The prognostic role of CD5 negativity in B-cell chronic lymphocytic leukaemia: a case–control study

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Abstract—B cells in chronic lymphocytic leukaemia (CLL) usually express the CD5 antigen, which appears to participate in the pathogenesis of autoimmune phenomena. However, 7–20% of B-CLL patients are CD5⁻. The aim of this study was to assess whether CD5 expression could be used as a discriminating factor for two subgroups of B-CLL. Twenty-nine CD5⁻ B-CLL patients were compared in terms of clinico-biological characteristics and survival with a control group of 29 sex- and age-matched, consecutive CD5⁺ B-CLL subjects. B-CLL was considered to be CD5⁻ when less than 5% of mononuclear cells expressed CD5 after subtraction of the number of T cells. Splenomegaly, lymph node involvement, and haemolytic anemia were found in CD5⁻ patients in a significantly higher proportion than in their CD5⁺ counterparts, who presented with an earlier stage of disease. CD5⁻ patients had a median survival of 97.2 (22–130) months, exceeding CD5⁺ patients significantly [84.0 (19–120) months, \( p = 0.0025 \)]. CD5⁻ patients seemingly present with milder disease and have a favourable prognosis compared with the vast majority of B-CLL patients who express CD5.

Key words: CD5; chronic lymphocytic leukaemia; prognosis.

INTRODUCTION

Chronic lymphocytic leukaemia (CLL) is the most common form of adult leukaemia in Western countries. It is usually defined as a proliferation of mature lymphocytes with an absolute, sustained for at least 4 weeks, peripheral blood lymphocyte count

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of more than $10 \times 10^9$ per litre, marrow involvement by at least 30% of lymphocytes, and a majority of peripheral blood lymphocytes with B-cell markers [1].

In 95% of cases, CLL develops from the malignant transformation of a single B lymphocyte and its clonal expansion; in less than 5% of cases, it involves T lymphocytes [2]. CLL cells usually express a low level of surface immunoglobulin (S-Ig) and are positive for CD19, CD20, CD5, and CD23. A unique property of CLL B-cells is the presence of the CD5 molecule. This antigen is a 67 kD membrane glycoprotein, which is present on the surface of normal T-lymphocytes. However, a subgroup of B lymphocytes expressing CD5 was isolated on 1–7% of the peripheral lymphocytes of normal adults, whereas CD5$^+$ cells are the predominant B-cell subset (40–60%) in fetal human tissues and have been shown to produce polyreactive antibodies of the Ig-M type that seem to be protective against infections [3, 4]. Several of these antibodies were described as having autoreactivity and the increased number of CD5$^+$ B cells found in patients with rheumatoid arthritis, systemic lupus erythematosus, and after allogeneic bone marrow transplantation suggested a possible involvement of CD5$^+$ B cells in the pathophysiology of these disorders. Although the role and origin of CD5$^+$ B cells remain controversial, they may well participate in the pathogenesis of autoimmune phenomena in CLL [5].

Of all cases of CLL, the incidence of CD5$^-$ B-CLL varies from 7% to 20% [5]. In this article, we report a series of 29 cases of CD5$^-$ B-CLL and compare their clinical, biological, and prognostic characteristics with a control group of 29 cases of CD5$^+$ B-CLL.

PATIENTS AND METHODS

Study design and data collection

In this prospective study, B-CLL patients were recruited from January 1990 through January 1998 from the Haematology Unit of the Third University Department of Medicine, Sotiria General Hospital, Athens, Greece. Twenty-nine CD5$^-$ patients were enrolled during this period. Eligible controls were 29 newly diagnosed, uns-screened with regard to tumour burden, CD5$^+$ B-CLL patients, matched by sex and age in 5-year bands. Control patients entered the study consecutively, according to the time of diagnosis, in order to avoid selection bias. At the same time, the overall B-CLL population in the department mentioned-above consisted of 175 patients, CD5$^-$ subjects accounting for 16.5% of cases. Study participants were followed until January 2002. Diagnosis was established according to the International Workshop recommendations (IW-CLL). Tumour burden was estimated by physical examination, chest X-ray, and abdominal CT scan. Classification at diagnosis was made according to the Binet and Rai staging systems. The two groups were compared in terms of clinical, laboratory, and immunophenotyping parameters, and survival.