

## Diagnosis and treatment of chronic lymphocytic leukaemia: practical remarks

Commentary on

### Graves' thyrotoxicosis in a patient with metastatic differentiated thyroid carcinoma and chronic lymphocytic leukaemia (CLL)

Jacek Makarewicz, Sławomir Mikosiński, Antoni Rutkowski, Zbigniew Adamczewski, Andrzej Lewiński

*Arch Med Sci* 2007; 3, 2: 179-84

---

Lukas Smolej

2<sup>nd</sup> Department of Internal Medicine, Department of Clinical Haematology, University Hospital and Medical School, Hradec Kralove, Czech Republic

**Submitted:** 13 November 2007

**Accepted:** 7 December 2007

*Arch Med Sci* 2007; 3, 4: 407-408  
Copyright © 2007 Termedia & Banach

**Corresponding author:**

Lukas Smolej, MD  
2<sup>nd</sup> Department of Internal Medicine  
Department of Clinical Haematology  
University Hospital and Medical School  
Sokolska 581, Hradec Kralove  
500 05, Czech Republic  
Phone: +42 077 670 49 87  
Fax: +42 049 583 20 11  
E-mail: smolej@seznam.cz

Dr Makarewicz et al. recently published an interesting case report on autoimmune thyrotoxicosis and metastatic thyroid carcinoma in a chronic lymphocytic leukaemia (CLL) patient [1]. From a haematologist's point of view I would like to comment on several aspects regarding the diagnosis and management of CLL. Firstly, diagnosis of CLL should not be made on the basis of plain cytology (irrespective of peripheral blood or bone marrow) because it is not possible to cytologically distinguish other lymphoproliferative disorders such as disseminated follicular lymphoma, mantle cell lymphoma or splenic lymphoma with villous lymphocytes with 100% certainty. Therefore, internationally accepted diagnostic criteria for CLL require not only absolute lymphocytosis of  $5 \times 10^9/l$  but also the characteristic immunophenotype of malignant cells ( $CD5^+/19^+/23^+/sIg^{low}$ ) obtained by flow cytometry [2]. On the other hand, examination of bone marrow is not routinely required for diagnosis of CLL. Secondly, steroids are not recommended as the treatment of choice in CLL unless autoimmune haemolytic anaemia or autoimmune thrombocytopenia is present [3]. In order to determine the cause of thrombocytopenia, the patient should have HAD bone marrow cytology or biopsy. In the case of autoimmune anaemia or thrombocytopenia, the recommended dose of steroids is 1 mg/kg [4]; if thrombocytopenia results from marked bone marrow infiltration, the patient should receive either chlorambucil (reserved for elderly or severely comorbid patients) or a combination protocol based on purine analogues such as fludarabine or cladribine (particularly popular in Poland) used in younger and fit patients [5]. Thirdly, CLL was historically not considered to be associated with radiation (as the authors state). However, several studies have recently shown increased incidence of CLL among nuclear facility workers, uranium miners and victims of the Chernobyl disaster [6-8]. Lastly, CLL is due to complex immune derangement associated not only with autoimmune phenomena and diseases but also with increased incidence of various secondary malignancies [9]. As the majority of CLL patients are nowadays diagnosed

due to the incidental finding of leukocytosis (during routine check-ups, before operations, etc.) during the asymptomatic phase of the disease (which may actually last dozens of years), one may speculate that the patient has already had CLL for some time before the actual diagnosis and that immunosuppression caused by a CLL clone may have led to the development of thyroid carcinoma.

## References

1. Makarewicz J, Mikosiński S, Rutkowski A, Adamczewski Z, Lewiński A. Graves' thyrotoxicosis in a patient with metastatic differentiated thyroid carcinoma and chronic lymphocytic leukaemia (CLL). *Arch Med Sci* 2007; 3: 179-84.
2. Cheson BD, Bennett JM, Grever M, et al. National Cancer Institute-sponsored Working Group guidelines for chronic lymphocytic leukemia: revised guidelines for diagnosis and treatment. *Blood* 1996; 87: 4990-7.
3. Oscier D, Fegan C, Hillmen P, et al. Guidelines on the diagnosis and management of chronic lymphocytic leukaemia. *Br J Haematol* 2004; 125: 294-317.
4. Hallek M. Chronic Lymphocytic Leukemia (CLL): First-Line Treatment. *Hematology Am Soc Hematol Educ Program* 2005; 285-91.
5. Diehl LF, Ketchum LH. Autoimmune disease and chronic lymphocytic leukemia: autoimmune hemolytic anemia, pure red cell aplasia, and autoimmune thrombocytopenia. *Semin Oncol* 1998; 25: 80-97.
6. Schubauer-Berigan MK, Daniels RD, Fleming DA, et al. Chronic lymphocytic leukaemia and radiation: findings among workers at five US nuclear facilities and a review of the recent literature. *Br J Haematol* 2007; 139: 799-808.
7. Abramenko I, Bilous N, Chumak A, et al. Chronic lymphocytic leukemia patients exposed to ionizing radiation due to the Chernobyl NPP accident-With focus on immunoglobulin heavy chain gene analysis. *Leuk Res* 2007; Sep 24 [Epub ahead of print].
8. Rericha V, Kulich M, Rericha R, Shore DL, Sandler DP. Incidence of leukemia, lymphoma, and multiple myeloma in Czech uranium miners: a case-cohort study. *Environ Health Perspect* 2006; 114: 818-22.
9. Robak T. Second malignancies and Richter's syndrome in patients with chronic lymphocytic leukemia. *Hematology* 2004; 9: 387-400.