


## CASE REPORT

# Co-occurrence of *JAK2* V617F-mutated essential thrombocythemia and chronic lymphocytic leukemia harboring der(8;17)(q10;q10)

Masahiro Manabe<sup>1</sup>  | Nao Tanizawa<sup>1,2</sup> | Satoru Nanno<sup>1</sup> | Yuuji Hagiwara<sup>3</sup> | Reiko Asada<sup>3</sup> | Ki-Ryang Koh<sup>1</sup>

<sup>1</sup>Department of Hematology, Osaka General Hospital of West Japan Railway Company, Osaka, Japan

<sup>2</sup>Hematology, Graduate School of Medicine, Osaka City University, Osaka, Japan

<sup>3</sup>Department of Clinical Laboratory, Osaka General Hospital of West Japan Railway Company, Osaka, Japan

## Correspondence

Masahiro Manabe, Department of Hematology, Osaka General Hospital of West Japan Railway Company, 1-2-22 Matsuzaki-cho, Abeno-ku, Osaka 545-0053, Japan.  
Email: [m1153564.osaka.cu@gmail.com](mailto:m1153564.osaka.cu@gmail.com)

## Abstract

**Background and Case:** We herein present a case of the co-occurrence of *JAK2*-mutated essential thrombocythemia (ET) with chronic lymphocytic leukemia (CLL) harboring the recurrent and rare whole-arm translocation, der(8;17)(q10;q10). The co-existence of lymphoproliferative neoplasms and myeloproliferative neoplasms is suggested to be a rare event. Under this condition, the lymphoproliferative disorder presents a clinically indolent course with a low-risk biological profile. However, the present case showed aggressive disease progression, reflecting a poor prognostic factor; that is, the loss of 17p caused by the whole-arm der(8;17)(q10;q10) translocation.

**Conclusion:** The present case report emphasizes the importance of considering the involvement of a genetically poor prognostic factor, regardless of the co-occurrence of CLL and ET.

## KEYWORDS

cytogenetics, hematological cancer, pathology

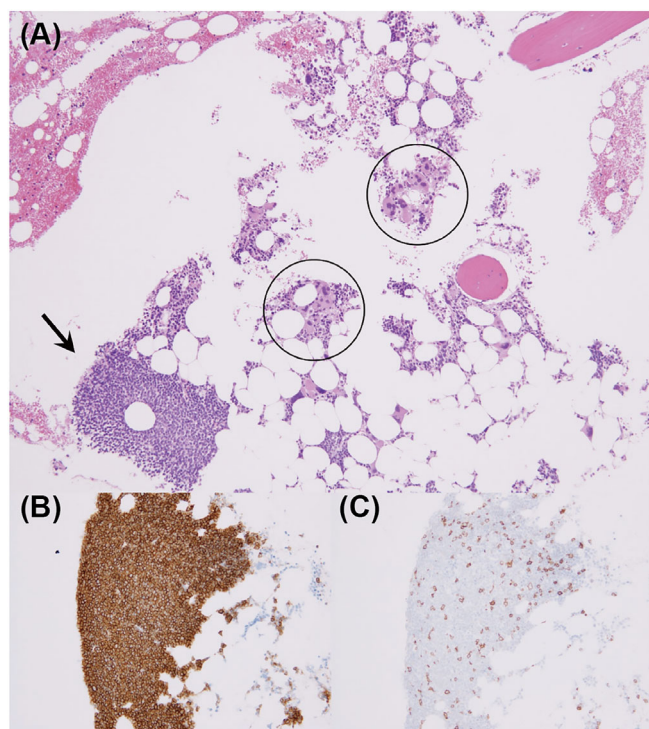
## 1 | INTRODUCTION

Whole-arm translocations are considered to be rare in hematological malignancies.<sup>1</sup> der(8;17)(q10;q10) is a recurrent and rare chromosomal aberration associated with lymphoid neoplasms.<sup>1–6</sup> The co-existence of lymphoproliferative neoplasms and myeloproliferative neoplasms is suggested to be a rare event, and the lymphoproliferative disease demonstrates a clinically indolent course with a low-risk biological profile.<sup>7,8</sup> We herein report a case of the co-occurrence of Janus kinase 2 (*JAK2*)-mutated essential thrombocythemia (ET) and chronic lymphocytic leukemia (CLL) harboring der(8;17)(q10;q10), which resulted in the loss of 17p,

considered to be a poor prognostic factor, and showed steady progression.

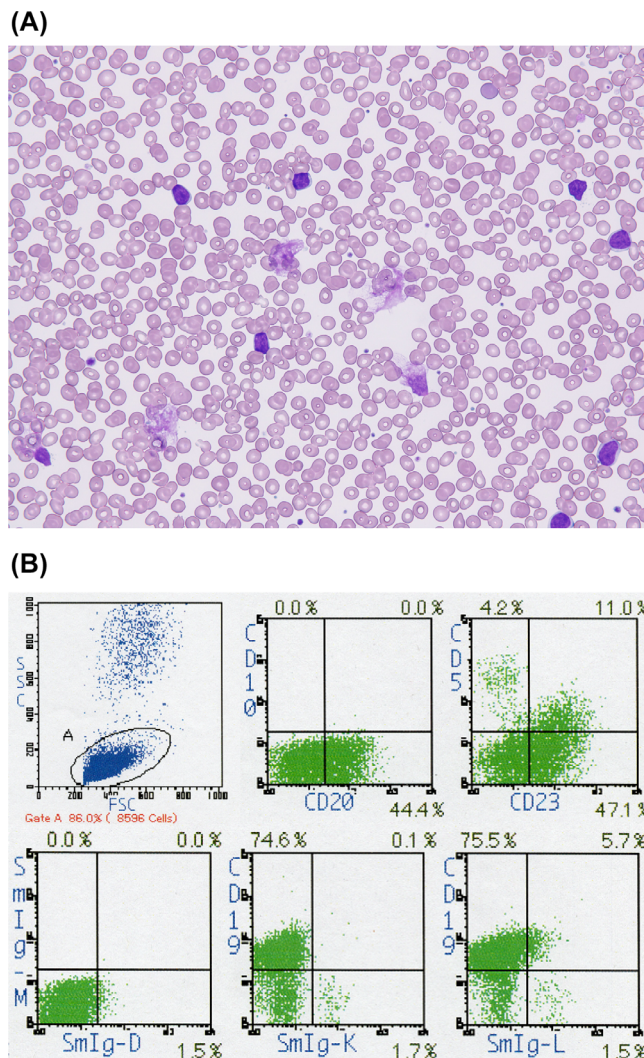
### 1.1 | Case presentation

A 74-year-old male was referred to our hospital (Osaka General Hospital of West Japan Railway Company, Osaka, Japan) with thrombocythemia in September 2015. His medical history included hypertension, which was being treated with oral amlodipine besilate. Although a physical examination showed mild splenomegaly, palpable lymph nodes were absent. The initial complete blood



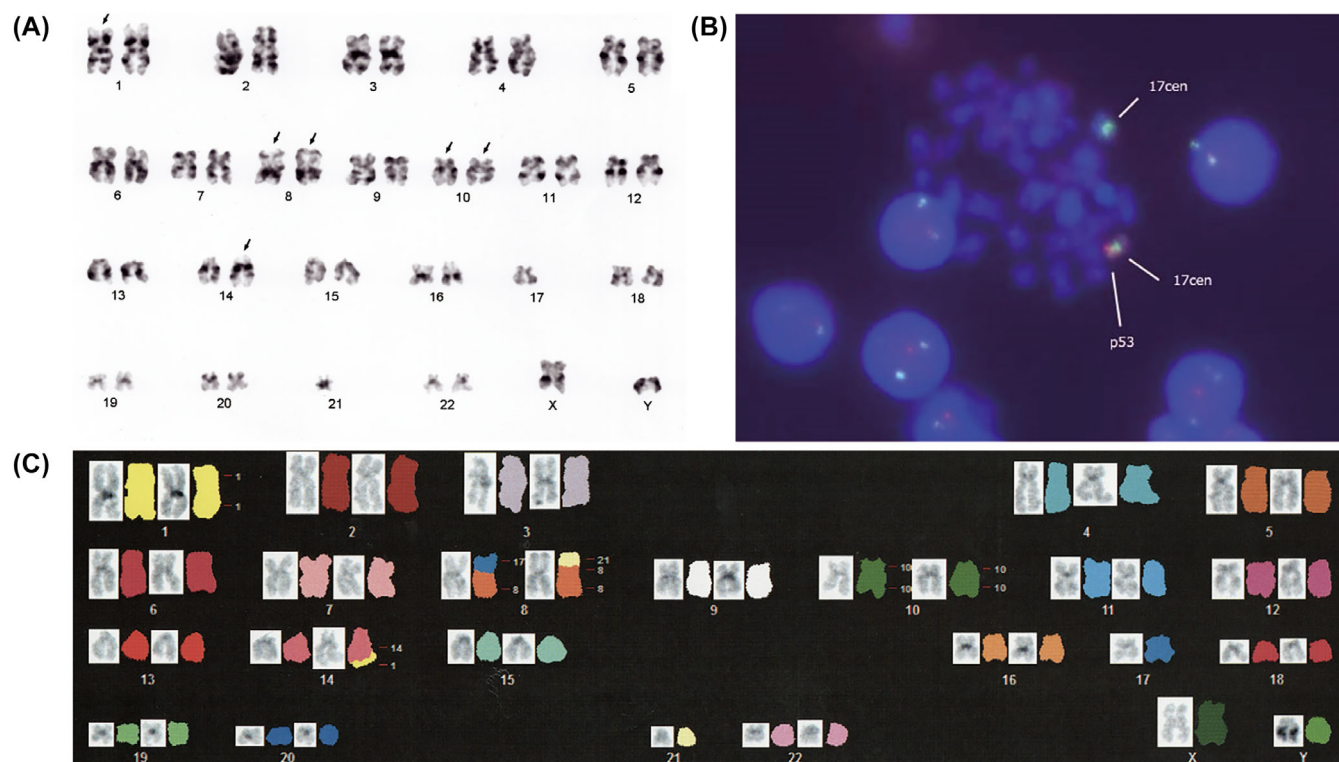
**FIGURE 1** Pathological images of bone marrow biopsy. (A) Proliferation of megakaryocytes (circles) and clusters of small lymphocytes (arrow) were observed (hematoxylin and eosin staining,  $\times 100$ ). (B, C) Immunohistochemistry demonstrated that lymphocytes were positive for CD23 (B,  $\times 200$ ) and aberrantly positive for CD5 (C,  $\times 200$ ).

count test showed a white blood cell (WBC) count of  $12.2 \times 10^9/L$  (reference range,  $3.4\text{--}8.4 \times 10^9/L$ ) with 73.5% neutrophils, 2.5% eosinophils, 6.5% basophils, 2.5% monocytes, and 15% lymphocytes. The concentration of hemoglobin was 13.2 g/dL (reference range, 14.0–18.0 g/dl) and the platelet count was  $1224 \times 10^9/L$  (reference range,  $130\text{--}320 \times 10^9/L$ ). A polymerase chain reaction revealed the JAK2-V617F mutation in peripheral blood cells. Bone marrow biopsy showed the proliferation of megakaryocytes and clusters of small lymphocytes (Figure 1). Immunohistochemical staining revealed that small lymphocytes were positive for CD23 and CD79a, aberrantly positive for CD5, and negative for cyclin D1. A chromosomal study of bone marrow cells showed a normal karyotype of 46,XY[20]. Based on these findings, the patient was diagnosed with the co-occurrence of ET and monoclonal B-cell lymphocytosis (MBL). Although he was treated with hydroxyurea (500 mg per day) and aspirin for ET, only watchful waiting was performed for MBL because a treatment intervention was not indicated at this point. In November 2017, a gradual increase in the WBC count was noted. Laboratory data included a WBC count of  $23.6 \times 10^9/L$  with 49% lymphoid cells, a hemoglobin concentration of 10.8 g/dL, and platelet count of  $294 \times 10^9/L$ . In a surface marker analysis, lymphoid cells in peripheral blood showed CD19, CD20, CD23, and CD5 (weak) expression (Figure 2). A follow-up cytogenetic analysis revealed the following abnormal karyotype:



**FIGURE 2** (A) Peripheral blood smear at the diagnosis of CLL (May-Giemsa staining,  $\times 400$ ). (B) Flow cytometric analysis of peripheral blood cells by SSC/FSC gating. The corresponding cell percentage demonstrated by the gate is 86.0%. The results of two-color analyses with CD10 and CD20, CD5 and CD23, surface (s-)IgM and s-IgD, CD19 and s-Igk, and CD19 and s-Igλ for the gated cells are shown. Corresponding cell percentages in each fraction are indicated. The gated cells are positive for CD20, CD23, and CD19 and weakly positive for CD5. Strong positivity for surface immunoglobulin was not detected.

44,XY,t(1;14)(p36.1;q32),der(8)t(8;21)(p21;q?),der(8;17)(q10;q10),del(10)(p13)  $\times 2$ , -21 [3]/46,XY[17]. In addition, a fluorescent in situ hybridization analysis showed the loss of the p53 signal in 94% of cells (Figure 3). Therefore, the patient was diagnosed with CLL that evolved from MBL. At this point, oral hydroxyurea was discontinued due to anemia. Leukocytosis and anemia reflecting the progression of CLL gradually progressed in April 2018 (WBC,  $28.7 \times 10^9/L$ ; hemoglobin, 9.3 g/dl). Hemolysis was not detected. Although we proposed the initiation of ibrutinib monotherapy because anemia was an indication for treatment, the patient did not wish to be treated for financial reasons. Only follow-up surveillance was



**FIGURE 3** (A) G-banded karyogram obtained in the present case. The arrows indicate derivative chromosomes. (B) FISH image showing the loss of one copy of the *TP53* gene. Red signal, the p53 probe; green signal, chromosome 17 centromere. (C) Spectral karyotyping of the metaphase spread after a spectrum-based classification (left, counterstained with 4',6-diamino-2-phenylindole dihydrochloride; right, SKY).

continued; however, lymphocytosis became more prominent in April 2019 (WBC,  $71.8 \times 10^9/L$ ; lymphocytes, 83%), and the patient eventually died of pneumonia.

## 2 | DISCUSSION

Regarding cytogenetic abnormalities among CLL, an abnormality of chromosome 17 is the most frequent in cases involving complex karyotypes.<sup>9</sup> On the other hand, only seven cases of mature lymphoproliferative disorders (six of CLL<sup>1–5</sup> and one of Waldenström's macroglobulinemia<sup>6</sup>) involving the der(8;17)(q10;q10) translocation have been reported in the literature; therefore, this translocation is considered to be recurrent and rare. Furthermore, it was impossible to establish the prognostic significance of this translocation on the prognosis of the patient because the majority of previous case reports mainly focused on the chromosomal abnormality itself or described a case series. Among CLL cases, the loss of 17p is associated with a poor prognosis and *TP53* mutations. der(8;17)(q10;q10) results in the loss of 8p and 17p due to the unbalanced nature of the translocation. Besides the simple deletion of 17p, the unbalanced translocation resulted in the loss of 17p, such as dic(17;18)(p11.2;p11.2),<sup>10</sup> which may correlate with a poorer outcome. Regarding the abnormality in 14q32 in the present case, a recent study indicated that chromosome 14q32 rearrangements/

translocations involving the immunoglobulin heavy chain (*IGH*) were associated with an intermediate-adverse outcome.<sup>11</sup> The co-existence of lymphoproliferative neoplasms and myeloproliferative neoplasms is suggested to be a rare event. Under this condition, the lymphoproliferative disorder presents a clinically indolent course with a low-risk biological profile.<sup>7,8</sup> However, regardless of the co-occurrence of CLL and ET, a genetically poor prognostic factor was considered to be strongly involved.

## 3 | CONCLUSION

The co-occurrence of myeloproliferative neoplasms and CLL rarely occurs and presents an indolent clinical course. However, clinicians need to be aware that chromosomal abnormalities with a poor prognosis have a strong negative impact on the prognosis of patients.

## AUTHOR CONTRIBUTIONS

**Masahiro Manabe:** Conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); project administration (lead); resources (lead); writing – original draft (lead); writing – review and editing (lead). **Nao Tanizawa:** Investigation (equal); methodology (equal); writing – review and editing (equal). **Satoru Nanno:** Investigation (equal); methodology (equal); writing – review and editing (equal). **Yuuji Hagiwara:** Data curation (equal);





investigation (equal); methodology (equal); writing – review and editing (equal). **Reiko Asada:** Data curation (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Ki-Ryang Koh:** Investigation (equal); methodology (equal); writing – review and editing (equal).

## ACKNOWLEDGMENTS

The authors thank Medical English Service (<https://www.med-english.com>) for English language editing.

## CONFLICT OF INTEREST

No conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

## ETHICS STATEMENT

Written informed consent was obtained from the patient for the publication of case details and the use of images.

## ORCID

Masahiro Manabe  <https://orcid.org/0000-0002-9065-2437>

## REFERENCES

1. Adeyinka A, Wei S, Sanchez J. Loss of 17p is a major consequence of whole-arm chromosome translocations in hematologic malignancies. *Cancer Genet Cytogenet*. 2007;173:136-143.
2. Döhner H, Fischer K, Bentz M, et al. p53 gene deletion predicts for poor survival and non-response to therapy with purine analogs in chronic B-cell leukemias. *Blood*. 1995;85:1580-1589.
3. Geisler CH, Philip P, Christensen BE, et al. In B-cell chronic lymphocytic leukaemia chromosome 17 abnormalities and not trisomy 12 are the single most important cytogenetic abnormalities for the prognosis: a cytogenetic and immunophenotypic study of 480 unselected newly diagnosed patients. *Leuk Res*. 1997;21:1011-1023.
4. Schlette E, Bueso-Ramos C, Giles F, Glassman A, Hayes K, Medeiros LJ. Mature B-cell leukemias with more than 55% prolymphocytes. A heterogeneous group that includes an unusual variant of mantle cell lymphoma. *Am J Clin Pathol*. 2001;115:571-581.
5. Tang G, Banks HE, Sargent RL, Medeiros LJ, Abruzzo LV. Chronic lymphocytic leukemia with t(14;18)(q32;q21). *Hum Pathol*. 2013;44:598-605.
6. Wang KF. Waldenström macroglobulinemia with a novel der(8;17)(q10;q10). *Cancer Genet Cytogenet*. 2003;141:83-85.
7. Laurenti L, Tarnani M, Nichele I, et al. The coexistence of chronic lymphocytic leukemia and myeloproliferative neoplasms: a retrospective multicentric GIMEMA experience. *Am J Hematol*. 2011;86:1007-1017.
8. Masarova L, Newberry KJ, Pierce SA, et al. Association of lymphoid malignancies and Philadelphia-chromosome negative myeloproliferative neoplasms: clinical characteristics, therapy and outcome. *Leuk Res*. 2015;39:822-827.
9. Costa D, Granada I, Espinet B, et al. Balanced and unbalanced translocations in a multicentric series of 2843 patients with chronic lymphocytic leukemia. *Genes Chromosomes Cancer*. 2022;61:37-43.
10. Woyach JA, Heerema NA, Zhao J, et al. Dic(17;18)(p11.2;p11.2) is a recurring abnormality in chronic lymphocytic leukaemia associated with aggressive disease. *Br J Haematol*. 2010;148:754-759.
11. Pérez-Carretero C, Hernández-Sánchez M, González T, et al. Chronic lymphocytic leukemia patients with IGH translocations are characterized by a distinct genetic landscape with prognostic implications. *Int J Cancer*. 2020;147:2780-2792.

**How to cite this article:** Manabe M, Tanizawa N, Nanno S, Hagiwara Y, Asada R, Koh K-R. Co-occurrence of JAK2 V617F-mutated essential thrombocythemia and chronic lymphocytic leukemia harboring der(8;17)(q10;q10). *Cancer Reports*. 2022;5(10):e1658. doi:10.1002/cnr2.1658