Anti-Cancer Drugs 1997, 8, pp. 468–469

Case report

Severe adverse skin reaction to chlorambucil in a patient with chronic lymphocytic leukemia

Ismet Aydogdu, Cevher Ozcan, Murat Harputluoglu, Yelda Karincaoglu,[1] Oguz Turhan[2] and Atilla Ozcanu[1]

Departments of Hematology, [1]Dermatology and [2]Pathology, School of Medicine, Inonu University, Turgut Ozal Medical Center, Malatya, Turkey. Fax: (+90) 422 341 0728.

Chlorambucil, an alkylating agent, is used primarily as a daily palliative therapeutic agent for chronic lymphocytic leukemia (CLL) and low-grade non-Hodgkin's lymphomas. The important side effect of a therapeutic dose is depression of bone marrow, and subsequent leukopenia and thrombocytopenia.[1] Reported allergic skin reactions, especially toxic epidermal necrolysis (TEN), due to chlorambucil are rare in the English literature.[2,3] In this brief report, we describe a case of severe cutaneous reaction during treatment of CLL with chlorambucil.

A 60-year-old male was admitted to the hospital with symptoms of anemia and abdominal discomfort. He was diagnosed with B cell CLL 6 years ago. He was treated with chlorambucil, prednisolone and received splenic radiotherapy at the time of diagnosis. He was doing well for 5 years. The patient was suffering from symptoms of anemia and abdominal discomfort due to huge splenomegaly. Blood counts revealed anemia, thrombocytopenia and peripheral lymphocytosis, Rai stage IV. Bone marrow aspirate and trephine biopsy revealed a dense infiltrate of small lymphocytes. Immunophenotyping of peripheral blood mononuclear cells confirmed the diagnosis of B cell CLL. Chlorambucil, 10 mg/daily before breakfast, was started. On day 20 of chlorambucil treatment, he was admitted to hospital again because of the skin lesions. Physical examination revealed diffuse maculopapular erythema with flaccid bullae of skin, and edema of face, legs, neck, scrotum and trunk. He also had fever rising up to 38°C, pharyngitis and conjunctivitis. Blood counts revealed lymphocytosis, eosinophilia, anemia and thrombocytopenia. Skin biopsy was reported as chronic vasculitis. TEN was diagnosed and chlorambucil was stopped. Skin lesions improved within 3 weeks.

The incidence of severe skin lesions due to side effects of drugs such as TEN are very rare, ranging from 0.4 to 1.2 per million per year.[4] The most common drugs involved in this condition are sulfonamides, anticonvulsants, allopurinol and non-steroidal anti-inflammatory agents. TEN is characterized by fever and a diffuse wide-spread macular erythema precedes the formation of large flaccid bullae. Mucosal lesions such as stomatitis, pharyngitis and conjunctivitis are also common.[5] To date, only one case of TEN has been reported due to the use of chlorambucil in a patient with CLL in the English literature.[2] Our patient with CLL is the second case of TEN associated with chlorambucil treatment. Delayed allergic reactions by chlorambucil have also been reported in another patient with CLL.[3] Accurate diagnosis of TEN and cessation of the drug is essential because of a high incidence of mortality.[4,5] Diagnosis must be confirmed by cutaneous biopsy. TEN associated with chlorambucil is a rare syndrome and should be kept in mind in patients with CLL receiving chlorambucil treatment.

Correspondence to I Aydogdu

References

1. Polliack A. *A handbook of essential drugs and regimens in hematological oncology.* Philadelphia, PA: Harwood 1991: 28–9.
2. Pietrantonio F, Moriconi L, Torino F, Romano A, Gargovich A. Unusual reaction to chlorambucil: a case report. *Cancer Lett* 1990; **54**: 109–11.
3. Torricelli R, Kurer SB, Kroner T, Wuthrich B. Delayed allergic reaction to chlorambucil (Leukeran). Case

report and literature review. *Schweiz Med Wochenschr* 1995; **125:** 1870–3.
4. Wolkenstein P, Revuz J. Drug-induced severe skin reactions. Incidence, management and prevention. *Drug Safety* 1995; **13:** 56–68.
5. Hood AF. Cutaneous manifestations of drug reactions. In: Stein JH, ed. *Internal medicine*, 4th edn. St Louis, MO: Mosby 1994: 2547–50.

(Received 21 January 1997; Revised form accepted 18 March 1997)