a means of demonstrating the extent of subcutaneous lesions (as compared to physical examination alone), and to identify nodal and visceral involvement.

The pattern of widespread subcutaneous uptake on ^{18}F-FDG PET scans have been reported in cases of SPTLs[15,16] and intravascular large B-cell lymphomas,[17] which may be indistinguishable from lobular panniculitis (e.g. lupus panniculitis). The likelihood of FDG avidity in CTCL appears to depend on the tumour stage (i.e. cutaneous or extracutaneous).[5,13,18] Feeney et al[19] found high rates of FDG positivity in a number of T-cell lymphoma subtypes, which they tried to characterise with PET/CT scans. The mean SUVmax of SPTLs they reported was 5.7 (range, 1.5-13.1), while that of mycosis fungoides was 3.8 (range, 1.4-8.9) and for transformed mycosis fungoides it was 11.3 (range, 2.3-25.0).

In conclusion, we report a case of CGD-TCL (stage IV) with demonstrated widespread subcutaneous uptake on a PET/CT scan, which has rarely been described. Despite a low positive rate in most cutaneous lesions of T/NK-cell lymphomas, PET/CT is potentially helpful in delineating the extent of subcutaneous lesions. Possibly it could also illustrate that such a lesion could be the distinct primary site of disease, and detect any nodal or visceral involvement. Distinction between SPTL with an SPTL-AB and subcutaneous presentation of CGD-TCL is crucial, as the latter carries a much poorer prognosis and warrants different treatment strategies.

REFERENCES

1. Willemze R, Jansen PM, Cerroni L, et al. Subcutaneous panniculitis-like T-cell lymphoma: definition, classification, and prognostic factors: an EORTC Cutaneous Lymphoma Group Study of 83 cases. Blood. 2008;111:838-45.
2. Kempf W, Sander CA. Classification of cutaneous lymphomas — an update. Histopathology. 2010;56:57-70.
3. Lee HJ, IM JG, Goo JM, et al. Peripheral T-cell lymphoma: spectrum of imaging findings with clinical and pathologic features. Radiographics. 2003;23:7-28.
4. Cronin CG, Swords R, Truong MT, et al. Clinical utility of PET/CT in lymphoma. AJR Am J Roentgenol. 2010;194:W91-W103.
5. Kako S, Izutsu K, Ota Y, et al. FDG-PET in T-cell and NK-cell neoplasms. Ann Oncol. 2007;18:1685-90.
6. Khong PL, Pang CB, Liang R, Kwong YL, Au WY. Fluorine-18 fluorodeoxyglucose positron emission tomography in mature T-cell and natural killer cell malignancies. Ann Hematol. 2008;87:613-21.
7. Ko YH, Kim CW, Park CS, et al. REAL classification of malignant lymphomas in the Republic of Korea: incidence of recently recognized entities and changes in clinicopathologic features. Hematolymphoreticular Study Group of the Korean Society of Pathologists. Revised European-American lymphoma. Cancer. 1998;15:806-12.
8. Lee SS, Cho KJ, Kim CW, Kang YK. Clinicopathological analysis of 501 non-Hodgkin's lymphomas in Korea according to the revised European-American classification of lymphoid neoplasms. Histopathology. 1999;35:345-54.
9. Salar A, Fernández de Sevilla A, Romagosa V, et al. Distribution and incidence rates of lymphoid neoplasms according to the REAL classification in a single institution. A prospective study of 940 cases. Eur J Haematol. 1997;59:231-7.
10. Rodriguez-Abreu D, Filho VB, Zucca E. Peripheral T-cell lymphomas, unspecified (or not otherwise specified): a review. Hematol Oncol. 2008;26:8-20.
11. Burg G, Kempf W. Epidemiology. In: Burg G, Kempf W, editors. Cutaneous lymphomas. New York: Taylor & Francis; 2005. p 13-20.
12. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105:3768-85.
13. Valencak J, Becherer A, Der-Petrossian M, Trautinger F, Raderer M, Hoffmann M. Positron emission tomography with [18F] 2-fluoro-D-2-deoxyglucose in primary cutaneous T-cell lymphomas. Haematologica. 2004;89:115-6.
14. Kuo PH, McClennan BL, Carlson K, et al. FDG-PET/CT in the evaluation of cutaneous T-cell lymphoma. Mol Imaging Biol. 2008;10:74-81.
15. Wang SY, Wu YW, Hsiao CH, Li MF, Hsu PY, Yen RF. F-18 FDG PET images for subcutaneous panniculitis-like T-cell lymphoma. Clin Nucl Med. 2011;36:66-9.
16. Huang CT, Yang WC, Lin SF. Positron-emission tomography findings indicating the involvement of the whole body skin in subcutaneous panniculitis-like T cell lymphoma. Ann Hematol. 2011; 90:853-4.
17. Lu PH, Kuo TT, Yu KH, Lin TL, Chang SL, Yang CH. Intravascular large B-cell lymphoma presenting in subcutaneous fat tissue and simulating panniculitis clinically. Int J Dermatol. 2009;48:1349-52.
18. Cheson BD. The role of positron emission tomography in T-cell lymphoma and T-cell specific response criteria. Hematology Meeting Reports. 2009;3:20-7.
19. Feeney J, Horwitz S, Gönen M, Schöder H. Characterization of T-Cell lymphomas by FDG PET/CT. AJR Am J Roentgenol. 2010;195:333-40.