causapedia
hakemli olgu dergisi

e-ISSN:2147-2181

Chronic Lymphocytic Leukemia and JAK2 V617F Positive Essential Thrombocythemia: Distinct Clonal Diseases?

Kronik Lenfositik Lösemi ve JAK2 V617F Pozitif Esansiyel Trombositemi: Farklı Klonal Hastalıklar mı?

Hematoloji

Başvuru: 11.07.2014
Kabul: 30.09.2014
Yayın: 28.10.2014

Deniz Çetin[1], İrfan Yavaşoğlu[1], Gürhan Kadıköylü[1], Gökay Bozkurt[1], Zahit Bolaman[1]

[1] Adnan Menderes Üniversitesi Tıp Fakültesi

Özet

Myeloproliferatif neoplazi ve kronik lenfositik lösemi birlikteliği nadir görülen bir durumdur. Bu birlikteliğin altta yatan patogenetik mekanizması bilinmemektedir. Burada JAK2 V617F mutasyonu pozitif olan esansiyel trombositemi ve kronik lenfositik löseminin eş zamanlı saptandığı bir olguyu sunmaktayız. Olgumuzda JAK2 V617F mutasyonunu lenfoid seri hücrelerinde saptamadık. Bu durum iki ayrı klonal hematolojik hastalık için öne sürülen ortak başlatıcı pluripotent kök hücre teorisi olasılığını azaltmaktadır. Kronik lenfositik lösemi ve esansiyel trombositemi birlikteliğinin rastlantısal olması muhtemeldir.

Anahtar kelimeler: *Kronik lenfositik lösemi, Esansiyel trombositemi JAK2 mutasyonu*

Abstract

The coexistence of myeloproliferative neoplasia and chronic lymphocytic leukemia is a rare entity. The underlying pathogenetic mechanism of this association is unknown. Here, we present a case who had JAK2 V617F mutation positive essential thrombocythemia and chronic lymphocytic leukemia simultaneously. In our patient, we did not detect JAK2 V617F mutation in lymphoid lineage cells. This situation reduces the possibility of a common initiative pluripotent stem cell theory for these two distinct clonal haematological diseases. It is likely that the association between chronic lymphocytic leukemia and essential thrombocythemia is coincidental.

Keywords: *Chronic lymphocytic leukemia, Essential thrombocythemia JAK2 mutation*

Introduction

The coexistence of myeloproliferative neoplasia (MPN) and chronic lymphocytic leukemia (CLL) is a rare entity. The underlying pathogenetic mechanism of this association is unknown [1]. Here, we present a case who had JAK2 V617F mutation positive essential thrombocythemia (ET) and CLL simultaneously.

Case Report

A 75-year-old male patient was admitted to our haematology department with complaints of weakness and exercise intolerance lasting for two months. Physical examination findings were conjunctival pallor, 3/6 degrees aortic systolic ejection murmur, bilateral cervical and axillary lymphadenopathy and hepatosplenomegaly. Hemoglobin level was 4.9 gr/dL, hematocrit 18.2%, white blood cell count was $22.9x10^9$/L and platelet count was $1157x10^9$/L. The patient had absolute lymphocytosis with a number of $12.5x10^9$/L. The peripheral blood smear revealed hypochromia, 26% neutrophils, 70% lymphocytes, 2% monocytes, 2% eosinophils and smudge cells. Direct Coombs test was negative and no evidence of hemolysis was detected. Bone marrow aspiration and biopsy revealed erythroid hypoplasia, normal myeloid maturation, increased small mature lymphocytes with a percentage of 40% and also increased megakaryocytes with dysplastic changes. Flow cytometric analysis of bone marrow aspirate showed CD20 (60%), CD5 (80%), CD5-20 (59.7%), CD23 (54.1%) positivities supporting CLL.

Sorumlu Yazar: Deniz Çetin, Adnan Menderes Üniversitesi Tıp Fakültesi
Adnan Menderes Üniversitesi Tıp Fakültesi İç Hastalıkları A.D., Aydın
drdenizcetin48@hotmail.com

e-ISSN:2147-2181

Thoracoabdominal computerized tomography scan showed no lymphadenopathy. 13q deletion and 17p deletion were negative by fluorescence in situ hybridization (FISH). BCR-ABL translocation was not detected by RT-PCR analysis and by FISH. JAK2 V617F mutation was detected heterozygous by PCR. ET and CLL were diagnosed simultaneously. We have separated the mononuclear cells from the heparinized venous blood of the patient by density gradient centrifugation method (Biocoll density 1.077 g/mL, isotone). JAK2 V617F mutation was negative in isolated lymphocytes by PCR. Hepatosplenomegaly was thought to be related with MPN. CLL stage was considered as Rai 1, Binet A. Hydroxyurea and acetylsalicylic acid treatment was started.

Discussion

MPNs are clonal haematopoietic stem cell disorders characterized by proliferation of one or more lineages of the myeloid, erythroid and megakaryocytic cell lines. The JAK2 V617F mutation is present in approximately 50-55% of the ET patients [2,3]. The risk of developing lymphoproliferative neoplasia is significantly increased in patients with MPN, especially harboring JAK2 V617F mutation [4]. A retrospective multicenter study (Gruppo Italiano Malattie EMatologiche dell'Adulto - GIMEMA) reported 46 patients affected by CLL/ Monoclonal B-cell lymphocytosis (MBL) and concomitant MPN diagnosed between 1985-2010 [1]. Coexistence of CLL/MBL and ET was detected in 18 cases in this study. In review of the literature about coexistence of CLL and MPN (56 cases) in the same study, 12 cases had been reported as CLL/ET and ET occurred simultaneously or preceded the development of CLL [4-10]. However, GIMEMA series also demonstrated that ET could be subsequent to the diagnosis of CLL. The coexistence of these two distinct clonal haematological diseases raises the possibility of a common initiative pluripotent stem cell [4,5]. Henry et al. reported the absence of JAK2 V617F mutation in lymphoid cells of a case in whom CLL was diagnosed after ET and hydroxyurea treatment. The mutagenic role of hydroxyurea remains controversial and no increased frequency of lymphoproliferative neoplasia has been reported after hydroxyurea treatment [7]. Kodali et al. reported the presence of JAK2 V617F mutation in B lymphocytes but not in T lymphocytes in a patient with CLL coexisting MPN simultaneously[11]. Likewise, Eskazan et al. detected JAK2 V617F mutation in both lymphoid and myeloid lineages in a patient with CLL coexisting MPN simultaneously in 2011 [12]. Clonal involvement of lymphoid lineage is still controversial because of conflicting data.

In our patient, we did not detect JAK2 V617F mutation in lymphoid lineage cells. This situation reduces the possibility of a common initiative pluripotent stem cell theory for these two distinct clonal haematological diseases. It is likely that the association between CLL and ET is coincidental.

References

1. Laurenti L, et al. The coexistence of chronic lymphocytic leukemia and myeloproliperative neoplasms: a retrospective multicentric GIMEMA experience. Am J Hematol. 2011;86:1007-12.
2. Koopmans SM, van Marion AM, Schouten HC. Myeloproliferative neoplasia: a review of clinical criteria and treatment. Neth J Med. 2012;70:159-67.
3. Tefferi A. Polycythemia vera and essential thrombocythemia: 2012 update on diagnosis, risk stratification, and management. Am J Hematol. 2012;87:285-93.
4. Vannucchi AM, et al. Increased risk of lymphoid neoplasms in patients with Philadelphia chromosome-negative myeloproliferative neoplasms. Cancer Epidemiol Biomarkers Prev. 2009;18:2068-73.
5. Tabaczewski P, Nadesan S, Lim SH. Zap-70 positive chronic lymphocytic leukemia co-existing with Jak 2 V617F positive essential thrombocythemia: a common defective stem cell? Leuk Res. 2009;33:854-5.
6. Bizzaro N. Chronic lymphocytic leukemia in a patient with essential thrombocythaemia. Clin Lab Haematol. 1998;20:377-9.
7. Henry L, et al. Association of essential thrombocythemia and chronic lymphocytic leukemia: absence of

e-ISSN:2147-2181

the V617F JAK2 mutation in the lymphoid compartment. Am J Hematol. 2007;82:500-1.
8. Gabrail NY, Martin TW. Coexistence of essential thrombocythemia and chronic lymphocytic leukemia. Acta Haematol. 1991;85:31-3.
9. Marcos Sánchez F, et al. Simultaneous presentation of chronic lymphocytic leukosis and essential thrombocythemia. An Med Interna. 1995;12:566.
10. Robak T, et al. Coexistence of chronic lymphocytic leukemia and essential thrombocythemia. Leuk Lymphoma. 2003;44:1425-31.
11. Kodali S, et al. JAK2 mutation in a patient with CLL with coexistent myeloproliferative neoplasm (MPN). Leuk Res. 2009;33:236-9.
12. Eskazan AE, et al. Chronic lymphocytic leukemia developing in a patient with Janus kinase 2 V617F mutation positive myeloproliferative neoplasm. Ann Hematol. 2012;91:305-6.