QUIZ SECTION

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Multiple Erythematous Nodules on the Trunk: A Quiz

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A 75-year-old male patient presented with multiple erythematous skin nodules. The rash began as a solitary abdominal lesion a month before presentation and gradually spread across the trunk, including the back and abdomen. Three years earlier, the patient had been diagnosed with myelodysplastic syndromes (MDS) based on a bone marrow examination after pancytopenia was detected during a routine health checkup. However, as he has mild cytopenia with no systemic symptoms and exhibited a normal karyotype on G-banding analysis, he was classified as having low-risk MDS and remained under observation without any treatment. His medical history included heart failure and diabetes mellitus, both of which he had been managed with stable medication regimens for over 10 years. Physical examination revealed multiple erythematous nodules on the back and abdomen (Fig. 1). The lesions were non-pruritic and non-tender. No mucosal involvement or lymphadenopathy was noted, and no other systemic abnormalities were detected. Laboratory tests revealed anaemia (8.9 g/dL), thrombocytopenia ($91 \times 10^3/\mu L$), and leukopenia ($2.7 \times 10^3/\mu L$); however, no blast cells were detected in the peripheral blood. Inflammatory markers, infection screening, antinuclear antibodies, and eosinophil counts were all within normal limits. Computed tomography revealed no significant abnormalities.

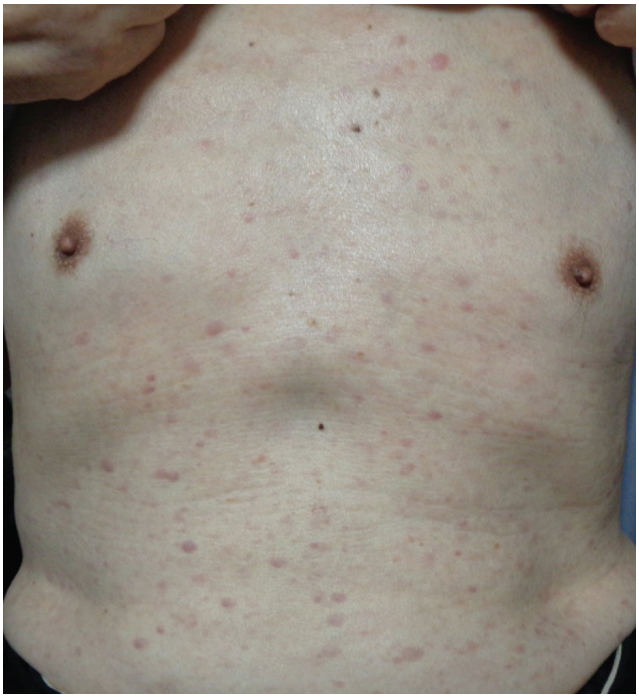

Fig. 1. Clinical photo: multiple erythematous nodules on the trunk.

What is your diagnosis?

1: Leukaemia cutis in myelodysplastic syndromes

2: Sweet syndrome

3: Primary cutaneous lymphoma

4: Lichen planus

See next page for answer.

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ANSWERS TO QUIZ

Multiple Erythematous Nodules on the Trunk: A Commentary

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Diagnosis: **leukaemia cutis in myelodysplastic syndromes**

Histopathological examination of the multiple nodules revealed lymphocyte-like cell infiltration in the dermis (Fig. 2). Immunostaining showed positivity for myeloperoxidase (MPO) and CD117, whereas CD3, CD20, CD34, and CD30 were negative (Fig. 3A, B). Bone marrow analysis revealed a hypercellular marrow with a predominance of myeloid precursors and 5% blasts. Ineffective haematopoiesis was observed, consistent with myelodysplastic syndromes (MDS). There was no evidence of transformation to acute leukaemia. Immunohistochemical staining of bone marrow cells showed positivity for MPO and CD117 but negativity for CD3, CD20, and CD34 (Fig. 3C, D). These similar cellular compositions, observed in both bone marrow and skin biopsy specimens through immunohistochemical analysis, confirmed the diagnosis of MDS-associated leukaemia cutis (LC), resulting in the observation without any topical treatment.

MDS was first defined as a distinct disease entity by the French-American-British (FAB) Group in 1982 (1). MDS is a haematologic disorder characterized by cytopenia, particularly anaemia, with typically hypercellular bone marrow (1). Dysplastic haematopoiesis is observed across 1 or more cell lineages (1). MDS can present with various skin manifestations, classified as non-specific or specific lesions (2, 3). Non-specific lesions, including Sweet's syndrome, erythema nodosum-like eruptions, and pernio-like eruptions, are thought to be induced by excessive inflammatory cytokine production in MDS (2). Conversely, specific lesions, referred to as LC, involve direct infiltration of malignant hematopoietic cells into the skin (3). LC presents with diverse clinical manifestations, including skin-coloured or violaceous papules, plaques, ulcers, and nodules (4). LC is observed in approximately 3% of patients with acute leukaemia, and its incidence is considered to be even lower in chronic leukaemia (5). Although LC is commonly observed in patients with acute leukaemia, its occurrence in MDS is rarely reported. In most reported cases, the transformation of MDS into acute leukaemia coincides with the onset of skin lesions (4–6). Therefore, LC is considered an early indicator of the transformation into acute leukaemia and is associated with a poor prognosis (4–6). Even in the absence of visible skin lesions, leukemic blasts may infiltrate into the skin (7), suggesting that the transformation into acute leukaemia may begin even before the emergence of LC. Thus, when LC develops in patients with MDS, the possibility of the transformation into acute leukaemia must always be considered, necessitating early and proactive management (4–6).

No standardized treatment approach exists for LC in MDS, and a therapeutic consensus has yet to be established (4–6). Given that LC arises as a manifestation of MDS, its treatment focuses primarily on managing the underlying MDS (4–6). Most cases of MDS-associated LC progress to acute leukaemia and are ultimately fatal, with LC lesions persisting without regression. However, Katagiri et al. reported a case of MDS-associated LC in which azacitidine therapy led to the disappearance of bone marrow blasts and the resolution of LC lesions (8). Conversely, Kaiserling et al. reported a case of MDS-related LC that showed regression followed by transformation into acute leukaemia within months, resulting in death within 6 months (9). This suggests that LC regression does not necessarily indicate an improvement in the underlying haematologic disorders and may, in some cases, signal an impending aggressive transformation. In many cases of myeloid neoplasms presenting with cutaneous manifestations, shared clonal mutations have been identified in both skin and bone marrow specimens (10). Therefore, performing mutational analysis, such as next-generation sequencing (NGS), on both bone marrow and skin samples is considered highly valuable for understanding whether the clones at both sites share a common origin. However, in the present case, mutational analysis using a targeted panel with NGS was not performed on either the bone marrow or skin specimens, which represents a limitation in terms of fully investigating and confirming the clonal relationship between the 2 sites.

In our case, the bone marrow blast percentage remained at 5%, and the degree of pancytopenia was consistent with

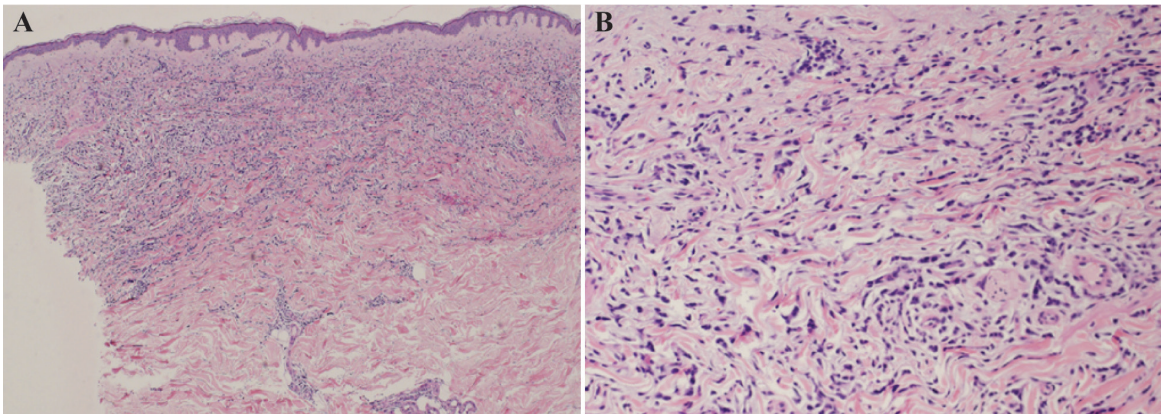

Fig. 2. Histopathological findings. Histopathological examination of the multiple nodules reveals significant infiltration of lymphocyte-like cells into the dermis. (A) Haematoxylin and eosin (HE) staining; ×40. (B) HE staining; ×200.

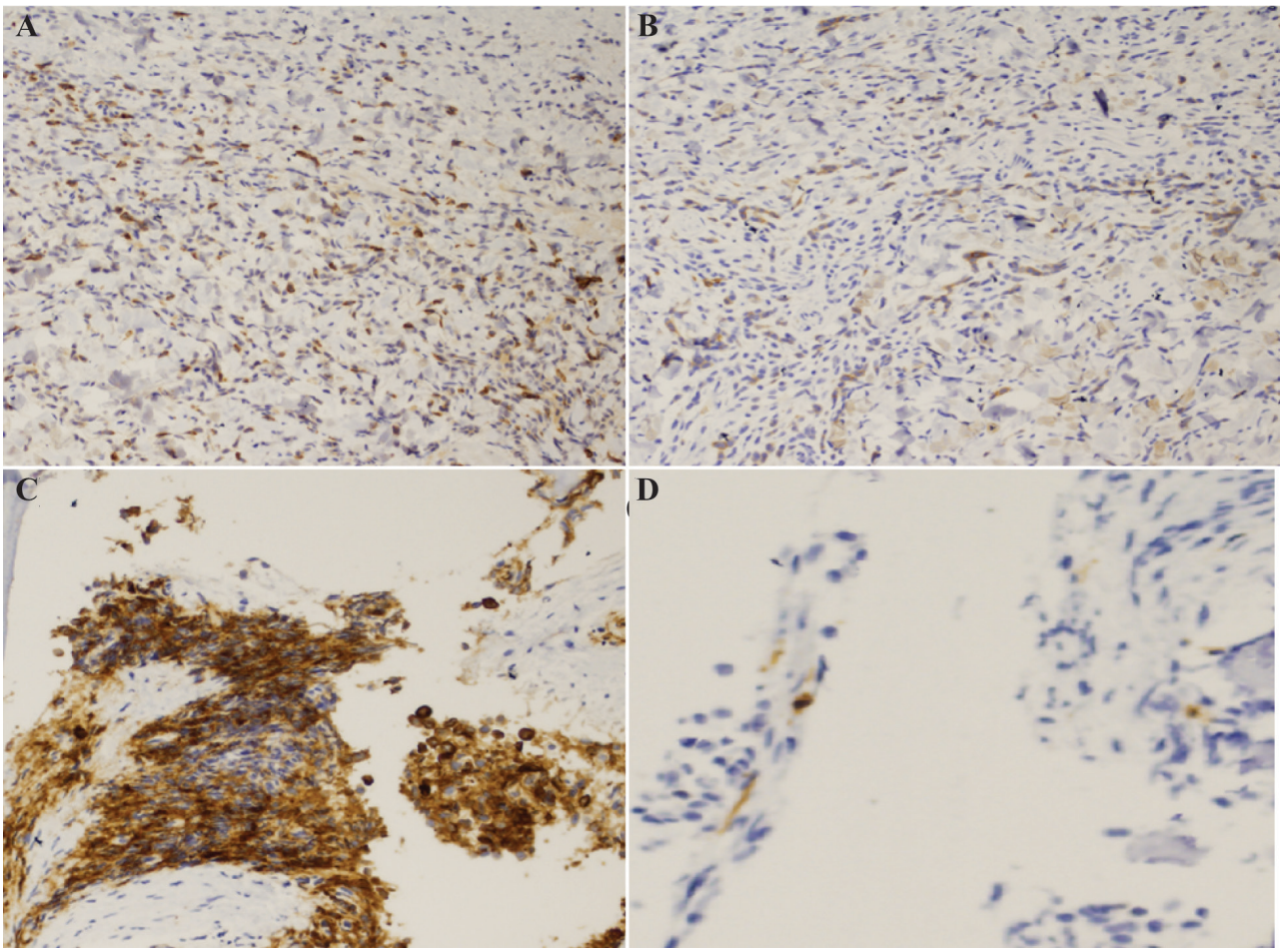

Fig. 3. Histopathological findings. Immunostaining of the multiple nodules shows positivity for (A) myeloperoxidase and (B) CD117 (x100). Immunostaining of the marrow cells was positive for (C) myeloperoxidase (x100) and (D) a little bit positive for CD117 (x400).

pre-existing levels before the appearance of LC lesions. Therefore, we are currently monitoring the patient closely for potential acute transformation while following a careful disease management strategy without the administration of chemotherapies. Skin manifestations in haematologic disorders may serve as crucial markers of disease progression. Dermatologists must collaborate with haematologists and other specialists to ensure comprehensive patient care. Further research is needed to elucidate the mechanisms underlying the development of MDS-associated LC and establish effective treatment strategies for LC in MDS.

The authors have no conflicts of interest to declare.

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