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LETTER TO THE EDITOR

Profuse erythema multiforme induced by chlorambucil

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Dear Editor,

Purine analogs replaced alkylating agents as the standard first-line agents for chronic lymphocytic leukemia (CLL); however, chlorambucil is still being used in some of selected patients, particularly who are not candidates for more aggressive therapies due to poor performance status or co-morbid diseases. Although myelosuppression is being the most common toxicity of chlorambucil therapy, rare but serious complications such as allergic skin reactions may also occur. In this paper, we report a CLL patient who developed profuse erythema multiforme (EM) induced by chlorambucil.

A 69-year-old woman had history of B cell CLL (Rai stage IV) diagnosis since 2002. She did not respond well to fludarabine therapy or to CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). After four cycles of CHOP therapy, the patient developed severe pneumonia. Therefore, CHOP therapy was discontinued. Four months later, during off-therapy, she presented with night sweats, malaise, and progressively increasing white blood cell count (WBC). At that time, her physical examination revealed pale appearance, multiple palpable lymph nodes, splenomegaly (13 cm), and hepatomegaly (5 cm). Peripheral blood picture showed: Hb 9.5 g/dl, WBC 125×10^9/l, and a platelet count of 58×10^9/l. Chlorambucil at a dose of 8 mg/day was commenced. Two weeks later, she was admitted to the hospital complaining of skin eruptions for the last 10 days. There was no preceding history of viral illness or vaccination. Her history revealed that the skin eruptions developed on the fourth day of chlorambucil therapy, which was then discontinued. On physical examination, several target lesions with a central blister and surrounding purplish dark erythema on the face, trunk, and extremities were observed (Fig. 1). Histopathological evaluation of lesions was compatible with EM. Blood cultures for bacteria were negative. Prednisone (1.5 mg/kg/day) was commenced promptly. However, 8 days later, she died due to development of pneumonia before the resolution of her skin lesions.

EM is an acute, self-limited skin disease characterized by the abrupt onset of symmetrical fixed red papules, some of which evolve into target lesions [1]. EM may occur in patients of all ages, particularly in adolescents and young adults [2]. Although many precipitating factors have been defined in EM, viral and bacterial infections and medicaments are the usual culprits. Nonetheless, chlorambucil-associated allergic skin reactions are very rare [3, 4]. Autoimmune disorders are well-known complications of CLL that may be observed either at presentation or during the course of the disease [5]. However, it is most likely that our patient has developed EM induced by chlorambucil, as:

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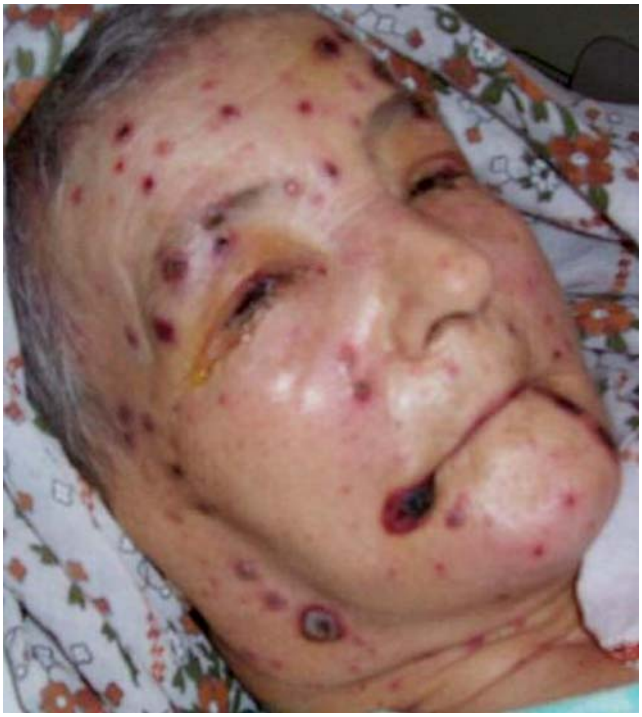

Fig. 1 Multiple typical and raised atypical target lesions in the face with labial and eye involvement

(1) there was no history of previous skin lesions not even with progressive disease, (2) there was no new medication except for chlorambucil, and (3) there was development of skin lesions soon after chlorambucil use.

Chlorambucil that has been used in the treatment of CLL and malign lymphomas is a well-tolerated alkylating agent. Myelosuppression is being the most common side effect. However, EM is rare and may be a life-threatening complication of chlorambucil. These observations should remind physicians about the risk and presenting clinical features of EM who are dealing with patients receiving chlorambucil.

Conflict of interest statement There was no conflict of interest among the authors.

References

1. Weston WL (1996) What is erythema multiforme? Pediatr Ann 25:106–109
2. Fritsch PO, Ruiz-Maldonado R (2003) Erythema multiforme, Steven-Johnson syndrome and toxic epidermal necrolysis. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Katz SJ et al (eds) Fitzpatrick dermatology in general medicine, 6th edn. McGraw-Hill, New York, pp 618–634
3. Libansky J, Trapl J (1960) Chlorambucil in erythrodermia. Lancet 1:732–733
4. Kilickap S, Kurt M, Aksoy S, Erman M, Turker A (2006) Extensive exfoliative dermatitis induced by chlorambucil. Am J Hematol 81:891–892
5. Mauro FR, Foa R, Cerretti R, Giannarelli D, Coluzzi S, Mandelli F, Girelli G (2000) Autoimmune hemolytic anemia in chronic lymphocytic leukemia: clinical, therapeutic, and prognostic features. Blood 95:2786–2792