case report

Coexistence of chronic lymphocytic leukemia and polycythemia vera: a case report and review of the literature

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Polycythemia vera is a Philadelphia chromosome-negative myeloproliferative neoplasm. Chronic lymphocytic leukemia is a monoclonal expansion of a CD5+ CD19+ B lymphocytes. Chronic myeloproliferative neoplasms may coexist with indolent B-cell malignant lymphomas of various types. The association of chronic lymphocytic leukemia with polycythemia vera is a rare event with only a few cases of coexistence ever reported. We report a 56-year-old man in whom these two disorders were diagnosed concomitantly. Possible etiopathogenic relationships between both disorders are discussed in this case report.

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Polycythemia vera (PV) is a Philadelphia chromosome-negative myeloproliferative neoplasm (MPN), according to the 2008 World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues.[1] Chronic lymphocytic leukemia (CLL) is a monoclonal expansion of a CD5+ CD19+ B lymphocytes expressing a unique antibody or B-cell antigen receptor (BCR). The association of CLL with PV is a rare event with coexistence reported in only a few patients.[2] We report a 56-year-old man in whom these two disorders were diagnosed concomitantly on the basis of peripheral blood count, cytology, and immunophenotyping, as well as exclusion criteria. Possible etiopathogenic relationships between both disorders are discussed.

CASE

A 56-year-old man presented with painful burning on both footpads for 2 months. On physical examination, plethora was evident, there was no lymphadenopathy; the liver and spleen were not enlarged. His medical history contained no abnormalities. Results of laboratory investigations on admission were as follows: elevated white blood cell (WBC) count up to 28.3×10^9/L, platelet (PLT) count up to 937×10^9/L, and elevated hemoglobin (Hgb) count up to 17.5 g/dL, with hematocrit as 57%. The circulating neutrophil and lymphocyte percentages were 89% and 11%, respectively, on peripheral blood smear. The other laboratory test results showed an elevation in potassium levels up to 5.8 mg/dL (Normal ranges for potassium; 3.5 - 5.1 mg/dL), and lactate dehydrogenase (LDH) up to 306 IU/L. Abdominal ultrasound scan and chest X-ray did not reveal any significant pathologies. Erythrocyte sedimentation rate (ESR) was 1 mm/h (range; 0-20 mm/hour) and C-reactive protein (CRP) was 3 mg/L (range; 0-5 mg/L). The peripheral venous blood was used to detect a JAK2V617F mutation. Its percentage was of 60% by RT-PCR technique, which did not reveal the bcr/abl fusion gene. The bone marrow (BM) findings were as follows: the cellularity was 60%, erythroid hyperplasia was prominent with a slight granulocytic hyperplasia, no dysplastic changes and no increase in blasts were noted; increased numbers of megakaryocytes were seen, and reticulin fibrosis was normal, so the net result was panmyelosis. The erythropoietin level was 2 mLU/mL, which was reduced below the normal range (normal range: 2.59-18.5 mLU/mL). The patient was diagnosed as having PV based on

the WHO criteria.[1] The patient was started on hydroxyurea 2 g/day (per oral), aspirin 100 mg/day (per oral), allopurinol once a day (per oral), and normalization of the peripheral blood count was achieved after 2 months. At 3 months, on his third visit, hemogram parameters were as follows: hemoglobin concentration 14.3 g/dL, hematocrit 43%, WBC 14.1×10^9/L, PLT 307×10^9/L, reticulocyte count of 1.22%. Biochemistry showed that normal potassium concentration of 4.5 mg/dL, and normal LDH activity (205 IU/L), and direct and indirect Coombs tests were negative. Serum iron level, iron binding capacity, and coagulation parameters were within normal ranges. The circulating lymphocyte percentage was 78% on peripheral blood smear. Review of the peripheral blood smear showed an increased number of typical small lymphocytes with spherical nuclei, coarse chromatin, and scanty cytoplasm; smear cells were also seen. Flow cytometry confirmed the diagnosis of CLL [65% of CD5/CD19 (+) cells displaying the following phenotype: CD20/CD22 (-), CD23 (+), FMC7 (-), with kappa monoclonality. Cytogenetic analysis of the BM revealed a normal karyotype. The typical characteristics of BCLL, such as trisomy 12 and the deletions of 11q22.3, 13q14 and 17p13, were not detectable by fluorescent in situ hybridization. The patient was diagnosed with coexisting B cell CLL Rai '0' Binet A according to the WHO and International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria.[3] A quantitative immunoglobulin test revealed a normal IgG, IgM and IgA concentrations. The "watch and wait" strategy was applied to CLL. The patient was observed in our outpatient clinic and 3 months later his general condition was fine, erythromelalgia was lost and his laboratory investigations were in the normal range (hydroxyurea dose was reduced to 1 g/day). His CLL was still in the indolent phase and was being monitored without therapeutic intervention at the follow-up visit.

DISCUSSION

Chronic myeloproliferative neoplasms (MPNs) may coexist with indolent B-cell malignant lymphomas of various types. This coexistence of MPNs and CLL is much less common than with other neoplasms, especially solid cancers. As of the date of this publication, only 28 JAK2 V617F-positive BCLL patients have been identified.[4] All of these patients exhibited a Ph negative MPN concomitantly. Although the coexistence of CLL and MPN has been only sporadically reported, a systematic study on this disease association has been published by Italian GIMEMA group.[5] They retrospectively analyzed 46 patients affected by CLL/MPN. MPN consisted of essential thrombocythemia in 18 cases, polycythemia vera in 10 cases, chronic myeloid leukemia in 9 cases, primary myelofibrosis in 6 cases, and MPN/myelodysplastic syndrome in 3 cases.[5] They concluded that the diagnosis of concomitant CLL/MPN is a rare event and lymphoproliferative disorders present a clinical indolent course with a low-risk biological profile. MPN therapy does not interfere with the prognosis of patients with CLL.[5] Possible pathogenetic mechanisms might include independent proliferation of two distinct cell lines,[6] bilineage development of a common pluripotent stem cell proliferation, or an accidental situation.[7] Vannuchi et al (2009) concluded that the risk of secondary lymphoproliferative disorder is significantly increased in MPN patients compared to the general population (the cumulative risk at 5 and 10 years being 1% and 3%, respectively), particularly in males.[8] They found that the risk was higher in JAK2V617F positive patients. In conclusion, they indicated that MPN patients presented a 12-fold risk of developing CLL.[8] Due to very sporadic simultaneous occurrence of myelo- and lymphoproliferative neoplasms, further multicenter studies are needed to assess the epidemiology and molecular pathogenesis of these disorders.

Consent

The patient gave written informed consent for publication.

Conflict of interest

The authors report no conflict of interest.

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