A Case of Leukemia Cutis Showing Annular Erythema during the Course of Philadelphia Chromosome-Positive Acute B-lymphoblastic Leukemia

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August 3, 2023

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The authors received no financial support for this study.

The authors have no conflicts of interest to declare.

Key words: leukemia cutis, annular erythema, acute B-lymphoblastic leukemia

Key Clinical Message

We report a case of leukemia cutis showing annular erythema during the course of Philadelphia chromosome-positive acute B-lymphoblastic leukemia. The annular appearance may be developed by immunomodulatory effects of blinatumomab.

Introduction

Leukemia cutis (LC) is a cutaneous disease caused by the infiltration of neoplastic leukocytes into the skin. The cutaneous manifestations of LC commonly present as patches of homogeneous erythema, papules, and nodules [1]. Only one case showing annular erythema as LC due to T-cell acute lymphocytic leukemia (T-ALL) has been reported to date [2]. Furthermore, there has been no case showing annular erythema as LC due to B-cell ALL (B-ALL).

Blinatumomab is an antibody drug that mediates the formation of a synapse between T-cells presenting the CD3 antigen and tumor cells presenting the CD19 antigen, resulting in the redirected lysis of CD19-positive B-ALL cells [3]. A phase 2 clinical trial showed that the number of neoplastic leukocytes (tumor cells) decreased below the detection limit within a few days and this effect persisted during the period of blinatumomab treatment [3]. This trial concomitantly demonstrated that the number of cytotoxic T-cells rapidly decreased within 1 day after the administration of blinatumomab and recovered above the base number within 1 week, the so-called redistribution phenomenon [3]. Although immune-modulating drugs, such as blinatumomab, potentially affect the cutaneous manifestations of LC through cytotoxic T-cells, limited information is currently available.

We herein report a case of B-ALL-induced LC with the annular appearance of multiple erythema potentially modified by blinatumomab.

Case report

A 64-year-old man was referred to our Department of Dermatology with a 1-day history of annular erythema on his trunk. The patient was diagnosed with Philadelphia chromosome-positive B-ALL based on the finding of the infiltration of leukemia cells with CD79α, CD10, and terminal deoxynucleotidyl transferase (Tdt) antigens into the bone marrow 9 months previously. The patient was treated with combination chemotherapy consisting of cyclophosphamide, vincristine, doxorubicin, and dexamethasone, resulting in complete remission, followed by consolidation therapy with dasatinib. However, the recurrence of B-ALL was confirmed 5 months previously based on the detection of bcr/abl mRNA of 4,100,000 copies/μg RNA by a real-time polymerase chain reaction. Therefore, the patient was referred to our Department of Oncology/Hematology and was treated with blinatumomab (1 course of 42 days; 9 μg/day on days 1 to 7, 28 μg/day on days 8 to 28, and washout on days 29 to 42).

On day 5 in the 4th course of blinatumomab, the patient developed erythema on his trunk. On day 6, he visited our Department of Dermatology for the eruption and we noted multiple erythema with an annular appearance and ranging in size from 2 to 5 cm in diameter on his trunk (Figure 1). A histopathological examination of erythema showed that mononuclear cells with dense chromatin and mild atypia infiltrated the nucleus around the vessels and adnexa in the dermis and a few mitotic cells were present (Figure 2a and 2b). An immunohistochemical analysis revealed that infiltrating mononuclear cells were reactive to anti-CD79α, CD10, and terminal Tdt antibodies (Figure 2c, 2d, and 2e, respectively), which was compatible with the bone marrow findings observed 9 months previously. Cutaneous manifestations were diagnosed as LC due to B-ALL and disappeared on day 7 in the 4th course, leaving only pale pigmentation when treated with topical corticosteroids.

Discussion

The mechanisms underlying the annular appearance of LC remain unknown; however, an immune reaction against tumor cells may be associated with this phenotype. Previous cases of the skin metastasis of breast cancer showed annular erythema[4-6]. The underlying mechanisms have been explained as follows: i) tumor cell embolization into the blood and lymph vessels result in local blood congestion and edema, leading to patches of homogeneous erythema centered around emboli; ii) emboli consisting of tumor cells are attacked by cytotoxic T-cells and emboli resolve; iii) blood congestion and edema are sequentially released from the center to the edge of erythema, resulting in the development of the annular appearance of erythema. In the present case, blinatumomab, which may cause an immune reaction against tumor cells, was administered. Immunosuppression may have been induced by the rapid decrease in cytotoxic T-cells immediately after the initiation of the 4th course, leading to tumor cell embolization and the development of patches of homogeneous erythema as LC. Immediately after this condition, the number of anti-tumor cytotoxic T-cells may have increased and these cells may have attacked tumor emboli located in the center of LC, resulting in the annular appearance of erythema temporally.

The present case provides evidence to support the potential involvement of immune-modulating drugs in the phenotype of annular erythema through cytotoxic T-cell reactions against tumor cells. Oncologists and

dermatologists need to consider characteristic cutaneous adverse events, particularly in patients treated with immune-modulating drugs.

Acknowledgment: None

Statement of Ethics: The study protocol was approved by The Ethics Committee of The Jikei University School of Medicine and the patient provided written informed consent.

Consent statement: Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Data Availability Statement: Additional data sharing is not applicable to this article due to ethical restrictions.

Author Contributions

Hizuru Tomita: The author contributed to data curation, resources, and drafting the original paper.

Yoshimasa Nobeyama: The author contributed to conceptualization and project administration.

You Sakayori: The author contributed to resources and preparation for paper writing.

Rika Matsumoto: The author contributed to resources and preparation for paper writing.

Satomi Chujo: The author contributed to resources and preparation for paper writing.

Hikaru Suzuki: The author contributed to resources and preparation for paper writing.

Akihiko Asahina: The author contributed to review and supervision.

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Figure legends

Figure 1. Clinical manifestations in the first visit

Erythema of various sizes with an annular appearance are scattered on the trunk.

Figure 2. Histopathological findings of annular erythema

(a) A monotonous dense infiltration is observed around vessels and adnexa in the dermis and subcutaneous tissue (hematoxylin-eosin stain, loupe image). (b) Mononuclear cells with dense chromatin and mild atypia in the nucleus are present. A few mitotic cells are observed (hematoxylin-eosin stain, ×1000). (c, d, e) Immunohistochemical analysis (×400). Infiltrating cells are reactive to the anti-CD79α antibody (c), CD10 (d), and terminal deoxynucleotidyl transferase (e).