Painless Red Nodule on the Right Cheek of a Young Woman: A Quiz

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A 45-year-old woman presented with an erythematous nodule on her right cheek since 3 months. She reported that the skin lesion manifested suddenly with the appearance of a small painless erythematous papule, which enlarged slowly. The patient was in good general health with no underlying diseases. She was not taking any regular medication, and denied fever, recent infections or insect bites. There was no family history of skin cancer.

Clinical examination revealed a circular erythematous nodule 0.5 cm in diameter (Fig. 1A), which was moveable on palpation. Dermoscopy revealed a vascular pattern characterized by an orange-pink background with overlying serpiginous blood vessels (Fig. 1B). There was no lymphadenopathy. Blood tests (haemogram and general blood chemistry) were normal. A punch excision of the entire lesion was performed.

What is your diagnosis?

Differential diagnosis 1: Primary cutaneous CD4$^+$ small/medium T-cell lymphoproliferative disorder
Differential diagnosis 2: Amelanotic melanoma
Differential diagnosis 3: Dermal naevus
Differential diagnosis 4: Merkel cell carcinoma

See next page for answer.

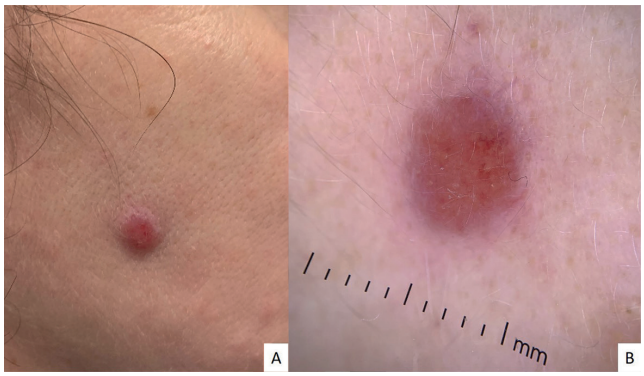

Fig. 1. Clinical presentation. (A) A solitary erythematous nodule 0.5 cm diameter on the right cheek. (B) Dermoscopy revealing a well-vascularized nodule characterized by an orange-pink background with overlying serpiginous blood vessels.

ANSWERS TO QUIZ

Painless Red Nodule on the Right Cheek of a Young Woman: A Commentary

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Diagnosis: **Primary cutaneous CD4⁺ small/medium T-cell lymphoproliferative disorder**

Punch biopsy revealed a dense dermal infiltrate of small- to medium-sized slightly pleomorphic CD4⁺ lymphocytes with increased proliferative activity (20% MiB1-positive cells) without epidermotropism. The cells were immunoreactive for PD-1 and ICOS. There was no increase in CD30 expression and a balanced ratio of kappa/lambda light chain immunoexpression (1:1). PCR revealed a biclonal rearrangement of the T-cell receptor gene yielding 2 clones of 232-bp (type V-II) and 240-bp (type III) length (Fig. 2). These findings allowed a diagnosis of a primary cutaneous CD4⁺ small/medium T-cell lymphoproliferative disorder to be established. The punch excision wound healed spontaneously. At subsequent follow-ups there were no signs of recurrence.

Primary cutaneous CD4⁺ small/medium T-cell lymphoproliferative disorder (PCSMLPD) is a provisional entity within the spectrum of primary cutaneous T-cell lymphomas (1). The WHO revised and updated the classification of lymphoid neoplasms in 2016, and primary cutaneous CD4⁺ small- to medium-sized T-cell lymphoma was reclassified as primary cutaneous CD4⁺ small- to medium-sized T-cell lymphoproliferative disorder (PCSMLPD) (1). PCSMLPD is generally considered to be a low-grade lymphoma, meaning that it has a relatively slow growth rate and tends to be limited to the skin (2).

The exact cause and pathogenesis of PCSMLPD is not fully understood. This disorder most commonly affects middle-aged adults (women > men) (3).

PCSMLPD usually presents as 1 or more red/purple skin nodules. The most commonly affected body regions are the head and/or neck, but the trunk or limbs may also be affected (2).

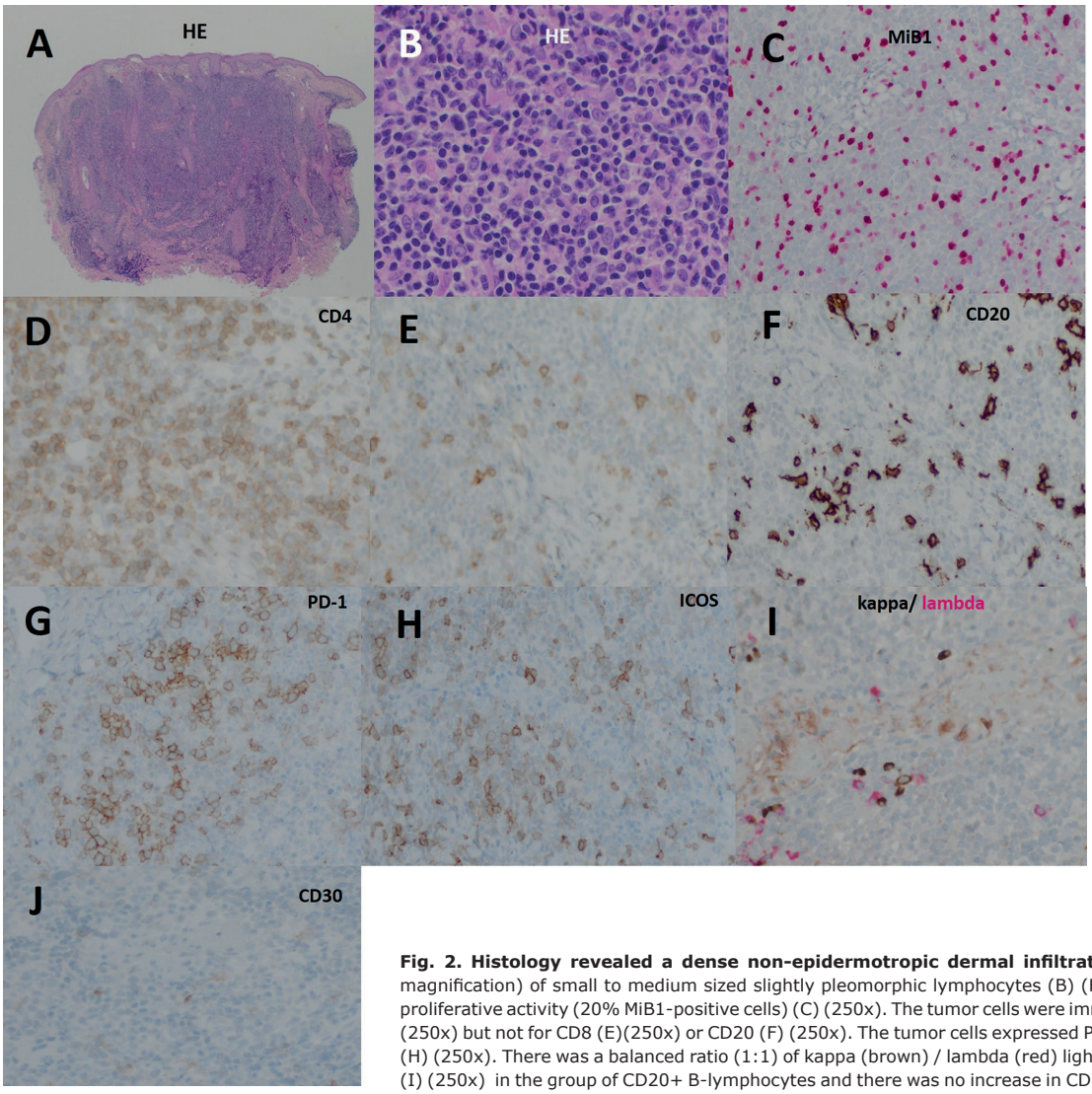

Fig. 2. Histology revealed a dense non-epidermotropic dermal infiltrate (A) (HE staining, 40x magnification) of small to medium sized slightly pleomorphic lymphocytes (B) (HE, 250x) with increased proliferative activity (20% MiB1-positive cells) (C) (250x). The tumor cells were immunoreactive for CD4 (D) (250x) but not for CD8 (E)(250x) or CD20 (F) (250x). The tumor cells expressed PD-1 (G) (250x) and ICOS (H) (250x). There was a balanced ratio (1:1) of kappa (brown) / lambda (red) light chain immunexpression (I) (250x) in the group of CD20+ B-lymphocytes and there was no increase in CD30 expression (J) (250x).

Diagnosis of PCSMLPD involves a combination of clinical examination, imaging studies and biopsy of the affected skin. Histologically, PCSMLPD shows an infiltrate composed mainly of small- to medium-sized slightly pleomorphic lymphocytes, and the percentage of any large atypical cells is <30% (4). Some plasma cells, eosinophils, and histiocytes may also be present. The dermal infiltrate may have a nodular or band distribution and, as in the current case, a border zone separating it from the epidermis. Occasionally, epidermotropism or extension into the subcutaneous fat tissue may also occur (4–6).

Treatment for PCSMLPD depends on the extent and severity of the disease. Localized lesions can be treated with surgery (7), radiation therapy (8), topical steroids (2) or topical chemotherapy (7). Systemic therapy, such as chemotherapy or immunotherapy, may be used for more extensive disease (7). The prognosis for PCSMLPD is generally favourable, with most patients experiencing long-term remission after treatment. However, there is a risk of recurrence; hence, close monitoring and follow-up care are important (9).

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