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SHORT COMMUNICATION

Generalized Granulomatous Dermatitis Accompanied by Myelodysplastic Syndrome

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Cutaneous manifestations associated with myelodysplastic syndrome (MDS) are uncommon. Recognizing MDS skin manifestations is important as they can precede blood or bone marrow transformation to leukaemia and are associated with a poor prognosis (1, 2). Recently, 2 cases of granulomatous dermatitis associated with MDS were reported as non-specific cutaneous manifestations of MDS, with subsequent development into acute myeloid leukaemia with leukaemia cutis (1, 2). An imbalance of T-cell subsets, regulatory T cells (Tregs) and Th17 in MDS is also correlated with disease progression (3, 4). We describe here a case of granulomatous dermatitis accompanied by MDS, which we hypothesized might show correlations with Tregs and interleukin (IL)-17 producing cells. We therefore employed immunohistochemical staining for Foxp3 and IL-17 to characterize the granuloma.

CASE REPORT

A 65-year-old Japanese man with a one-year history of pruritic eruption on his face, trunk and extremities visited our outpatient clinic. He had been treated with topical steroids and anti-histamine for one year with no improvement. On his initial visit, physical examination revealed erythroderma overlapping with groups of firm nodules on the trunk and extremities (Fig. 1). A biopsy specimen from his right lower leg revealed interstitial, dermal granulomatous inflammation with multinucleated giant cells without blasts, neutrophils or atypical cells (Fig. 2A, B). Eosinophils were not prominent. Immunohistochemical staining revealed that these infiltrating cells were mainly positive for CD3, CD4, CD5, CD7 and CD8, and negative for neutrophil elastase, myeloperoxidase (MPO), Alcian blue and Ziehl-Neelsen stain. The Ki67 score was approximately 10%. Immunohistochemical staining for Foxp3, IL-17 and CD163 revealed dense, massive infiltration of $Foxp3^+$ Tregs throughout the granuloma tissue (Fig. 2C, D), which were surrounded by $CD163^+$ M2 macrophages (Fig. 2E). IL-17-producing cells were scattered in the granuloma tissue (Fig. 2F). A full blood count revealed prominent upregulation of monocytes (45%, 2,750/mm^3). Bone marrow biopsies revealed increased numbers of megakaryocyte (313/μl) and a high ratio of myeloblasts (15.4%). The karyotype of this patient is 46, XY, and the chromosome aberration test revealed 2 types of abnormalities in chromosome (46, XY, der (1) (qter-q21::p32-qter), and 46, XY, t(3; 16) (q27;p11.2)). From the above findings, we diagnosed this patient with generalized granulomatous dermatitis accompanied by myelodysplastic syndrome (Refractory Anemia with Excess of Blasts, type 2 (RAEB2), International Prognostic Scoring System (IPSS) score 2.0) (5). We administered oral prednisolone 30 mg/day, nicotinic acid amide 1.5 mg/day and doxycycline hydrochloride 200 mg/day. His pruritus and eruption improved, although there was no change in the firm nodules on the trunk and extremities.

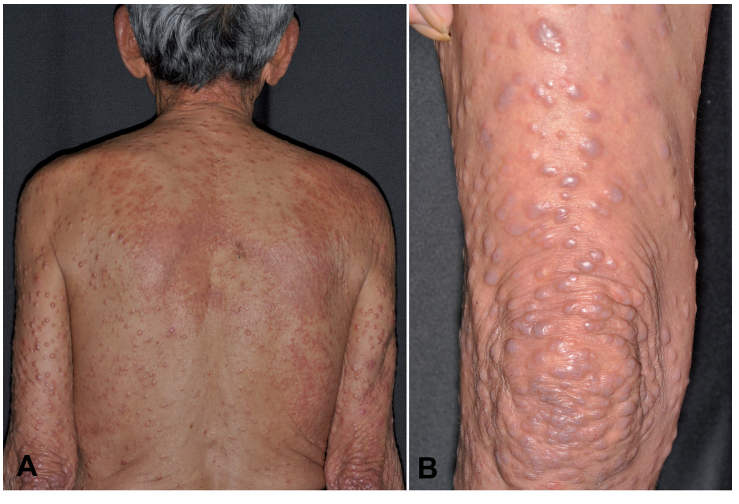

Fig. 1. Erythroderma overlapping with groups of firm nodules on (A) the trunk and (B) extremities.

DISCUSSION

Cutaneous manifestations of myelodysplastic syndrome (MDS) are uncommon and can occur as specific neoplastic infiltrations of malignant hematopoietic cells or various non-specific lesions (3, 4, 6, 7). Among them, granulomatous dermatitis has rarely been reported as a manifestation of MDS (1, 2). Recently, Balin et al. (1) reported a case of granulomatous dermatitis accompanied by MDS, and concluded that granulomatous dermatitis might be the first sign of underlying MDS.

The contribution of an imbalance in T-cell subsets, regulatory T cells (Tregs) and Th17, to MDS has been reported previously (3, 4, 6, 7). In fact, Kordasti et al. (3) reported a significant correlation between increased numbers of $CD4^+$ Tregs and MDS subgroups with disease progression. Moreover, they reported in another study that the Th17:Treg ratio was significantly higher in low-risk MDS compared with high-risk MDS (4). Overall, the prognosis of MDS is strongly correlated with Tregs and Th17. On the other hand, we recently reported the distribution of $Foxp3^+$ Tregs and IL-17-producing cells in several cases of cutaneous granulomatous

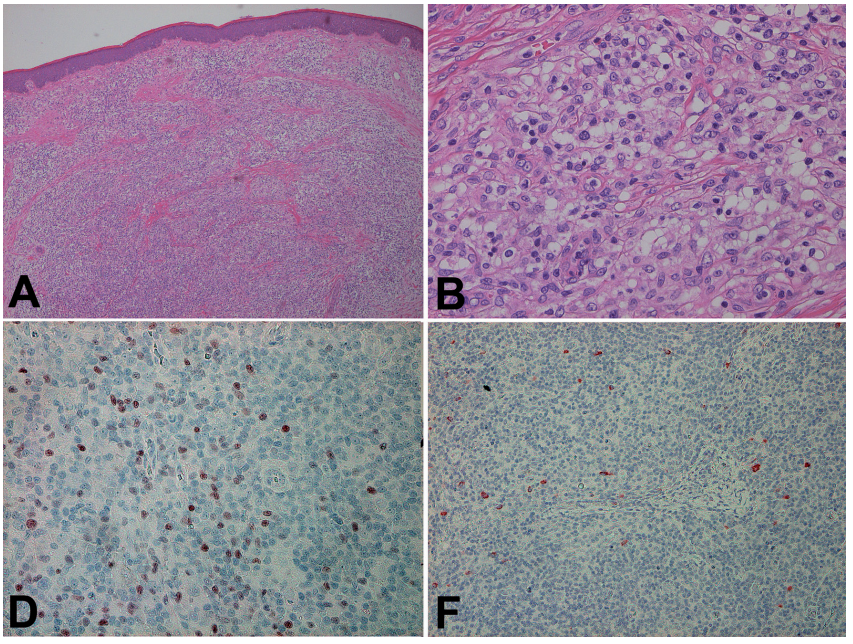

Fig. 2. (A, B) Interstitial, dermal granulomatous inflammation with multinucleated giant cells. The paraffin-embedded tissue sample was deparaffinized and stained using (D) anti-Foxp3 Ab or (F) anti IL-17 Ab. The sections were developed with liquid permanent red. The central area of granuloma is positive for $Foxp3^+$ and negative for $CD163^+$ macrophages. Peripheral areas of granuloma positive for $CD163^+$ macrophages and negative for $Foxp3^+$ Tregs. (Original magnification (A) × 50, (F) × 200, (B) × 400). (Complete figure available from https://doi.org/10.2340/00015555-1656).

dermatitis, including sarcoidosis, granuloma annulare, necrobiosis lipoidica, granulomatous pigmented and purpuric dermatitis (8–10). Therefore, since we hypothesized that our present case, granulomatous dermatitis accompanied by MDS, might show correlations with Tregs and IL-17-producing cells, we employed immunohistochemical staining for Foxp3 and IL-17 to characterize the granuloma. As we expected, based on previous reports (3, 4, 6–10), $Foxp3^+$ Tregs were predominant in the granuloma cells, similar to sarcoidosis, whereas IL-17-producing cells were scattered. In addition, $CD163^+$ M2 macrophages, which are also known to correlate with Th2 and Tregs (11, 12), were detected around the granuloma. Like suppressive macrophages, myeloid-derived suppressor cells in tumour-bearing host (13), these $CD163^+$ M2 macrophages might be related to the induction of Tregs in granuloma. Since we did not directly assess the suppressive function of these infiltrating Tregs and M2 macrophages, further research into the mechanisms underlying this phenomenon may provide fundamental insights into the mechanisms of granulomatous dermatitis with MDS.

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