

Multimodal Imaging-Assisted Diagnosis of a Rare Primary Cutaneous T-Cell Lymphoma Secondary to Imatinib plus Sintilimab in a Postoperative GIST Patient

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Case Report

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Abstract

Background: Primary cutaneous T cell lymphoma represents a heterogeneous subgroup of extranodal non-Hodgkin lymphoma and frequently presents with non-specific cutaneous manifestations that contribute to high rates of misdiagnosis. Emerging evidence suggests combined treatment with tyrosine-kinase inhibitors and PD-1 immune checkpoint inhibitors may drive secondary lymphomagenesis. This case adds to literature by highlighting the diagnostic value of multimodal non-invasive skin imaging (dermoscopy plus high-frequency ultrasound) as ancillary clues before definitive histopathological confirmation.

Case Summary: A 58-year-old male with completely-resected high-risk gastrointestinal stromal tumor (GIST) developed progressive generalized skin lesions following imatinib and single-dose sintilimab therapy. He presented with widespread purplish-red scaly papules and plaques accompanied by pruritus, eyebrow loss and palpable peripheral lymphadenopathy. Routine laboratory tests revealed mild monocytosis and slight anaemia. Multimodal imaging including high-frequency ultrasound and dermoscopy identified characteristic cutaneous changes. Histopathology together with immunohistochemistry confirmed the diagnosis of primary cutaneous T-cell lymphoma. Unfortunately, the patient was lost to follow-up after hospital discharge, so post-discharge therapeutic response could not be evaluated.

Conclusion: Multimodal non-invasive skin imaging assists early suspicion of PCTCL; definitive diagnosis still depends on histopathology and immunohistochemistry. Clinicians should remain alert for secondary cutaneous lymphoproliferative disorders among patients receiving combined targeted-immune anticancer therapy.

Introduction

Primary cutaneous T-cell lymphoma (PCTCL) is the most common subtype of primary cutaneous lymphoma, accounting for approximately 70%-80% of all primary cutaneous lymphomas[1]. It is a heterogeneous group of malignancies originating from mature T lymphocytes, with diverse clinical manifestations, insidious onset, and a long disease course. The typical clinical features include chronic pruritic erythema, plaques, and tumors involving the skin, which can progress to systemic involvement in advanced stages, seriously affecting the patient's quality of life and prognosis[2].

In recent years, with the widespread application of targeted therapy and immunotherapy in the treatment of malignant tumors, the incidence of secondary tumors related to these therapies has gradually attracted clinical attention. Tyrosine kinase inhibitors (TKIs) such as imatinib are widely used in the treatment of gastrointestinal stromal tumors (GIST), chronic myeloid leukemia, and other tumors, and their potential immunomodulatory effects may affect the occurrence and development of secondary malignancies[3]. PD-1 inhibitors represented by sintilimab have achieved remarkable curative effects in the treatment of various solid tumors and hematological malignancies, but they may also induce

abnormal T-cell clonal expansion and immune-related adverse reactions, including the occurrence of secondary lymphomas[4].

Case Presentation

A 58-year-old male patient presented to our hospital on October 30, 2024, due to progressive skin lesions for 1 month. The patient initially developed erythema on the face 1 month ago, accompanied by mild pruritus and burning sensation. He applied hydrocortisone butyrate cream topically by himself without obvious improvement. The skin lesions gradually expanded to the trunk and limbs, presenting as generalized purplish-red papules and plaques covered with scales. Physical examination showed crusting on the face, eyebrow loss, and persistent pruritus.

Past medical history

In April 2024, the patient was diagnosed with "gastrointestinal stromal tumor". He underwent "laparoscopic resection of huge abdominal tumor + partial gastrectomy + splenectomy + fenestration and unroofing of hepatic cysts", and recovered well after the operation. He has been regularly taking "imatinib 0.4g once daily" till now. On October 18, 2024, he received "sintilimab injection 200mg intravenously once". There was no history of allergies, hypertension, diabetes, or other chronic diseases.

Physical examination: The general condition of the whole body was good. Enlarged lymph nodes were palpable in the bilateral neck, groin, and axilla, with the largest being 3×2cm, which were mobile and non-tender. Skin examination: Erythema and plaques on the face, fused into sheets; dry skin and scales on the limbs; generalized purplish-red papules and plaques on the trunk and limbs, covered with scales on the surface; crusting on the face and eyebrow loss. A 15cm old surgical scar was visible in the left lower abdomen (Fig. 1).

Laboratory examinations: Routine blood test showed: monocyte ratio 0.108 (elevated), monocyte count $0.757 \times 10^9/L$ (elevated), hemoglobin concentration 123g/L (decreased), red blood cell count $4.01 \times 10^{12}/L$; coagulation function (five items), D-dimer, tumor markers (seven items), pancreatitis indicators (two items), electrolytes (six items), blood lipids (complete set), renal function (five items), and liver function (seven items) were all within the normal range.

Imaging examinations: Color Doppler ultrasound examination: Diffuse thickening of the affected skin, with a maximum thickness of about 7mm, uneven internal echo, no obvious cystic space or calcification, and abundant blood flow signals in the affected skin layer shown by CDFI (Fig. 2). Dermoscopy (waist): The microscope showed a red background with a little yellowish-white scales; yellowish-white flaky structures with follicular keratotic plugs were visible in the skin lesions, accompanied by scattered punctate and linear blood vessels (Fig. 3).

Histopathological and immunohistochemical examinations: Histopathological examination of the waist skin lesion showed irregular hyperplasia of the spinous layer of the covering squamous epithelium with

mild hyperkeratosis, intact granular layer; liquefaction of the epidermis and hair follicle basement membrane with irregular lymphocyte infiltration and pigment incontinence; irregular lymphocytes, histiocytes, and a small number of neutrophils and eosinophils infiltrated around the blood vessels in the superficial dermis. Special staining: PAS positive (microspores were seen in the stratum corneum and follicular keratotic plugs), melanin negative. Immunohistochemical staining showed: CD3 (T cells positive), CD7 (T cells positive), CD4 (T cells positive), CD8 (T cells positive), CD56 (negative), Ki-67 (positive, approximately 90% in the basal layer), CD20 (a small number of B cells positive). Combined with morphological and immunohistochemical results, the diagnosis of primary cutaneous T-cell lymphoma was confirmed (Fig. 4).

Treatment and follow-up

Considering the patient's history of GIST and current use of imatinib and sintilimab, the treatment plan was formulated according to the patient's general condition and the stage of PCTCL. However, the patient was lost to follow-up after discharge, and further treatment and prognosis could not be tracked.

Discussion

The clinical manifestations of PCTCL are diverse[5], and the early lesions are often non-specific, which are easily misdiagnosed as eczema, psoriasis, and other inflammatory skin diseases, leading to delayed treatment[6]. In this case, the patient initially presented with facial erythema and pruritus, which was misdiagnosed as common inflammatory skin disease by himself, and the condition progressed to generalized skin lesions, which is consistent with the insidious and non-specific characteristics of early PCTCL.

The diagnosis of PCTCL relies on the combination of clinical manifestations, imaging examinations, and pathological examinations, among which histopathological and immunohistochemical examinations are the gold standard[7]. In this case, the patient's skin lesions showed typical clinical features of PCTCL, such as generalized purplish-red papules, plaques, and eyebrow loss. Dermoscopy and high-frequency ultrasound, as non-invasive imaging techniques, provided important clues for early diagnosis[8]. Dermoscopy showed punctate and linear blood vessels, which is consistent with the microvascular characteristics of early PCTCL reported in the literature[9]. Manal Bosseila et al. pointed out that neovascular proliferation is significant in early mycosis fungoides lesions, and punctate blood vessels are the characteristic dermoscopic sign of PCTCL[10]. Ping Xu et al. further found that thin linear blood vessels and orange-yellow patchy areas can be used as auxiliary diagnostic clues for early lesions[11]. High-frequency ultrasound showed diffuse skin thickening and abundant blood flow signals, which is related to the inflammatory infiltration and abnormal angiogenesis of PCTCL lesions[12]. The synergistic application of dermoscopy and high-frequency ultrasound can realize the multi-dimensional evaluation of "superficial morphology-deep structure", which is helpful for the early identification of suspicious lesions, guiding targeted biopsy, and improving the diagnostic efficiency. However, it should be emphasized that imaging examinations can only provide auxiliary diagnostic clues, and the definitive

diagnosis still needs to rely on histopathological and immunohistochemical examinations. In this case, the histopathological examination showed atypical T-cell infiltration, and the immunohistochemical results showed positive expressions of CD3, CD4, CD7, CD8, and high expression of Ki-67, which fully met the diagnostic criteria of PCTCL[13].

Imatinib, as a TKI, mainly exerts its anti-tumor effect by inhibiting the activity of tyrosine kinase, but it also has certain immunomodulatory effects, which may affect the balance of the immune system and promote the clonal expansion of abnormal T cells[4]. Saleh JS et al. reported that some patients developed secondary tumors during imatinib treatment, including lymphoma and solid tumors, but there is no conclusive evidence that imatinib significantly increases the risk of secondary tumors[5]. Sintilimab, as a PD-1 inhibitor, can block the PD-1/PD-L1 pathway, activate the anti-tumor immune response of T cells, but it may also lead to abnormal activation and clonal expansion of T cells, thereby inducing immune-related adverse reactions and even secondary tumors[11]. Yasutoshi Hida et al. reported a case of malignant melanoma patient who developed cutaneous T-cell lymphoma 1.5 years after receiving nivolumab treatment, which was considered to be related to PD-1 inhibitor-induced abnormal T-cell clonal expansion and EBV infection[6]. At present, there is no direct report on the coexistence or causal relationship between sintilimab and PCTCL. Therefore, it is speculated that the long-term use of imatinib and the single use of sintilimab in this patient may have synergistically affected the immune microenvironment of the skin, promoted the clonal proliferation of abnormal T cells, and ultimately led to the occurrence of PCTCL. However, due to the lack of long-term follow-up data and relevant molecular biological detection results (such as EBV detection, T-cell receptor gene rearrangement detection), the causal relationship between targeted/immune therapy and PCTCL in this case cannot be completely confirmed, which needs to be further verified by more clinical cases and basic research.

In terms of the treatment and follow-up of PCTCL, the treatment plan should be formulated according to the patient's age, general condition, and disease stage[9]. For early PCTCL, local treatment (such as topical glucocorticoids, nitrogen mustard) or phototherapy can be used; for advanced cases, systemic treatment such as chemotherapy, immunotherapy, and targeted therapy is needed. In this case, considering the patient's history of GIST and current use of imatinib and sintilimab, the treatment plan needs to be individualized to avoid drug interactions and excessive immune suppression. This also reminds clinicians that for patients receiving targeted/immune therapy, regular follow-up should be strengthened, and any new skin lesions should be paid attention to, so as to realize early detection, early diagnosis, and early treatment of secondary tumors.

Declarations

Ethical Approval and Consent to Participate

This study has been approved by the Ethics Committee of The First Affiliated Hospital of Guangdong Pharmaceutical University. Written informed consent has been obtained from the patient's for

participation in the study and the collection and analysis of relevant data. All research procedures comply with the ethical principles of the Helsinki Declaration.

Consent for Publication

The patient's have provided written consent for the publication of this case report and related clinical data (including imaging pictures, laboratory test data, and treatment records), and have signed the informed consent form for publication, agreeing to the use of relevant materials for academic exchange and publication.

Conflicts of Interest

All authors declare that they have no conflicts of interest related to the research content (including but not limited to commercial interests, academic interests, and personal interests) during the conduct of this study and the publication of related results.

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Author Contribution

Y.C., H.Z. and W.D. collected clinical-laboratory data, performed literature retrieval, and drafted the original manuscript. R.W. conceived and designed the case report, supervised data interpretation, critically revised the manuscript, and took overall responsibility for this work. All authors read and approved the final manuscript.

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Data Availability

The existing “Availability of Data and Materials” section within the manuscript will be automatically extracted for formal publication.

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Figures

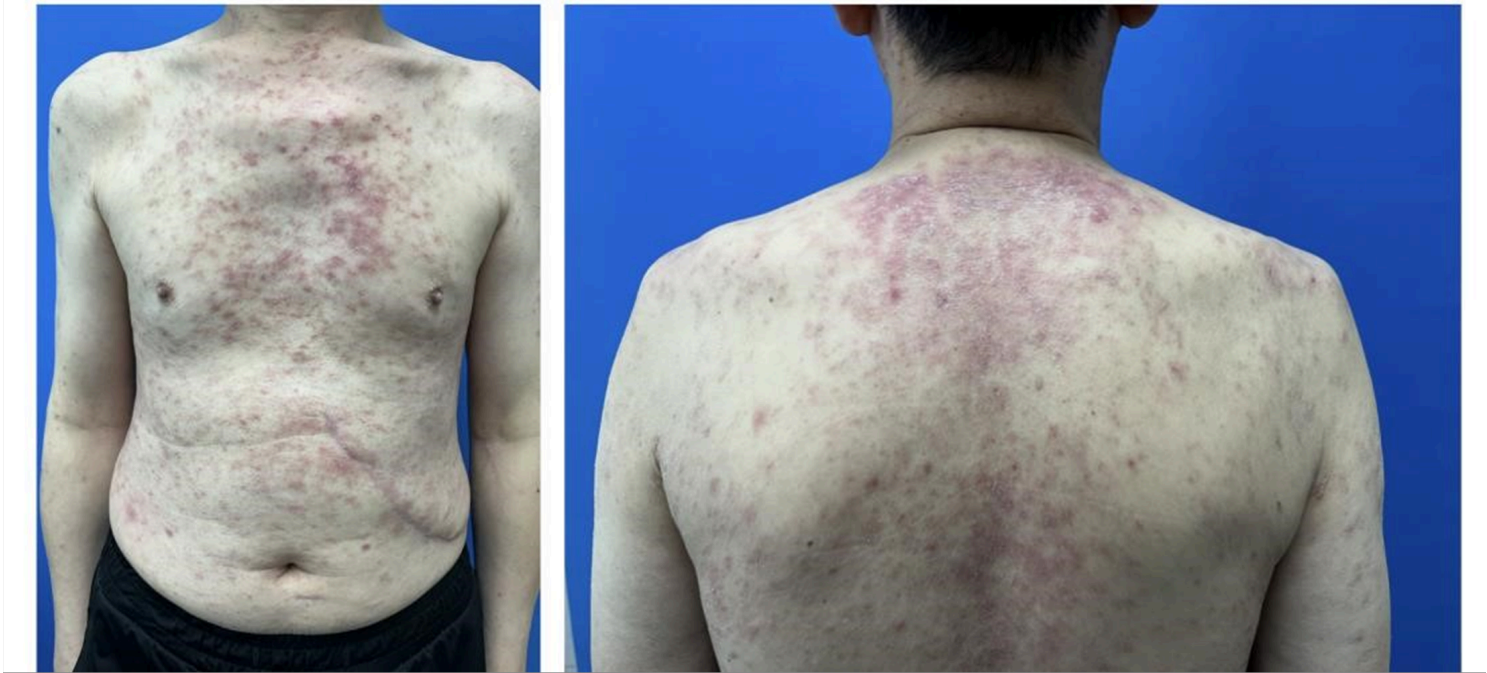


Figure 1

Trunk skin lesions of a 58-year-old male patient with PCTCL. Generalized purplish-red papules and plaques covered with scales can be seen on the trunk.

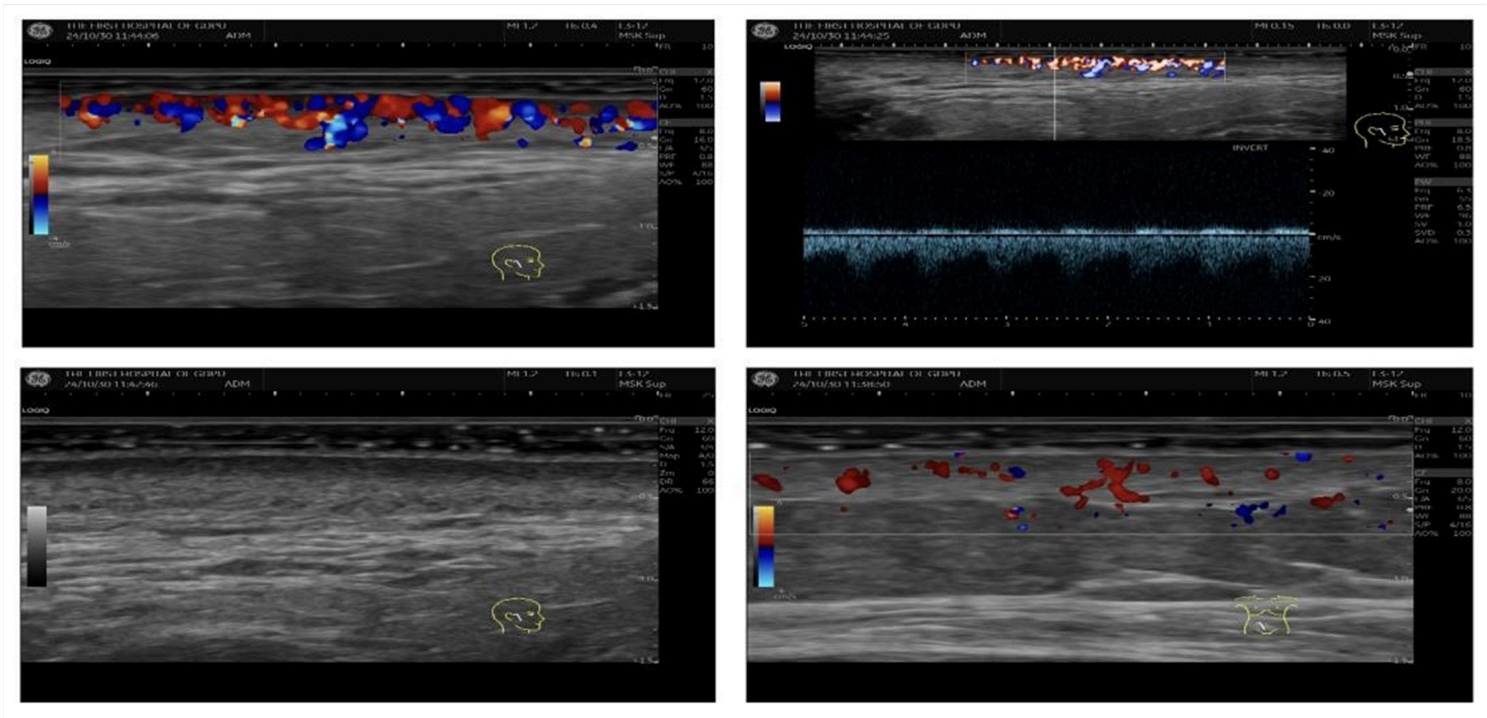


Figure 2

High-frequency color Doppler ultrasound of the waist skin lesion in a 58-year-old male patient with PCTCL. Diffuse thickening of the skin (maximum thickness of 7 mm), uneven internal echo, and

abundant blood flow signals in the skin layer are shown.

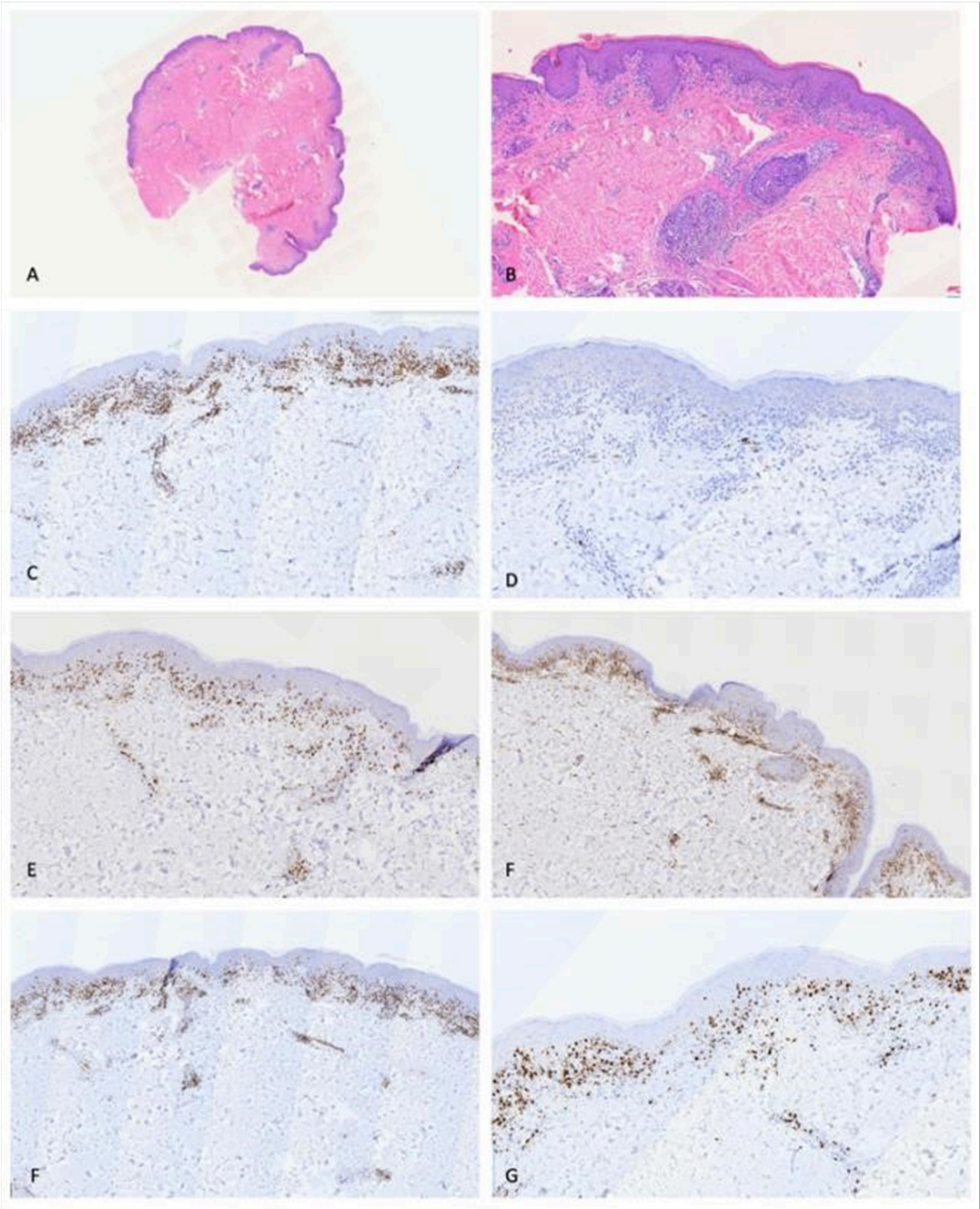


Figure 3

Dermoscopy of the waist skin lesion in a 58-year-old male patient with PCTCL (IDS-1100, Illuco Corporation Ltd., Gyeonggi-do, South Korea; magnification $\times 10$). A red background with yellowish-white

scales, yellowish-white flaky structures with follicular keratotic plugs, and scattered punctate and linear blood vessels are visible.

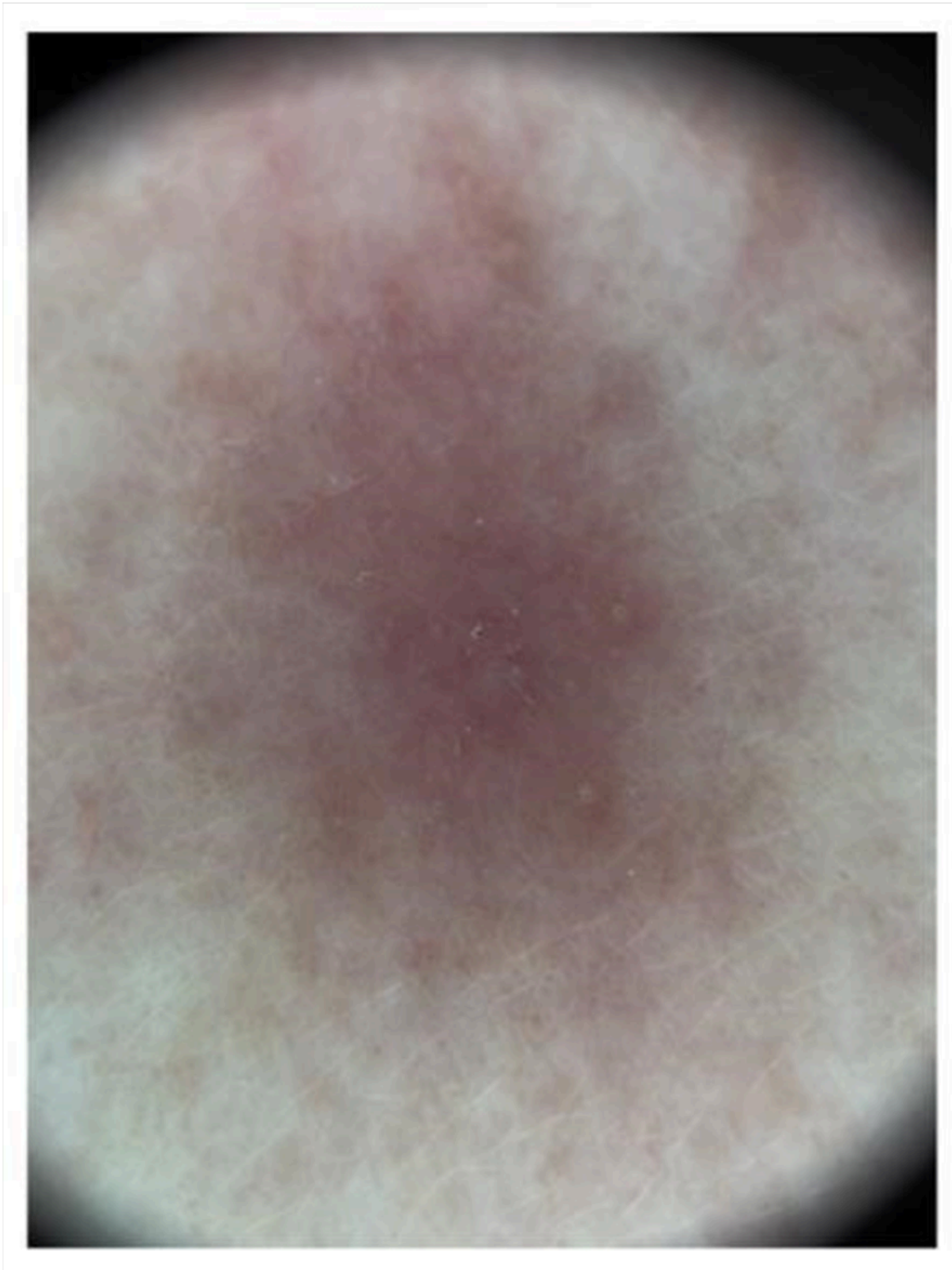


Figure 4

Histopathological and immunohistochemical findings of the waist skin lesion in a 58-year-old male patient with PCTCL. A, B: Irregular hyperplasia of the spinous layer of the covering squamous epithelium

with mild hyperkeratosis, intact granular layer; liquefaction of the epidermis and hair follicle basement membrane with irregular lymphocyte infiltration and pigment incontinence; irregular lymphocytes, histiocytes, and a small number of neutrophils and eosinophils infiltrated around the blood vessels in the superficial dermis (A: HE staining $\times 10$; B: HE staining $\times 40$). C: Immunohistochemical staining shows positive expression of CD3 ($\times 40$). D: Immunohistochemical staining shows a small number of CD20-positive cells ($\times 40$). E: Immunohistochemical staining shows positive expression of CD8 in some T cells ($\times 40$). F: Immunohistochemical staining shows positive expression of CD7 ($\times 40$). G: Immunohistochemical staining shows positive expression of Ki-67, approximately 90% in the basal layer ($\times 40$).