Simultaneous Occurrence of Chronic Lymphocytic and Chronic Myeloid Leukemia

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ABSTRACT

The coexistence of chronic lymphocytic (CLL) and chronic myeloid leukemia (CML) in the same patient has only been reported occasionally. Most of these cases represent the patients who developed CLL during the course of CML. Reviewing the literature, only a few cases of simultaneous occurrence of CLL and CML were found. Here we represent a previously healthy 50-year old man in whom the diagnosis of CLL and CML was established by FNAB of the bone marrow. The diagnosis was then confirmed by histopathology, immunophenotypization of the peripheral blood and by a cytogenetic study of the bone marrow. Four years after the diagnosis the patient is well, with leucocytosis of 40×10⁹/L, and lymphocytosis of 93%.

Key words: chronic lymphocytic leukemia, chronic myeloid leukemia, simultaneous occurrence

Introduction

The coexistence of chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) in the same patient is very rare. Most of these cases represent the patients who developed chronic lymphoid leukemia (CLL) during the course of chronic myeloid leukemia (CML), so the leukemogenic effect of the therapy claimed as a possible risk factor for second malignancy¹–¹³. The impaired immune response associated with CLL could also contribute to the increased risk of second neoplasia, but CLL patients mostly develop non-Hodgkin lymphoma and solid tumors and rarely acute myeloid leukemia, myelodysplastic syndromes and CML¹⁴. Reviewing the literature, only a few cases of CLL and CML were found¹,⁵,⁶,⁸,⁹. Here we represent a patient with a simultaneous occurrence of CLL and CML. The diagnosis was established by FNA of the bone marrow and was confirmed by histopathology, immunophenotypization of the peripheral blood and by a cytogenetic study of the bone marrow.

Case Report

A previously healthy 50-year old man was referred to our clinic after the discovery of leucocytosis and thrombocytosis. Physical examination was normal, without any lymphadenopathy or hepatosplenomegaly. The hemoglobin (Hb) was 166g/L, white blood cell count (WBC) 17×10⁹/L (neutrophils 49%, eosinophils 2%, basophils 1%, lymphocytes 45% and monocytes 3%, with numerous «smudge cells»), and platelet count (Plt) 720×10⁹/L. The serum lactat dehydrogenase (LDH) level was 198 U/L (norm. 114–241 U/L). The bone marrow aspirate was hypercellular, with abundant thrombopoiesis, a few micromegakaryocytes, and platelets in clusters. There were also a slightly increased number of mature eosinophilic forms (Figure 1). The number of lymphocytes was increased (28–33% of all cells) (Figure 2). The cytological diagnosis was myeloid and lymphoproliferative disease. The bone marrow biopsy was performed, and revealed as well a hypercellular bone marrow aspirate with an increased number of eosinophils and large, hyperlobulated megakaryocytes. Some small lymphoid nodules and interstitial accumulation of lymphocytes were also found, so the diagnosis was chronic lymphocytic and chronic myeloid leukemia. The cytogenetic study of the bone marrow made by FISH showed the Ph chromosome, and PCR of the bone marrow revealed the clonal rearrangement of gene for immunoglobulin heavy chain (IgH). Immunophenotypization of peripheral blood lymphocytes demonstrated the expression of mature B-cell markers (CD19, CD20, CD23) and also CD5 positive cells. A year after the...
diagnosis the WBC was 24×10⁹/L and Plt were 1007×10⁹/L, so hydroxyurea was introduced in the therapy and six months later also was imatinib mesylate. After 6 months of the imatinib mesylate therapy, control cytogenetic FISH and molecular RT-PCR analyses were done and Ph chromosome and bcr/abl transcript were negative. Four years after the diagnosis, the patient is well, without lymphadenopathy and splenomegaly. The WBC is 40×10⁹/L and lymphocytosis is 93%. Interesting is, that a year after the diagnosis, the patient’s father also developed CLL.

Discussion

Sequential and simultaneous occurrence of CLL and CML has been reported only occasionally. The coexistence of these two hematologic malignancies leads to some questions about their cell of origin. The CML and CLL association might be explained that both diseases originate from a unique stem cell capable of differentiating into two different cell lines. However, some studies⁶,⁷,⁸,¹⁵ results demonstrated independent bi-clonal evolution of these two diseases and a different origin of CLL and CML leukemic cells. Zollino et al.⁷ analyzed, in a patient with CML following CLL, the expression of molecular markers specific for CLL and CML proliferation, (bcr/abl rearrangement for CML and J segment of heavy chain immunoglobulin (JH) for CLL). They detected bcr/abl rearrangement in the granulocytic, but not in the mononuclear cell fraction, probably composed mainly of CLL cells. On the contrary, they observed by JH rearrangement analysis a characteristic JH band corresponding to a monoclonal lymphoid population in the lymphoid-enriched but not in the myeloid blood fraction. There is also a case¹⁶ of a patient who developed CLL some years after the diagnosis of CML with a molecular data documenting a separate clonal origin. In the reported patient a population of clonal CD19+ B cells was detected, without an expression of bcr/abl, and bcr/abl positive CML clone was also found in the granulocyte and mononuclear cell fractions. The documented data indicate that CLL leukemic cells developed from other different cell than a CML pluripotent progenitor cell. One of the bcr/abl negative mature B cell clone was transformed resulting in clonal lymphoid proliferation and a subsequent development of CLL. Esteve et al.¹⁷ showed a patient with a coexistent CML and early stage CLL, who further developed B-lineage lymphoid blast crisis. The analysis of JH rearrangement pattern of sequential samples supports the origin of the diseases in two different cell clones. Moreover, «our patient’s» father developed CLL, implicating that the two malignant diseases, as well as the familial occurrence of the same disease, may be associated with genetic factors. Thus, Capablo S. et al.¹⁸ also found a high prevalence of CLL in the relatives of CLL patients.

In conclusion, the report of our patient with a simultaneous occurrence of CML and CLL contribute to other similar reports pointing to an increased risk for the secondary hematological malignancy in patients with the diagnosis of a hematoproliferative disease and many possible risk factors (cytostatic therapy, impaired immune response, genetic factors, etc) that may be involved in its occurrence. Immunophenotypic, cytogenetic and molecular analysis in most patients with the simultaneous or the subsequential CML and CLL revealed a rare event of hematologic leukemogenesis caused by the independent bi-clonal evolution. Our report points also to the importance of FNA diagnostics because the diagnosis of a simultaneous appearance of two hematological diseases was established by FNA of the bone marrow and confirmed afterwards by histopathology, cytogenetic and immunophenotypization of the bone marrow and peripheral blood.
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SIMULUTANA POJAVA KRONIČNE LIMFATIČNE I KRONIČNE MIJELOIČNE LEUKEMIJE U ISTOG PACIJENTA

SAŽETAK

Postojanje kronične limfatične (CLL) i kronične mijeloične leukemije (CML) u istog pacijenta vrlo je rijetka pojava. U većine bolesnika s te dvije hematološke bolesti, CLL se javlja nakon dijagnoze CML-a. U literaturi je opisano nekoliko bolesnika u kojih je dijagnosticirana CLL i CML i tek nekoliko s istovremenom pojavom obje navedene bolesti. U ovom je radu prikazan 50-godišnji pacijent koji je prethodno bio zdrav i u kojeg je dijagnoza CLL i CML postavljena citološkom punkcijom koštane srži, a potvrđena biopsijom i citogenetskom analizom koštane srži i imunofenotipizacijom limfocita periferne krvi. Četiri godine nakon postavljanja dijagnoze, pacijent je dobro s leukocitozom 40–10^9/L i limfocitozom od 93% u diferencijalnoj krvnoj slici.