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A case of e1a2 (minor, P190) *BCR-ABL* 1-positive chronic myeloid leukemia in Korea

TO THE EDITOR: Minor *BCR-ABL* 1-positive chronic mye-

loid leukemia (CML) is a very rare subtype of CML, with only 1-2% of patients with CML exhibiting this fusion gene as a sole rearrangement [1]. Amongst the several reported cases in literature, and to the best of our knowledge, only one case has been reported in Korea so far [2]. In this letter, we report a Korean patient diagnosed with minor *BCR-ABL* 1-positive CML.

An 81-year-old male with a history of hypertension and dyslipidemia was referred to our hospital because of marked leukocytosis. The complete blood count (CBC) at referral indicated anemia, leukocytosis, and thrombocytopenia, with a hemoglobin (Hb) level of 7.5 g/dL, white blood cell (WBC) count of $37.59 \times 10^9/L$, and a platelet count of $89 \times 10^9/L$. The differential counts of WBC were myelocytes 1%, metamyelocytes 2%, band neutrophils 13%, neutrophils 45%, eosinophils 2%, basophils 6%, lymphocytes 12%, and monocytes 19% (Fig. 1). Bone marrow (BM) biopsy and related cytogenetic studies were performed; bone marrow biopsy showed hypercellularity, with an estimated cellularity of 70-90% (Fig. 2) with granulocytic proliferation. Additionally, the number of megakaryocytes and dwarf megakaryocytes had increased (Fig. 3). Approximately 5.3% of all nucleated cells (ANCs) were counted as blasts, whereas the population co-expressing CD34(+), CD117(+), and myeloperoxidase corresponding to myeloblasts, was 2.28% of the total cells observed using flow cytometry (FCM). Pseudo-Gaucher cells were not observed. Monocytes accounted for 17.1% of the ANCs, consistent with the FCM results of 17.4%. Conventional chromosome analysis using BM cells exhibited 46,XY,t(9;22)(q34;q11.2)[20] (Fig. 4). Reverse transcriptase-polymerase chain reaction (RT-PCR) showed a minor (P190) *BCR-ABL* 1 transcript of the e1a2 type (Fig. 5). No major (P210) or micro (P230) *BCR-ABL* 1 transcripts were detected. Therefore, the patient was diagnosed with minor *BCR-ABL* 1-positive CML in chronic phase.

The Philadelphia chromosome, resulting from the chro-

Fig. 1. A peripheral blood smear showing leukocytosis with monocytosis (blue arrows), basophilia (red arrow) and left shift (yellow arrow) (white blood cell count $37.59 \times 10^9/L$ with 0.19 monocytes and 0.04 basophils, Wright-Giemsa stain, $\times 400$).

Fig. 2. Bone marrow biopsy showing hypercellularity (estimated cellularity of 70-90%, Hematoxylin & Eosin stain, $\times 200$).

Fig. 3. Dwarf megakaryocytes (yellow arrow) with hypolobated nuclei were seen in the bone marrow (Wright-Giemsa stain, $\times 400$).

Fig. 4. Karyotyping results exhibiting 46, XY, t(9;22)(q34;q11.2)[20].

mosomal translocation t(9;22), contains the *BCR-ABL1* fusion gene, which is a hallmark of CML. Over 95% of CML patients are *BCR-ABL1*-positive [3]. The fusion gene product varies in size depending on the breakpoint in the *BCR* gene. The fusion products thus formed are major p210, minor p190, and micro p230. The most common form—the major *BCR-ABL1* rearrangement—is mostly observed in patients with CML, whereas the minor *BCR-ABL1* rearrangement is more common among patients with acute lymphoblastic leukemia (ALL) [4]. Although our patient was positive for the minor *BCR-ABL1* rearrangement (Fig. 5), ALL was ruled out based on morphological and FCM results.

The case we have described here constitutes the second case of minor *BCR-ABL1*-positive CML reported in Korea [2]. Several similar reports have been made globally [5, 6]. Our case is in line with these prior reports with respect to minor *BCR-ABL1* CML being associated with significant monocytosis. The patient did not undergo tyrosine kinase inhibitor (TKI) therapy immediately after diagnosis owing

Fig. 5. The minor *BCR-ABL1* fusion gene was found as a sole rearrangement in the case presented here. Nested reverse transcriptase polymerase chain reaction revealed the minor *BCR-ABL1* fusion transcript (P190) with an approximately 320 bp length, indicating it to be the e1a2 type transcript. No amplicons corresponding to the 320 bp position were detected for the major *BCR-ABL1* transcripts.

to the presence of a ureter stone complicated by infection that required surgery. On November 26, the patient began treatment with dasatinib, a second-generation TKI. Thus, it was too early (<1 mo) to predict treatment response. Nevertheless, minor *BCR-ABL1*-positive CML has been correlated with a poor prognosis. CML patients with a minor *BCR-ABL1* fusion gene respond more slowly to TKI treatment and are less likely to achieve a major molecular response [7]. Accordingly, a less favorable outcome can be expected in our patient compared with that of a patient with a typical major *BCR-ABL1*-positive CML.

Yu Jeong Choi¹, Ja Yoon Heo², Jongha Yoo³

¹Department of Laboratory Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, ²Division of Hematology-Oncology, Department of Internal Medicine, ³Department of Laboratory Medicine, National Health Insurance Service Ilsan Hospital, Goyang, Korea

Correspondence to: Jongha Yoo

Department of Laboratory Medicine, National Health Insurance Service Ilsan Hospital, 100 Ilsan-ro, Ilsandong-gu, Goyang 10444, Korea
E-mail: jhyoo92@nhimc.or.kr

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Immune thrombocytopenic purpura worsened by COVID-19

TO THE EDITOR: Coronavirus disease (COVID-19) was

confirmed in an 88-year-old man on March 8, 2021 by reverse transcription-polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) RNA, when he was admitted for exertional dyspnea of vague onset with no fever, cough, or phlegm. His medical history revealed refractory/recurrent immune thrombocytopenic purpura (ITP) to high-dose immunoglobulin, immunosuppressive therapy including dexamethasone, vincristine, and cyclophosphamide, and splenectomy. He was treated with 25 mg eltrombopag, once a day (QD), in September 2020. A diagnosis of advanced prostate adenocarcinoma was made in May 2016, which was well controlled with androgen blockade until February 23, 2021, when 80 mg docetaxel was administered for tumor progression (Fig. 1). In April 2016, idiopathic pulmonary fibrosis was diagnosed. Additionally, hypertension and diabetes were diagnosed in April 2016 and treated with amlodipine 5 mg QD plus hydrochlorothiazide 25 mg QD and teneligliptin 10 mg QD plus metformin 500 mg QD, respectively. He underwent laparoscopic cholecystectomy in November 2017 for gallbladder stones and endoscopic sphincterotomy for common bile duct stone in October 2019, and bilateral gonarthrosis was diagnosed in 1990. His family history was unremarkable. He had not been vaccinated against COVID-19. Physical examination findings were unremarkable, with no fever, pallor, jaundice, lymphadenopathy, or bleeding tendency, except for bibasilar crackles and multiple abdominal surgical scars. The dyspnea experienced by the patient was attributed partly to two-vessel coronary arterial obstructive disease diagnosed by angiography and echocardiography in February 2021 and to COVID-19 to some extent. The patient did not develop pneumonia (Fig. 2). Further treatment with docetaxel was discontinued. Approximately 6 weeks after the first dose of docetaxel or 4 weeks after contracting COVID-19, sudden severe thrombocytopenia (7,000/ μ L) was recorded on April 2, 2021 (Fig. 1). This was despite the patient complying with the prescribed treatment of 25 mg eltrombopag QD,

Fig. 1. Platelet count dropped suddenly on day 181, and eltrombopag dose was tripled from 25 mg QD to 75 mg QD on the same day. The day of docetaxel administration is indicated by arrows. The platelet response to eltrombopag appears prominent on day 390 immediately after the second dose of docetaxel administered on day 388, similar to that seen on days 2–86 after the first dose of docetaxel was administered on day 1. Abbreviation: QD, one a day.