Cutaneous Metastases from Testicular Diffuse Large B-cell Malignant Lymphoma and Bowen Disease: 18F-FDG PET-CT Findings

Tatsuya MIKAMI[*1], Tamaki ICHIKAWA[*1], Toshiki KAZAMA[*1], Yasuyuki AOYAMA[*2], Tomotaka MABUCHI[*3], Haruka IKOMA[*4], Hiroshi KAJIWARA[*4], Yui NAGAFUJI[*1], Yuka SEKIGUCHI[*1], Eriko KODAMA[*1], Tsuyoshi FUKUZAWA[*5], Toshihisa KUROKI[*5], Ryouta NAGAO[*5] and Jun HASHIMOTO[*1]

[*1]*Department of Radiology, Tokai University School of Medicine*
[*2]*Department of Hematology and Oncology, Tokai University School of Medicine*
[*3]*Department of Dermatology, Tokai University School of Medicine*
[*4]*Department of Pathology, Tokai University School of Medicine*
[*5]*Department of Radiation oncology, Tokai University School of Medicine*

(Received January 9, 2020; Accepted February 28, 2020)

Here, we report the case of cutaneous metastases from testicular diffuse large B-cell malignant lymphoma (DLBCL) concurrent with Bowen disease evaluated with 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET-CT). A 60-year-old male underwent orchiectomy to remove his left testicle because of DLBCL. Multiple skin lesions appeared 1 month postoperatively. Furthermore, an intractable erythematous plaque localized to the right lower leg was present from 2 years before the operation. 18F-FDG PET-CT images revealed multiple skin lesions with marked FDG uptakes in the face, neck, and thigh of this patient, as well as a lower leg lesion with minimal FDG uptake. Biopsy of both lesions revealed cutaneous metastases from DLBCL and Bowen disease (BD) of the lower leg lesion. 18F-FDG PET-CT images following chemotherapy and resection of BD demonstrated no FDG uptake.

Key words: Bowen disease, malignant lymphoma, FDG

INTRODUCTION

Primary testicular lymphoma (PTL) is a type of extra-nodal lymphoma originating from the testicles [1, 2]. PTL constitutes approximately 1%–2% of all non-Hodgkin lymphomas and accounts for 1%–9% of all testicular tumors [2, 3]. The majority of patients affected by this disease are >60 years old [4]. Approximately 80%–98% of PTLs are diffuse large B-cell lymphomas (DLBCLs) [5, 6]. The most common metastatic sites for this disease are contralateral testicle, central nervous system, skin, adrenal glands, bone marrow, lung, and pleura [7]. Bowen disease (BD) is an epithelial limited squamous cell carcinoma (SCC) most commonly seen in elderly people [8]. Cutaneous malignant lymphoma concurrent with BD is extremely rare [9, 10]. 18F-fluorodeoxyglucose positron emission tomography with computed tomography (18F-FDG PET-CT) is useful for evaluation of skin malignancy and for the identification of malignant lymphomas [11–14]. In this paper, we report the case of cutaneous metastases from testicular DLBCL concurrent with BD evaluated with 18F-FDG PET-CT.

CASE

A 60-year-old male had undergone left orchiectomy at a previous hospital because of DLBCL. Multiple skin lesions in the form of small brown cutaneous nodules appeared one month postoperatively (Fig. 1a). An intractable erythematous plaque localized to the right leg had been already present from 2 years before the operation (Fig. 1b). Therefore, this patient referred to our institution to evaluate skin lesions that were suspected to indicate metastases from PTL. His lactate dehydrogenase (LDH) and soluble interleukin-2 receptor (sIL2R) levels were 152 U/L and 442 U/mL, respectively, and were within the normal range. Moreover, tumor markers including carcinoembryonic antigen and carbohydrate antigen 19-9 were negative.

Consequently, 18F-FDG PET-CT scanning was performed to identify metastases from PTL. Coronal maximum intensity projection image (Fig. 2a) revealed multiple small skin lesions with high FDG uptake [mean maximum standardized uptake value (SUVmax): 7.7 (5.1–8.1)] in the patient's face, neck and right thigh, left inguinal lymph nodes with moderate FDG uptake (SUVmax: 4.4), and a small skin lesion in the right lower leg with minimal FDG uptake (SUVmax: 0.9). Fused PET-CT axial images demonstrated marked FDG uptake in his cheek lesion (Fig. 2b) and a minimal FDG uptake in his lower leg lesion (Fig. 2c).

Biopsy of both lesions was performed; multiple skin lesions in the patient's face and thigh were pathologi-

Tamaki ICHIKAWA, Department of Radiology, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
Tel: +81-463-1121 Fax: +81-463-93-6827 E-mail: tamaki-i@is.icc.u-tokai.ac.jp

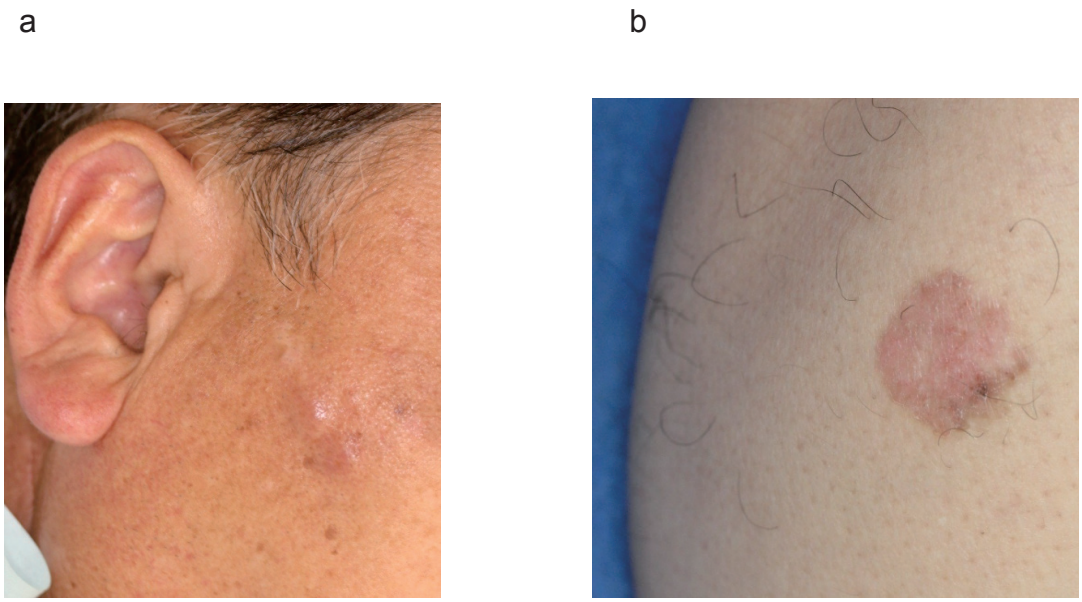

Fig. 1 Clinical images demonstrating a small brown cutaneous nodule on the right cheek (a) and an erythematous plaque on the right lower leg (b). The cheek lesion is smaller than the leg lesion. However, the leg lesion is thinner than the cheek lesion.

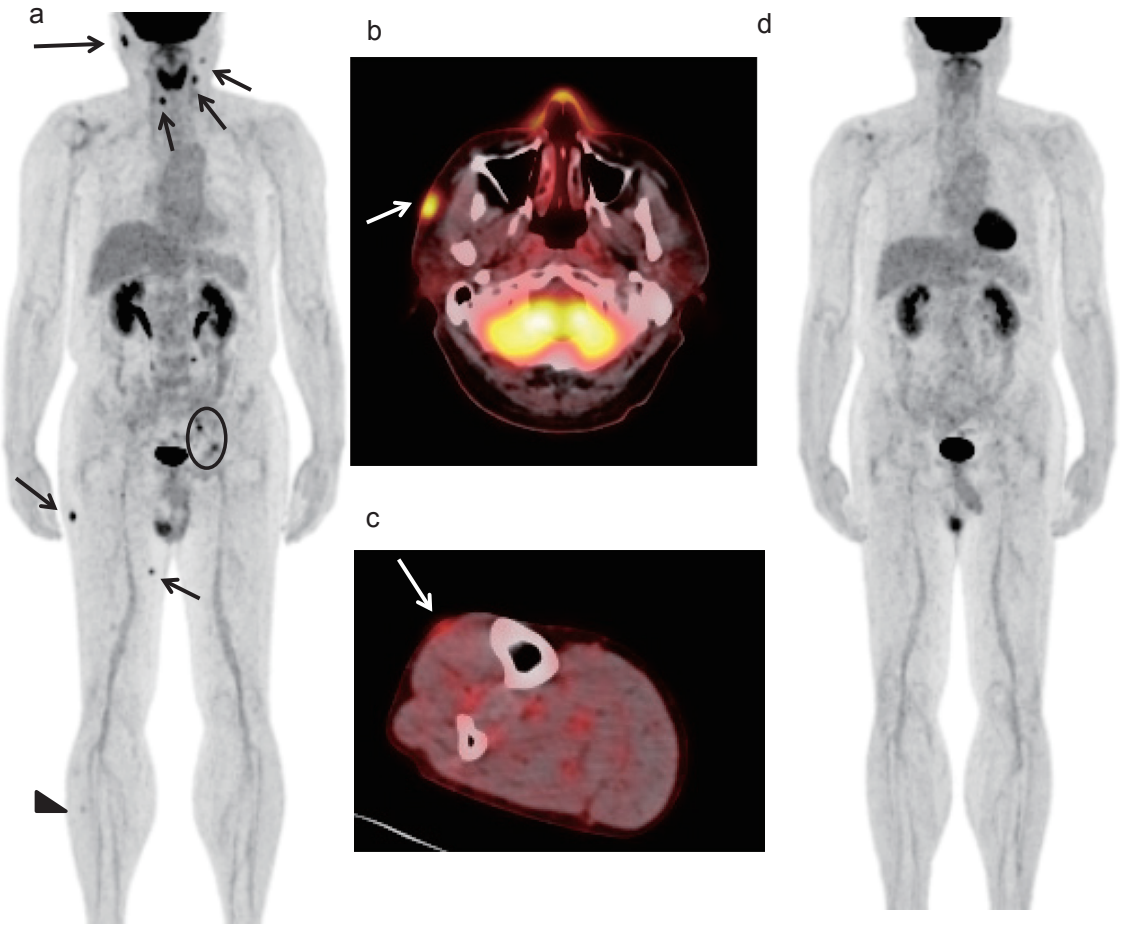

Fig. 2 PET and PET-CT images
Coronal maximum intensity projection image (a) shows multiple small skin lesions with high FDG uptake [mean maximum standardized uptake value (SUVmax): 7.7] in face, neck, and thigh (black arrows), left inguinal lymph nodes (circle) with moderate FDG uptakes (SUVmax: 4.4), and a small skin lesion in the right lower leg (arrow head) with minimal FDG uptake (SUVmax: 0.9). Fused PET-CT axial images shows a marked FDG uptake in the cheek lesion [(b) white arrow] and a minimal FDG uptake in the lower leg lesion [(c) white arrow]. No FDG uptake is identified following treatment (d).

Table Immunohistochemistry findings for the identification of cutaneous invasion of diffuse large B-cell lymphoma

CD3	negative
CD5	negative
CD10	negative
CD20	positive
BCL-2	positive
BCL-6	positive
MUM-1	positive
MIB-1	positive (70%)
C-MYC	positive (70%)
EBER RNA in situ hybridization	negative

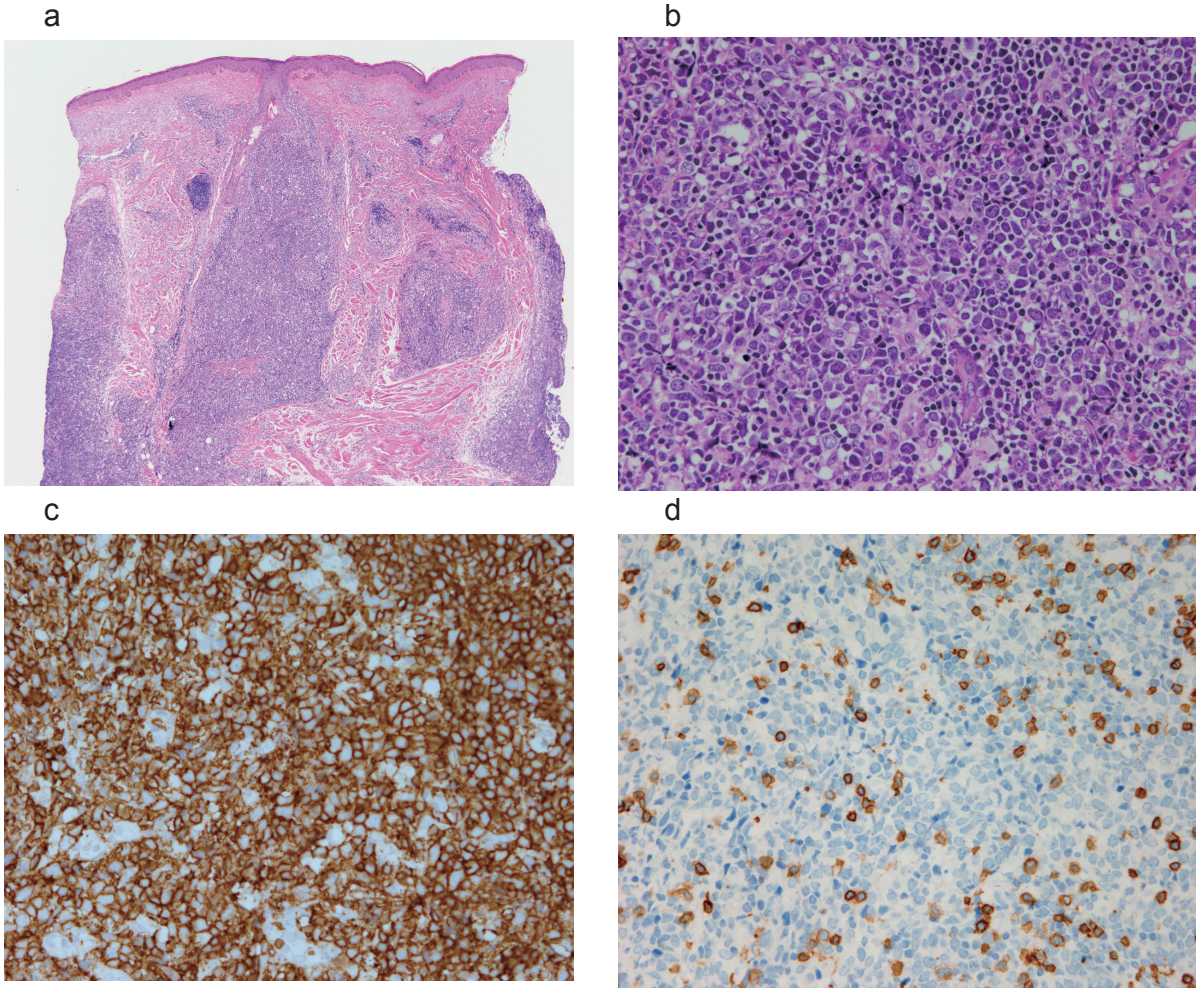

Fig. 3 Pathology of diffuse large B-cell lymphoma
A skin biopsy of the face. (a) Dense proliferation of atypical lymphoid cells in the entire dermis is observed [Hematoxylin and eosin (H&E, 40x)]. (b) Atypical cells had medium to large irregular shaped nuclei with prominent nucleoli (H&E, 400x). (c) Atypical cells are frequently positive for CD20 (400x). (d) Atypical cells are negative for CD3 (400x).

cally diagnosed as DLBCL with dermal invasion (Fig. 3), and the lower leg lesion was diagnosed as BD (Fig. 4). Table is shown immunohistochemistry finding of cutaneous invasion of DLBCL.

Consequently, chemotherapy using rituximab, cyclophosphamide, doxorubicin, and prednisolone (R-CHOP) and BD resection were performed. The PET-CT images following treatment showed no FDG uptake (Fig. 2d). Triple intrathecal therapy was added after R-CHOP. Complete remission has been successful.

DISCUSSION

Cutaneous lesions are commonly detected by imaging modalities. 18F-FDG PET-CT provides both morphological data and data regarding tumor meta-

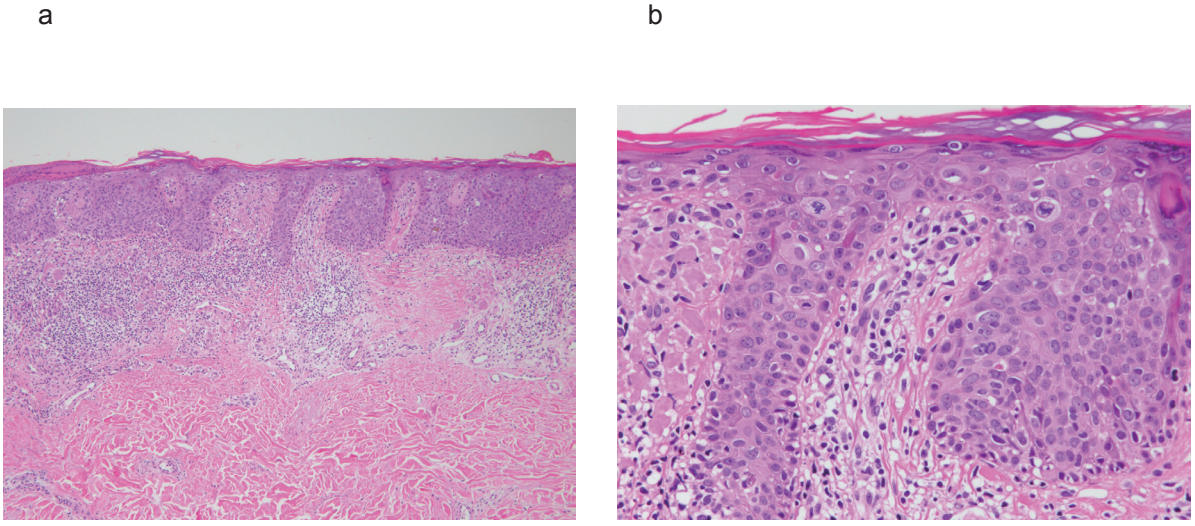

Fig. 4 Pathology of Bowen disease
A skin biopsy of the right lower leg. (a) Epidermis is acanthotic and accompanied with elongated rete ridge and an overlying hyperkeratotic scale (H&E, 100x). (b) Intraepidermal proliferation of atypical keratinocytespossessing irregular shaped large nuclei with prominent nucleoli. Mitotic figures are frequently observed (H&E, 400x).

bolic activity. Additionally, it can reveal potential subtle recurrences, micrometastases, and indeterminate nodal metastases resulting from various skin malignancies [11]. Furthermore, 18F-FDG PET-CT allows detection of cutaneous metastasis in locations that the patient is unable to notice, such as the lower back. However, 18F-FDG PET-CT has limitations because of false-positive findings from physiological uptake and infective or inflammatory conditions [13].

A majority of PTLs are DLBCLs, and most patients are >60 years of age [2, 4]. PTL yields poor prognosis, and its common metastatic sites include contralateral testicle, central nervous system, skin, and others [7]. 18F-FDG PET-CT is an excellent diagnostic tool for PTL disease-staging both before and during the follow-up period, as well as for the identification and diagnosis of primary and secondary malignant cutaneous lymphomas [1, 2, 12, 13]. PTL is a highly cellular tumor characterized by increased glucose metabolism, causing homogenous marked asymmetric testicular FDG uptake [2]. The semi-quantitative FDG uptake values measured by SUVmax have been reported to be within the range of 10–30 for PTL [2]. In our case, FDG uptake of PTL was unknown because 18F-FDG PET-CT was not performed at the previous hospital. Nonetheless, the SUVmax of cutaneous lesion was found to be 7.7, a value that was significantly lower than that usually observed in PTL because of the small metastatic volume.

BD is a skin condition described as SCC in situ and it is a very common epithelial malignancy in elderly people [8]. Progression to the invasive and metastatic forms occurs following a long period of time in only 3%–5% of diagnosed patients [8]. Outcomes can be favorable in selected cases even without any treatment involved [8]. FDG uptakes in primary lesions and lymph nodes or in distant metastatic sites are usually high when it on cutaneous SCC except BD [10, 13, 14]. Mahajan *et al.* reported that the mean value of SUVmax for primary lesions of cutaneous SCC was 10.2 [15]. On the other hand, the mean value of SUVmax for lymph node metastasis from cutaneous SCC has been reported to be 11 [13]. If the primary lesion suspected for BD has a marked FDG uptake, the lesion can develop into invasive SCC.

Concurrence of cutaneous malignant lymphoma and BD is extremely rare [9, 10]. However, the respective cutaneous features of the developed lesions are distinctly different. Mycosis fungoides is a cutaneous T-cell lymphoma whose morphology may mimic that of BD [16], where patients may typically present with multiple skin lesions [10]. The FDG uptakes in skin lesions depend on the thickness, size, and tumor volume [10]. In our case, the minimal FDG uptake of BD might be dependent on thickness rather than the size of the tumor, and it may be an indicative characteristic of low grade malignancy. In general, both LDH and sIL2R are effective biomarkers for follow-up of malignant lymphoma. However their values were found to be within normal range in our case study. Furthermore, 18F-FDG PET-CT was a very useful modality that could detect skin metastases stemming from PTL and patient's response to the underlying treatment.

In conclusion, this study evaluated the FDG uptakes of cutaneous metastases from testicular DLBCL and BD. FDG uptakes in cutaneous metastatic sites were found to be significantly higher than that related to BD.

REFERENCES

1) Cakiroglu B, Eyyupoglu SE, Dogan AN, Noseri U, Aksoy SH, Ozturk AB. Primary testicular lymphoma: Two case reports and review of the literature. Arch Ital Urol Androl 2016; 87: 332–4.
2) Okuyucu K, İnce S, Alagöz E, Ataş E, Arslan N. Utility of FDG PET/CT in the Management of Primary Testicular Lymphoma. Mol Imaging Radionucl Ther 2018; 27: 61–5.
3) Shahab N, Doll DC. Testicular lymphoma. Semin Oncol 1999; 26: 259–69.
4) Kim J, Yoon DH, Park I, Kim S, Park JS, Lee SW, *et al.* Treatment of primary testicular diffuse large B cell lymphoma without prophylactic intrathecal chemotherapy: a single center experience. Blood Res 2014; 49: 170–6.

5) Park BB, Kim JG, Sohn SK, Kang HJ, Lee SS, Eom HS, *et al*. Consideration of aggressive therapeutic strategies for primary testicular lymphoma. Am J Hematol 2007; 82: 840–5.
6) Cheah CY, Wirth A, Seymour JF. Primary testicular lymphoma. Blood 2014; 123: 486–93.
7) Lokesh KN, Sathyanarayanan V, Kuntegowdanahalli CL, Suresh TM, Dasappa L, Kanakasetty GB. Primary Diffuse large B-Cell lymphoma of testis: A single centre experience and review of literature. Urol Ann 2014; 6: 231–4.
8) Neagu TP, Ţigliş M, Botezatu D, Enache V, Cobilinschi CO, Vâlcea-Precup MS, *et al*. Clinical, histological and therapeutic features of Bowen's disease. Rom J Morphol Embryol 2017; 58: 33–40.
9) Starke WR. Bowen's disease of the palm associated with Hodgkin's lymphoma. Cancer 1972; 30: 1315–8.
10) Rivetti N, Cananzi R, Borroni RG, Croci GA, Vassallo C, Brazzelli V. Effectiveness of photodynamic therapy in refractory plaque-stage mycosis fungoides associated with Bowen's disease. Dermatol Ther 2017; 30: e12474.
11) Juan YH, Saboo SS, Tirumani SH, Khandelwal A, Shinagare AB, Ramaiya N, *et al*. Malignant skin and subcutaneous neoplasms in adults: multimodality imaging with CT, MRI, and 18F-FDG PET/CT. AJR Am J Roentgenol 2014; 202: W422–38.
12) Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. Radiographics 2010; 30: 269–91.
13) Fujiwara M, Suzuki T, Takiguchi T, Fukamizu H, Tokura Y. Evaluation of positron emission tomography imaging to detect lymph node metastases in patients with high-risk cutaneous squamous cell carcinoma. J Dermatol 2016; 43: 1314–20.
14) Cho SB, Chung WG, Yun M, Lee JD, Lee MG, Chung KY. Fluorodeoxyglucose positron emission tomography in cutaneous squamous cell carcinoma: retrospective analysis of 12 patients Dermatol Surg 2005; 31: 442–6.
15) Mahajan S, Barker CA, Singh B, Pandit-Taskar N. Clinical value of 18F-FDG-PET/CT in staging cutaneous squamous cell carcinoma. Nucl Med Commun 2019; 40: 744–51.
16) Yoo SS, Viglione M, Moresi M, Vonderheid E. Unilesional mycosis fungoides mimicking Bowen's disease. J Dermatol 2003; 30: 417–9.