



Case Report

Cutaneous Plasmacytosis Complicated with Chronic Lymphocytic Leukemia: A Case Report

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Abstract

In our case, we encountered a patient with a very rare complication who was diagnosed with chronic lymphocytic leukemia (CLL) combined with cutaneous plasmacytosis (C/SP). Cutaneous plasmacytosis is a rare and benign plasma cell proliferative disease, but a few reports suggesting that it has the potential to transform into malignant tumours. However, to date, there have been no reported cases of cutaneous plasmacytosis combined with chronic lymphocytic leukemia. Single cell RNA-seq analysis and clonotype tracking revealed co-expression of IGHV4-34 by malignant B-lymphocytes and monoclonal plasma cells. Interestingly, the presence of IGHV4-34, which is one of the most frequently used genes in CLL patients, has rarely been reported in plasma cell diseases. This indicated that there might be a similarity or homology between the malignant B-lymphocytes and monoclonal plasma cells in this particular patient.

Introduction

Chronic lymphocytic leukemia (CLL) is the most common mature B-cell neoplasm [1]. There have been substantial advances in the field of CLL research in the last decade, including the identification of recurrent mutations, and clarification of clonal architectures, signalling molecules, and the multistep leukemogenic process, providing a comprehensive understanding of CLL pathogenesis [2]. IGHV4-34 is one of the most frequently used genes in CLL patients, which usually display an indolent outcome [3]. C/SP is a rare and benign plasma cell proliferative disease [4,5], but a few reports suggesting that it has the potential to transform into malignant tumours [6,7]. However, to date, there have been no reported cases of C/SP combined with CLL. Here, we reported a patient with a very rare complication who was diagnosed with CLL combined with C/SP. Single cell RNA-seq analysis and clonotype tracking revealed co-expression of IGHV4-34 by malignant B-lymphocytes and monoclonal plasma cells, which indicated there might be a similarity or homology between

the malignant B-lymphocytes and monoclonal plasma cells in the particular patient.

Case Report

A 54-year-old man from southwestern China noticed the rapid growth of reddish-brown rash on his back without any discomfort in 2017 (Figure 1A). In 2020, the patient's rash worsened, accompanied by cervical lymphadenopathy, and he presented to a hospital in southwest China (Chongqing, China). A blood routine examination revealed significant increases in white blood cells and lymphocytes, while a skin biopsy showed infiltration of plasma cells in the dermis. Additionally, lymph node and bone marrow biopsies indicated the presence of malignant monoclonal mature B-lymphocytes. PET-CT scans showed enlarged lymph nodes in the bilateral neck, bilateral armpits and bilateral inguinal area, with increased FDG metabolism. The patient was diagnosed with chronic lymphocytic leukemia and prescribed ibrutinib at a dose of 80-160 mg/day for 12 cycles. After one-year treatment, the patient has achieved complete remission. The bone marrow flow pattern

showed that the residual malignant mature B-lymphocytes had decreased to less than 1%, but there was also infiltration of monoclonal plasma cells. Simultaneously, during the oral administration of ibutinib, the number of brownish-red spots on the skin gradually increased. A follow-up PET-CT scan revealed no significant change in lymphadenopathy compared to the pre-treatment condition, which could not be attributed to chronic lymphocytic leukemia alone. Further skin and lymph node biopsies were performed, revealing plasma cell infiltration (Figure 1B and Figure 1C), leading to the consideration of cutaneous plasmacytosis and chronic lymphocytic leukemia as diagnoses. To explore the relationship between the two diseases in the patient, bone marrow single-cell sequencing was conducted (Figure 2A). The results showed the presence of two groups of malignant B-lymphocytes and monoclonal plasma cells in the patient's bone marrow, with positive IgH and IgK rearrangement. Clonotype tracking revealed co-expression of IGHV4-34 by malignant B-lymphocytes and monoclonal plasma cells (Figure 2B).

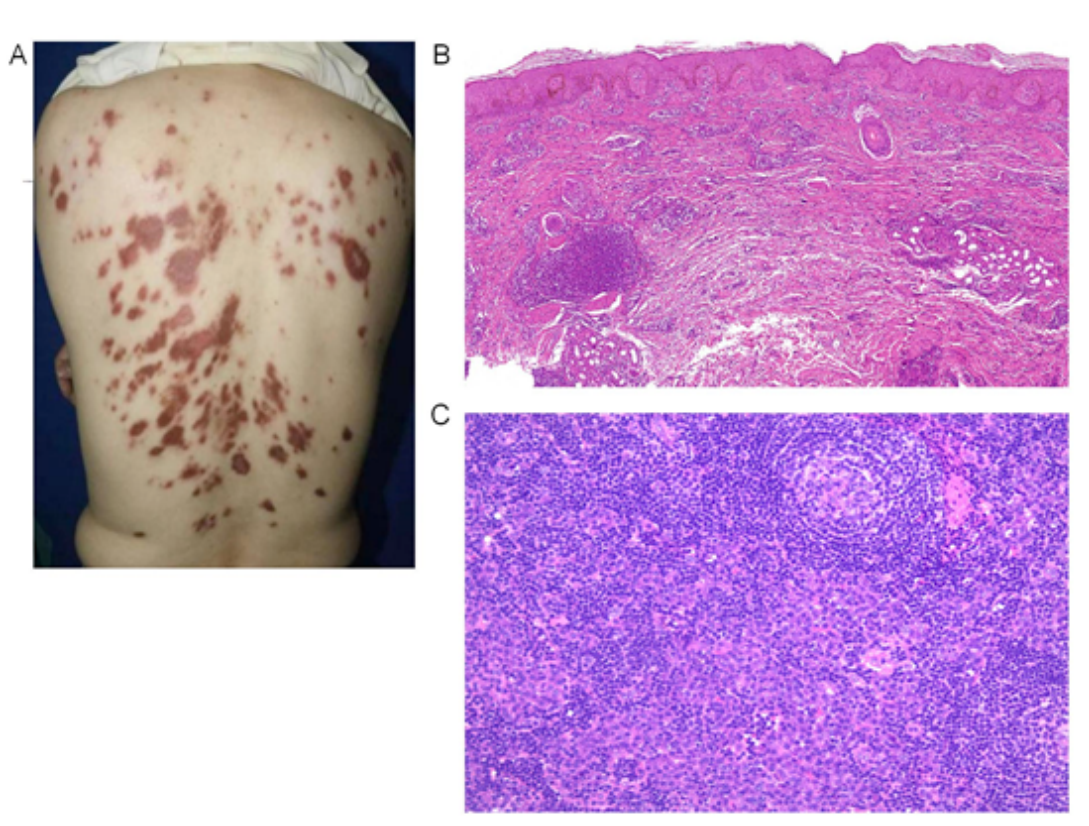


Figure1: Plasma cell infiltration in skin and lymph nodes. (A) General view of the patient's back. (B) Hematoxylin and eosin stain of skin biopsy (B, magnification $\times 20$). (C) Hematoxylin and eosin stain of lymph node (C, magnification $\times 400$).

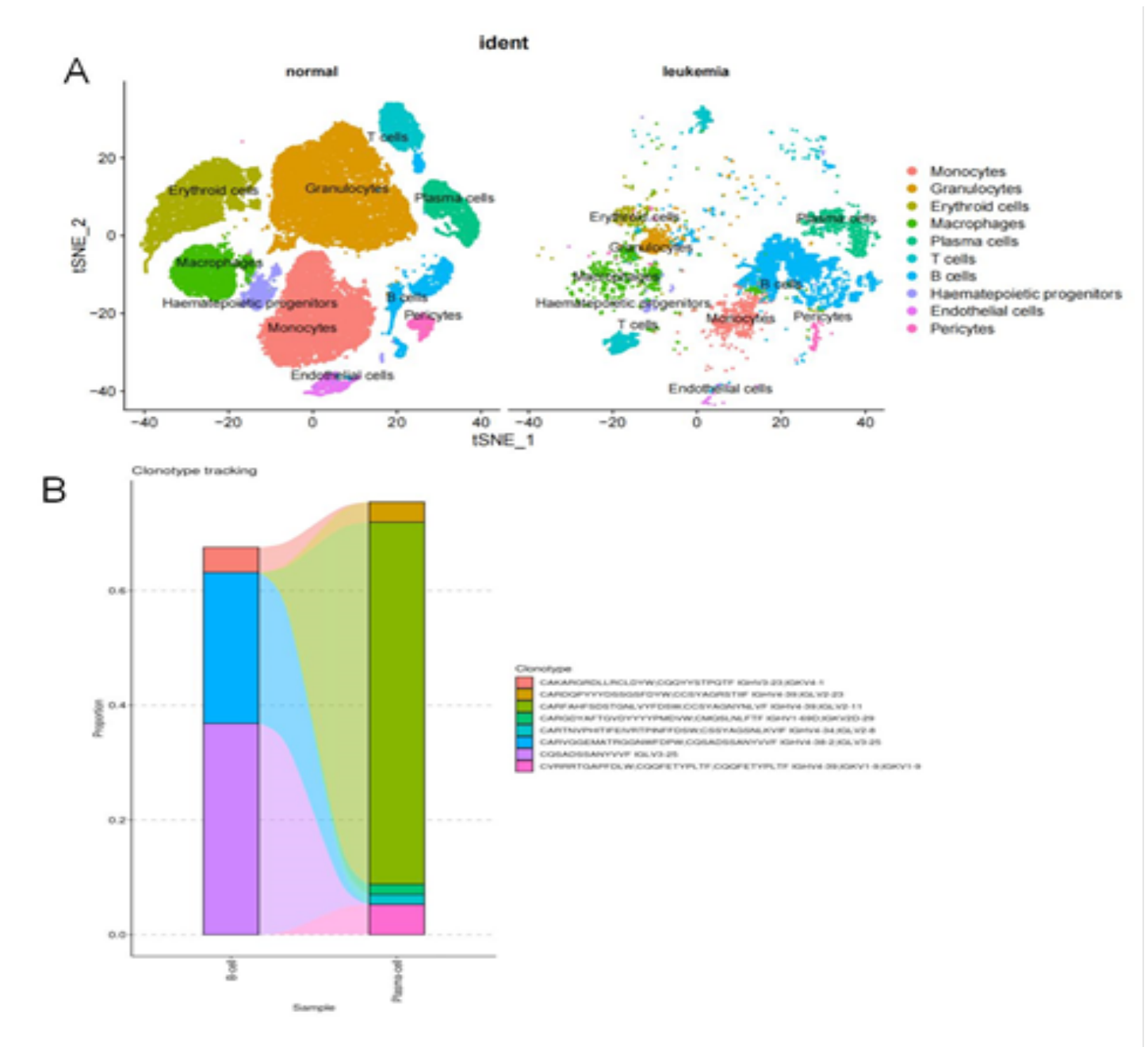


Figure 2: Bone Marrow Single-cell sequencing and B cell receptor Immuno Library Analysis. (A) Bone Marrow Single-cell sequencing. (B) BCR Clonotype tracking analysis.

Discussion

Cutaneous plasmacytosis is a plasma cell disorder characterized by reddish-brown patches, hypergammaglobulinemia and lymphadenopathy [8]. It is exceedingly rare and mostly reported in patients of Japanese and Chinese [9]. Systemic involvement may be manifested by hepatosplenomegaly. Cutaneous plasmacytosis progresses slowly and is reported as a benign disease in most cases. However, patients with systemic involvement may have variable constitutional symptoms such as fatigue, weight loss, and fever [10]. There are few reports the C/SP has the potential to transform into malignant tumors [6-7]. The degree to which C/SP overlaps with other plasma cell proliferative disorders and neoplasms is incompletely understood. Chronic lymphocytic leukaemia is characterised by the clonal proliferation and accumulation of mature and typically CD5-positive B-cells within the blood, bone marrow, lymph nodes, and spleen [11]. The status of the IGHV genes is also associated with survival, such as patients with unmutated IGHV genes have a more aggressive disease course than patients with mutated IGHV genes [12]. A preferential IGHV gene utilization has been revealed in CLL, IGHV4-34 are the most predominant and usually display an indolent outcome [3]. The IGHV4-34 gene encodes germline autoreactive antibodies by recognizing N-acetyllactosamine contained in self and exogenous antigens, as the I/i blood group antigen. It is usually intracellular and expressed in oxidized apoptotic cells, explaining why IGHV4-34 antibodies bind apoptotic B-cells removing cellular debris [13-14]. However, to date, there have been no reported cases of C/SP combined with CLL. In our case, the patient was diagnosed with CLL combined with C/SP. Interestingly, the presence of IGHV4-34, which is one of the most frequently used genes in CLL patients, has rarely been reported in plasma cell diseases. This indicated that there might be a similarity or homology between the malignant B-lymphocytes and monoclonal plasma cells in this particular patient.

Ethics Approval and Consent to Participate: The studies involving human participants were reviewed and approved by Ethics Committee of Southwest Hospital, the First Affiliated Hospital of Third Military Medical University, Chongqing. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

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revised the manuscript. All authors contributed to the article and approved the submitted version.

Data Availability Statement: All data generated and analyzed during this study are included in this published article and its additional file.

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References

1. Hampel PJ, Parikh SA. (2022) Chronic lymphocytic leukemia treatment algorithm 2022. *Blood Cancer J*. 12:161.
2. Kikushige Y. (2020) Pathogenesis of chronic lymphocytic leukemia and the development of novel therapeutic strategies. *J Clin Exp Hematop*. 60:146-158.
3. Stanganelli C, Torres DC, Ortega C, Márquez ME, Remedi V, et al (2022) Somatic hypermutation profiles in stereotyped IGHV4-34 receptors from South American chronic lymphocytic leukemia patients. *Ann Hematol*. 101:341-348.
4. Wagner G, Rose C, Klapper W, Sachse M. (2013) Cutaneous and systemic plasmacytosis[J]. *J DtschDermatol Ges*, 11: 1161-1167.
5. Leonard AL, Meehan SA, Ramsey D, Brown L, Sen F (2007) Cutaneous and systemic plasmacytosis[J]. *J Am Acad Dermatol*, 56:S38-S40.
6. Nitta Y. (1997) Case of malignant lymphoma associated with primary systemic plasmacytosis with polyclonal hypergammaglobulinemia[J]. *Am J Dermatopathol*19:289-93.
7. Turitto G, Tortoriello A, Facchini G, Lombardi R, Moscariello E, et al. (2000) Extramedullary primary cutaneous plasmacytoma. Description of a case[J]. *Recenti Prog Med*. 91:507-10.
8. Han XD, Lee SSJ, Tan SH, Chong W, Ng SK, et al. (2018) Cutaneous plasmacytosis: a clinicopathologic study of a series of cases and their treatment outcomes. *Am J Dermatopathol*. 40:36-42.
9. Wu YH, Liu C, Li Q. (2020) A case of cutaneous plasmacytosis. *Ann Dermatol Venerol*. 147:558-560.
10. Drissi M, Dunlap R, Clayton L, Raess PW, Mengden Koon S, et al (2018) Cutaneous Plasmacytosis and Idiopathic Multicentric Castleman Disease: A Spectrum of Disease? *Am J Dermatopathol*. 44:294-296.
11. Hallek M, Shanafelt TD, Eichhorst B. (2018) Chronic lymphocytic leukaemia. *Lancet*. 391:1524-1537.
12. Damle RN, Wasil T, Fais F, Ghiotto F, Valetto A, (1999) Ig V gene mutation status and CD38 expression as novel prognostic indicators in chronic lymphocytic leukemia. *Blood*. 94:1840-7.
13. Bhat NM, Bieber MM, Chapman CJ, Stevenson FK, Teng NN (1993) Human antilipid A monoclonal antibodies bind to human B cells and the i antigen on cord red blood cells. *J Immunol* 151:5011-5021
14. Smith G, Spellerberg M, Boulton F, Roelcke D, Stevenson F (1995) The immunoglobulin VH gene, VH4-21, specifically encodes autoantibodies against the I or i antigens. *Vox Sang* 68:231-235.