OMCR

Oxford Medical Case Reports, 2016, 28–30

doi: 10.1093/omcr/omw005
Letter to the Editor

LETTER TO THE EDITOR

Hairy cell leukemia followed by polycythemia vera: report of the first case

Yonal-Hindilerden Ipek[1,*], Hindilerden Fehmi[2], and Nalcaci Meliha[1]

[1]Istanbul University Istanbul Medical Faculty, Department of Internal Medicine, Division of Hematology, Istanbul, Turkey and [2]Istanbul Bakırkoy Sadi Konuk Training and Research Hospital, Hematology Clinic, Istanbul, Turkey

*Corresponding address. İstanbul Üniversitesi İstanbul Tıp Fakültesi, İç Hastalıkları ABD, Hematoloji BD, Fatih, Istanbul, Turkey. Tel: +905356875992; Fax: +902123153640; E-mail: ipekyonal@hotmail.com

To the Editor

Hairy cell leukemia (HCL) is a mature B-cell lymphoid neoplasm characterized by infiltration of bone marrow and splenic red pulp by small mature cells with oval nuclei and abundant cytoplasm with hairy projections [1]. HCL is a rare disease, constituting 2% of lymphoid leukemias. At initial diagnosis, patients are mostly middle-aged to elderly with a median age of 52 years with a male to female ratio of 5:1 [1]. Chronic myeloproliferative neoplasms (MPNs) represent a group of heterogeneous diseases of clonal origin characterized by abnormal proliferation of one or several myeloid lineages. Polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF) represent the three classical Philadelphia (Ph)-negative MPNs. Patients with ET and PV have life expectancies comparable with that of age-matched healthy individuals [2]. A population-based study including 3104 HCL patients demonstrated that patients with HCL are at increased risk of Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL) and solid cancers including thyroid cancer [1]. That study suggested that future studies are needed to address the role of immunologic impairment inherent to HCL, treatment modalities and other factors in the increased risk of second malignancies [1]. In contrast, in another long-term follow-up study including 241 HCL patients, subsequent malignancies did not appear to increase after pentostatin treatment [3]. Furthermore, the study by Federico *et al*. did not support the contention that HCL poses an increased risk for additional second malignancies, although the incidence of lymphoid neoplasms was significantly higher than expected [4]. The association of a Ph-negative MPN and lymphoproliferative neoplasm (LPN) in the same patient is a relatively uncommon event and has been reported mostly as case reports. Recently, in a study including the largest number of Ph-negative MPN and LPN patients, the incidence of concurrent Ph-negative MPN and LPN was reported as 0.3% [5]. LPN was diagnosed first in 47.1%, second in 44.1% and concurrently in 8.8% of patients [5]. The most common types of LPN were NHL and chronic lymphocytic leukemia (CLL) followed by HL and multiple myeloma (MM) [5]. PMF (41%), PV (24%) and ET (18%) were the most common MPNs, followed by MPN unclassifiable (MPN, U) and hypereosinophilic syndrome (HES) [5]. To our knowledge, there are only few reports describing a PV patient who subsequently develops HCL [6, 7]. Moreover, to date, only three reports have described a diagnosis of HCL variant developing in a background of PV [8–10]. We now report the first case of PV developed 3 years after the diagnosis of HCL.

A 58-year-old man presented 3 years earlier with fatigue, and his complete blood count showed the following: leukocyte 1400/mm^3 with 42.2% segmented neutrophils, 40% lymphocytes and 15.3% monocytes, hemoglobin 8 g/dl, MCV 107 fL and platelets 19 000/mm^3. His past medical history was significant for diabetes mellitus, hypertension and dyslipidemia. On physical examination, there was splenomegaly measuring 6 cm below the costal margin. Peripheral smear showed leukopenia with atypical lymphocytes displaying cytoplasmic projections (Fig. 1). Bone marrow biopsy demonstrated diffuse neoplastic infiltration consisting of cells with round, oval, regular nuclei and medium-sized, clear cytoplasm. Neoplastic cells expressed CD20, tartrate-resistant acid phosphatase (TRAP), LCA, CD79 alpha, CD11c, CD68 and annexin A1. Flow cytometry of bone marrow showed co-expression of B-cell marker CD19 and CD11c, CD25, CD103 and FMC7. Findings were consistent with HCL. Chemotherapy with the purine analog cladribine (2-chlorodeoxyadenosine) at a dose of 0.1 mg/kg per day for 7 days as continuous infusion was administered. Three months after the chemotherapy, complete remission was obtained with disappearance of hairy cells in bone marrow and splenomegaly. He remained disease free at regular follow-up visits. Approximately 3 years after the diagnosis of

Received: January 9, 2016. **Revised:** January 19, 2016. **Accepted:** January 21, 2016

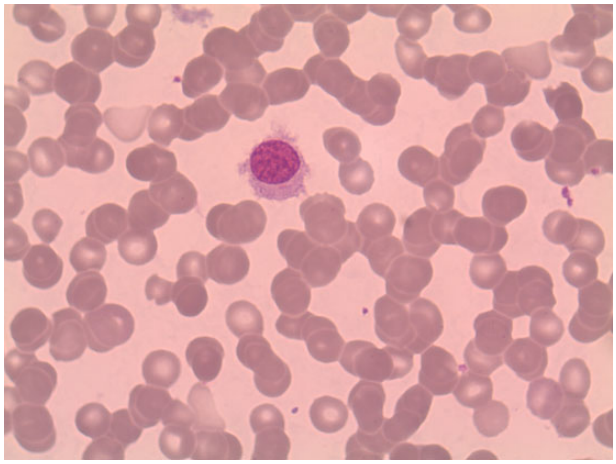

Figure 1: Peripheral smear demonstrating a circulating atypical lymphocyte with cytoplasmic projections.

HCL, he was examined for persistent headache. His complete blood count showed a hemoglobin level of 18.6 g/l, hematocrit of 55% and no other abnormalities. Examination of his arterial blood gases found no hypoxemia; erythropoietin level was 2.3 U/l (2.6–18.5), and lactate dehydrogenase (LDH) value was 520 U/l (normal value: <450 U/l). JAK2V617F mutation was found to be positive. His blood marrow biopsy revealed a slight hypercellularity with increased erythropoiesis. He was diagnosed with PV according to the 2008 WHO criteria. Because the patient was aged <60 years and had no history of thrombosis, hydroxyurea was not started. He was treated with phlebotomy to keep his hematocrit at 45% or lower. Also, twice-daily 100 mg/day acetylsalicylic acid (ASA) was started because of his cardiovascular risk factors including hypertension and diabetes mellitus.

There is increased recognition that patients with LPN are at higher risk of MPN or vice versa [5]. In such cases of concomitant MPN and LPN, it is hard to predict the chronologic evolution of the molecular events causing the two diseases. One group proposed that the two diseases originate from common progenitors. This notion would be supported by the presence of JAK2V617F mutation both in myeloid cells and B lymphocytes [11]. Other possible scenario supposes that MPN and LPN originate from different progenitors, which would be supported by the absence of JAK2V617F mutation from the lymphoid cells [12]. The latter condition can be explained by genomic instability, leading to the acquisition of JAK2V617F mutation in the myeloid progenitors, and to the acquisition of other mutations in the B lymphocytes progenitors [11, 12]. Chung *et al.* linked the pathogenesis of HCL to somatic BRAFV600E mutations arising in hematopoietic stem/progenitor cells (HSPCs) and suggest that chronic lymphoid malignancies may be initiated by aberrant hematopoietic stem cells (HSCs) [13]. Further studies are needed to demonstrate whether there is an inherent predisposition to second malignancies induced by immune dysfunction associated with HCL [1]. To our knowledge, there are only two previous reports of classic HCL developing in PV patients [6, 7]. One of these PV patients had received busulfan therapy, which might have contributed to the development of HCL [7]. The other PV patient received busulfan and radioactive phosphorus, which may be the cause for development of HCL [6]. To our knowledge, three HCL variant patients arising in the presence of PV have been described [8–10]. One of the aforementioned PV patients had received splenic irradiation, which has not been reported as a potential contributor to development of HCL variant [8]. Our case report is unique in that it is the first to describe PV occurring in a HCL patient. Physicians should be aware of such an association. It is to be elucidated whether or not the simultaneous presence of the two entities is purely coincidental, or there is a causal relationship between the two groups of diseases.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

None.

ETHICAL APPROVAL

None required.

CONSENT

Informed consent was obtained from all patients for being included in the study.

GUARANTOR

Ipek Yonal-Hindilerden is a guarantor of the study.

REFERENCES

1. Hisada M, Chen BE, Jaffe ES, Travis LB. Second cancer incidence and cause-specific mortality among 3104 patients with hairy cell leukemia: a population-based study. *J Natl Cancer Inst* 2007;**99**:215–222.
2. Cervantes F, Passamonti F, Barsi G. Life expectancy and prognostic factors in the classic BCR-ABL-negative myeloproliferative disorders. *Leukemia* 2008;**22**:905–914.
3. Flinn IW, Kopecky KJ, Foucar MK, Head D, Bennett JM, Hutchison R, *et al.* Long-term follow-up of remission duration, mortality, and second malignancies in hairy cell leukemia patients treated with pentostatin. *Blood* 2000;**96**:2981–2986.
4. Federico M, Zinzani PL, Frassoldati A, Vinceti M, Modè A, Annino L, *et al.* Risk of second cancer in patients with hairy cell leukemia: long-term follow-up. *J Clin Oncol* 2002;**20**:638–646.
5. Masarova L, Newberry KJ, Pierce SA, Estrov Z, Cortes JE, Kantarjian HM, *et al.* Association of lymphoid malignancies and Philadelphia-chromosome negative myeloproliferative neoplasms: clinical characteristics, therapy and outcome. *Leuk Res* 2015;**39**:822–827.
6. Mufti GJ, Hamblin TJ, Stevenson FK, Fitchett M. Polycythaemia rubra vera and hairy cell leukaemia in the same patient: studies on the spleen. *J Clin Pathol* 1982;**35**:1312–1315.
7. Lishner M, Jutrin I, Bar-Sela S, Josef D, Ravid M. Hairy cell leukemia in a patient with polycythemia vera. *Acta Haematol* 1984;**72**:49–51.
8. Kelly NP, Alkan S, Nand S. Hairy cell leukemia variant developing in a background of polycythemia vera. *Arch Pathol Lab Med* 2003;**127**:e209–e211.
9. Razaq M, Perumandla S, Mankan N, Sridhar S, Sanmugarajah J, Fernandez G, *et al.* Hairy cell leukemia variant transforming into aggressive lymphoma with prostatic involvement in a patient with polycythemia vera. *Leuk Lymphoma* 2006;**47**:754–757.
10. Kotchetkov R, Gupta V. Polycythemia vera followed by hairy cell leukemia variant. *Blood* 2012;**120**:5100.

11. Kodali S, Chen C, Rathnasabapathy C, Wang JC. JAK2 mutation in a patient with CLL with coexistent myeloproliferative neoplasm (MPN). *Leuk Res* 2009;**33**:e236–e239.
12. Hussein K, Brakensiek K, Ballmaier M, Bormann M, Göhring G, Buhr T, *et al*. B-CLL developing in a patient with PV is not affected by V617F mutation of the Janus kinase 2. *Eur J Haematol* 2006;**77**:539–541.
13. Chung SS, Kim E, Park JH, Chung YR, Lito P, Teruya-Feldstein J, *et al*. Hematopoietic stem cell origin of BRAFV600E mutations in hairy cell leukemia. *Sci Transl Med* 2014;**6**:238ra71.