Case report/Kazuistyka

Hairy cell leukemia and multiple myeloma: Two distinct entities or a single two-phase disease

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ABSTRACT

Hairy cell leukemia (HCL) and multiple myeloma (MM) originate from mature B-cell and they are characterized by different clinical symptoms and treatment. Their clinical outcome is also different. The introduction of 2-CdA makes HCL a potentially curable disease, but MM still remains incurable despite a therapeutic progress made in the recent years. We report a male patient who simultaneously developed HCL and MM. He was treated with combined therapy including 2-CdA and thalidomide and this approach resulted in complete remission (CR) of HCL and partial response (PR) of his MM. This patient continued MM treatment with CTD regimen (cyclophosphamide, dexamethasone, thalidomide) and he achieved >90% reduction of serum monoclonal protein. The attempt of stem cell collection failed and autologous transplantation has not been performed. Currently, one year off therapy he is remaining in very good PR of his MM and in CR of HCL. The possible explanations for the development of these two disorders have been discussed.

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Introduction

Hairy cell leukemia (HCL) and multiple myeloma (MM) are malignancies of B-cell origin [1, 2]. Although these hematologic malignancies originate from mature B-cell, they are characterized by different clinical symptoms and therapeutic approach [3, 4]. Typical manifestation of HCL includes pancytopenia, splenomegaly and presence of “hairy” lymphocytes in peripheral blood [1], whereas MM characterizes the overproduction of monoclonal protein, the presence of an increased number of plasma cells in bone marrow, bone lesions, and renal failure [2]. Their clinical outcome also varies. The introduction of 2-CdA makes HCL a potentially curable disease [3, 5, 6], but MM still remains incurable disorder despite a huge progress in the therapeutic approach seen in the recent years [4]. Herein we report a male with simultaneous occurrence of HCL and MM.

Case description

68-year-old male without any significant medical history was admitted to our Department in March 2011 because of accidentally found mild pancytopenia. He complained...
of easy fatigue. On admission physical examination revealed only paleness. The abdominal ultrasound examination showed hepatomegaly (AP diameter was 161 mm) and splenomegaly (longest diameter was 125 mm), without intra-abdominal lymphadenopathy. The X-ray skeletal survey disclosed generalized osteopenia, scoliosis and cervical, thoracic and lumbar discopathy. Full blood test showed pancytopenia. White blood cell (WBC) count was 1.9 × 10⁹/L with a predominance of small lymphocytes (1.14 × 10⁹/L). A small number of villous lymphocytes (0.3 × 10⁹/L) was found in differential. Hemoglobin (Hgb) concentration was 10.8 g/dL, and platelet count was 128 × 10⁹/L. Biochemistry was within normal range. Protein tests disclosed an increased IgG concentration (IgG = 22 g/L; normal range: 7–16 g/L), decreased IgA (IgA = 2.1; normal range: 0.7–4.0) and normal IgM concentration. An increased free light chains lambda (FLC λ = 80 mg/L; normal range: 5.7–26.3 mg/L) concentration, with an impaired free light chains ratio (FLC α/λ = 19; normal range 0.26–1.65) was also observed. A peak of monoclonal protein in gamma fraction of electrophoresis was detected and serum immunofixation confirmed the presence of IgG lambda monoclonal protein. Serum beta-2-microglobulin was within normal range and albumin concentration was decreased. 24-h proteinuria was absent. Bone marrow was occupied by plasma cells in 19%, and by lymphocytes in 22.5% – some of these cells had “hairy-like” cytoplasm projections. Immunophenotyping of these cells revealed the presence of two cell clones: 1) CD38+, CD138+, CD117+, s + α+ (11%) and 2) CD45+, CD19+, CD11c+, CD25+, CD103+/-, CD123+, CD24+/- (30%). This finding was consistent with coincidence of MM and HCL. Cytogenetic examination as well as fluorescence in situ hybridization (FISH) did not detect any abnormalities. MM stage was established to be IIB according to Durie-Salmon, and International Scoring System (ISS) was found to be 2. Patient was started with CC (2-CdA, Cyclophosphamide) regimen plus thalidomide at 100 mg daily a la longue. After 6 cycles of CC, he achieved a complete remission (CR) of HCL and there was only a small number of clonal plasma cells on flow cytometry (0.39%) and there was partial response (PR) according International Myeloma Working Group (IMWG) classification of his MM (>50% of M protein). Subsequently CD (cyclophosphamide, dexamethasone) was added. In total, he received 4 cycles of CTD which resulted in very good PR. He attempted to collect stem cells for autologous transplantation, but it failed. Currently, one year off therapy he is remaining in CR of HCL and in very good PR of his MM.

Discussion

MM and HCL are classified by World Health Organization (WHO) classification as mature B-cell neoplasms. They account for 10–15% of hematological malignancies and 2% of lymphoid leukemias, respectively [1, 2]. Coincidence of MM and HCL has rarely been reported so far [7, 8]. It could be suspected that these neoplasms originate from a single malignant cell clone. The study of 22 HCL patients in whose a phenotype and function of hairy cells have been evaluated, seems to confirm that hairy cells express B-cell restricted antigens (B4 and B1), plasma-cell associated PCA-1 antigen with the lack of IgD and B2, and this is typical for early B-cells. This finding may show the phenotypic similarities between hairy cells and pre-plasma cells and indicate the possibility of their common origin [9]. In regards to other malignancies, it was shown that chronic lymphocytic leukemia (CLL) cells induced by phorbol ester had the same morphology and cell-membrane-antigens, as HCL cells [10]. However, there was no similar observation regarding MM and HCL. The presence of the same light chain type on the surface of HCL cells in a patient with prior CLL may also point out the common origin of these two malignancies [11]. The transformation of large B-cell lymphoma (LBL) from HCL was also reported. It was explained by the presence of HCL-derived antigens (CD11c/CD22, CD25, CD103, FMC-7), strong tartrate-resistant acid phosphatase staining, and increase of Ki-67 expression on LBL cells [12]. On the other hand, some experts highlighted the development of a secondary malignancy instead of their joint root. This statement was supported by the presence of different heavy- and light-chain gene rearrangements in these entities [13]. It should be underlined that secondary neoplasms both in HCL [14] and in MM [15] were reported. Patients with MM are statistically more likely to develop melanoma, thyroid and urinary tract cancers, as well as hematological malignancies. Among hematological neoplasms the occurrence of acute leukemia, especially acute myeloid leukemia (AML) is the most frequent. Younger patients are more prone to suffer from AML than older [16]. However, patients with HCL if compared with a general population have an increased risk of Hodgkin and non-Hodgkin lymphomas, as well as thyroid cancers [17]. It was demonstrated that the occurrence of additional clonal populations in HCL increases during the course of disease [18]. It should be emphasized that impairment of immune system may correlate with an increased tendency to development of secondary neoplasms [19].

Both MM and HCL vary in treatment approach. “Wait and watch” strategy should be incorporated in patients with stable blood results [3, 4]. The presence of anemia, hepatosplenomegaly and general symptoms remain an indication for chemotherapy initiation. Our patient was started with 6 cycles of CC regimen and achieved CR of HCL. It was shown that use of 2-CdA in HCL results in a high percentage of long-lasting overall and complete response [6]. That data make 2-CdA-based regimens the therapy of choice in HCL [20]. It should be emphasized that even patients who relapsed after initial effective treatment could achieve complete or PR after repeated courses of 2-CdA [21]. 2-CdA-based therapy combined with thalidomide benefited in PR of MM. That may be explained by the observation that 2-CdA may impede cell proliferation and stimulates apoptosis of myeloma cells [22].

Authors’ contributions/Wkład autorów

KWP, GH – study design, data collection and interpretation, manuscript preparation, literature search. KW – data collection and interpretation. SKK – manuscript preparation. JDS – literature search.
Conflicts of interest/Finansowania

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Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES/PIŚMIENNICTWO