Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Asinari MB, Zeballos M, Alicia S, Ricchi BN, Basquiera AL. A case of chronic myeloid leukemia with the m-bcr (p190) molecular rearrangement identified during treatment. Rev Bras Hematol Hemoter 2015;37:55-7.
2. Yun JW, Yoon J, Kim JW, Kim SH, Jung CW, Kim HJ. Isolated monocytosis was the flag preceding abnormalities in other parameters of complete blood counts in chronic myeloid leukemia with e1a2 (minor, p190) BCR-ABL1 chimeric transcripts. Precis Future Med 2019;3:30-5.
3. Melo JV. The diversity of BCR-ABL fusion proteins and their relationship to leukemia phenotype. Blood 1996;88:2375-84.
4. Vardiman JW, Melo JV, Baccarani M, Radich JP, Kvasnicka HM. Chronic myeloid leukaemia, BCR-ABL1-positive. In: Swerdlow SH, Campo E, Harris NL, et al, eds. WHO classification of tumours of haematopoietic and lymphoid tissues. Revised 4th ed. Lyon, France: IARC Press, 2017:30-8.
5. Melo JV, Myint H, Galton DA, Goldman JM. P190BCR-ABL chronic myeloid leukaemia: the missing link with chronic myelomonocytic leukaemia? Leukemia 1994;8:208-11.
6. Gatti A, Movilia A, Roncoroni L, Citro A, Marinoni S, Brando B. Chronic myeloid leukemia with P190 BCR-ABL translocation and persistent moderate monocytosis: a case report. J Hematol 2018;7:120-3.
7. Gong Z, Medeiros LJ, Cortes JE, et al. Clinical and prognostic significance of e1a2 BCR-ABL1 transcript subtype in chronic myeloid leukemia. Blood Cancer J 2017;7:e583.

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 hydrochlorthaizide 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/μL) was recorded on April 2, 2021 (Fig. 1). This was despite the patient complying with the prescribed treatment of 25 mg eltrombopag QD,

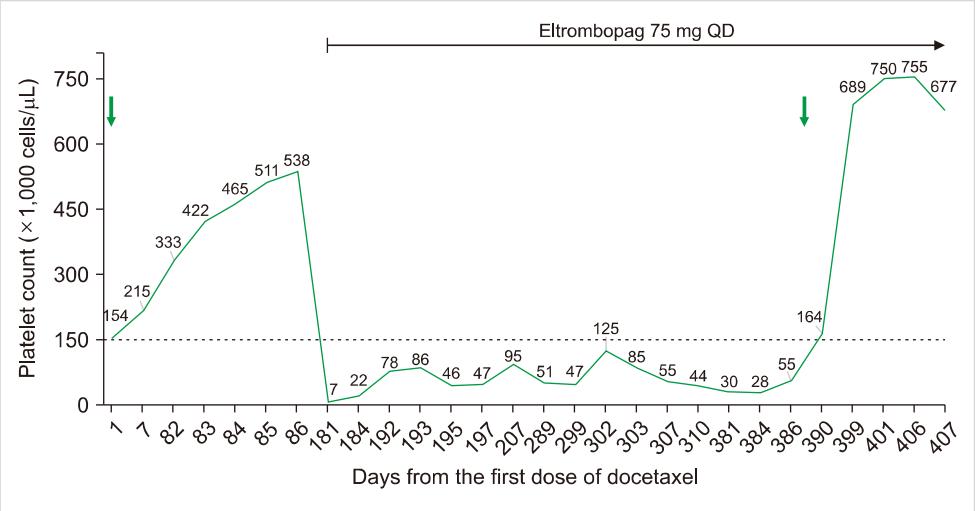

Fig. 1. Platelet count dropped suddenly on day 181, and eltrombopag dose was tripled from 25 mg QD to 75 mg QD on the same day. The day of docetaxel administration is indicated by arrows. The platelet response to eltrombopag appears prominent on day 390 immediately after the second dose of docetaxel 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.

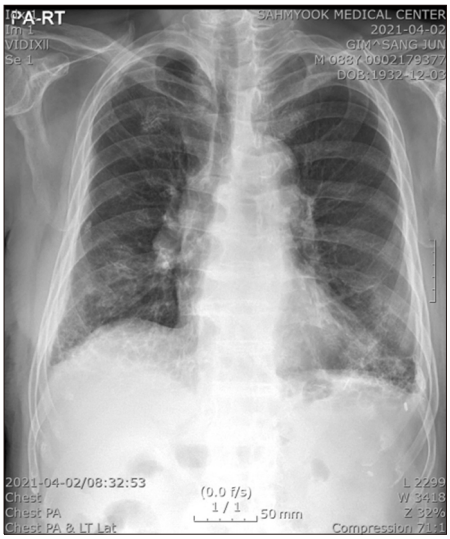

Fig. 2. Chest radiograph shows no evidence of pneumonia, except for persistent interstitial infiltrates due to chronic idiopathic pulmonary fibrosis.
Abbreviations: PA, posteroanterior; RT, right.

with no overt bleeding tendency or evidence of sepsis, disseminated intravascular coagulation (DIC), hemophagocytic lymphohistiocytosis (HLH), or thrombotic thrombocytopenic purpura (TTP) on anamnesis, physical examination, and laboratory tests. Laboratory findings were as follows: hemoglobin, 13.3 g/dL; white blood cells count, 11,300/μL (64% neutrophils and 22% lymphocytes); lactate dehydrogenase, 283 IU/L (reference value, 135–225 IU/L); and d-dimer, 0.53 μg/mL (reference value <0.5 μg/mL). The test results for *Campylobacter*-like organisms were negative. The eltrombopag dose was increased to 75 mg QD (Fig. 1), but platelet concentrate transfusion or corticosteroids administration was not performed. The elevated platelet count was in the range of 22,000–125,000/μL between April 5, 2021 and June 7, 2021. RT-PCR for SARS CoV-2 was negative on April 13, 2021. The second dose of docetaxel 80 mg was administered on June 9, 2021 (Fig. 1), 15 weeks after the first dose, with continuous administration of eltrombopag at 75 mg QD. The platelet count was >150,000/μL on June 11, 2021, which rose to >600,000/μL on June 20, 2012 when the dose of eltrombopag was reduced to 25 mg QD.

The severity of COVID-19 in our case was graded as either asymptomatic or mild, without pneumonia development. During the clinical course of COVID-19 in this patient, there were no complications, except for the ITP relapse. The thrombocytopenia relapse on April 2, 2021 was detected about 4 weeks after COVID-19 was confirmed on March 8, 2021. There was no bleeding tendency observed. The sudden drop in the platelet count to 7,000/μL on April 2, 2021 was not considered an adverse effect of docetaxel. It was not attributed to either marrow suppression or drug-induced ITP in view of the long interval (6 weeks) between drug administration and thrombocytopenia, paradoxical rise of platelet count immediately after docetaxel administration, and the absence of bleeding tendency usually seen with drug-induced ITP. The response to the thrombopoietin receptor agonist between April 5, 2021 and June 7, 2021 was a dramatic rise in the platelet count on June 11, 2021 (Fig. 1), immediately following the administration of 80 mg of docetaxel on June 9, 2021. This was indicative of the cytotoxic effect of chemotherapy on ITP as observed on two occasions of the seven previous administrations of intermittent parenteral cyclophosphamide at 1,500 mg. On the first occasion, the platelet count of 37,000/μL on day 1 showed a remarkable rise to 88,000/μL on day 2, 109,000/μL on day 3, and 174,000/μL on day 9. On the second occasion, the platelet count was 78,000/μL on day 1, which rose to 79,000/μL on day 2, 102,000/μL on day 3, 148,000/μL on day 5, 174,000/μL on day 6, 204,000/μL on day 10, and 250,000/μL on day 13. Dose escalation of eltrombopag was performed, but high-dose immunoglobulin was not attempted despite a theoretical advantage in cases of COVID-19, as there is no survival benefit of convalescent plasma in patients with COVID-19 pneumonia [1]. Corticosteroids were withheld, as the patient did not develop pneumonia requiring respiratory support [2].

The incidence of ITP associated with COVID-19 is rare. In total, 45 cases of new-onset ITP in conjunction with COVID-19 [3] were analyzed in terms of the clinical profile and outcomes through a literature review. The diagnosis of COVID-19-associated ITP should be made meticulously [3] by excluding concomitant factors that can cause thrombocytopenia in COVID-19 patients, such as sepsis, DIC, HLH, or TTP. ITP is common in elderly patients with moderate-to-severe COVID-19 [3]. The majority of ITP cases were detected over a week after the onset of COVID-19 symptoms, and some were even detected after clinical recovery [3]. ITP among asymptomatic COVID-19 patients accounted for 7% of the total cases, underscoring the need for COVID-19 testing in newly diagnosed ITP cases, regardless of the presence of COVID-19 symptoms [3]. The worsening of ITP in our COVID-19 case did respond to dose augmentation of the thrombopoietin receptor agonist, but there were no thromboembolic events. Among a few reports of worsening ITP affected by COVID-19, this is the first case report of recurrent ITP caused by COVID-19 that was successfully managed with eltrombopag alone [4-6].

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REFERENCES

1. Simonovich VA, Burgos Pratx LD, Scibona P, et al. A randomized trial of convalescent plasma in Covid-19 severe pneumonia. N Engl J Med 2021;384:619-29.
2. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;364:693-704.
3. Bhattacharjee S, Banerjee M. Immune thrombocytopenia secondary to COVID-19: a systematic review. SN Compr Clin Med 2020:1-11.
4. Hu Z, Chen W, Liang W, Xu C, Sun W, Yi Y. Severe exacerbation of immune thrombocytopenia and COVID-19: the favorable response to corticosteroid-based therapy-a case report. Ann Hematol 2021;100:2135-7.
5. Kondo Y, Kaneko Y, Oshige T, et al. Exacerbation of immune thrombocytopenia triggered by COVID-19 in patients with systemic lupus erythematosus. Ann Rheum Dis 2021;80:e77.
6. Merli M, Ageno W, Sessa F, et al. Recurrence of immune thrombocytopenia at the time of SARS-CoV-2 infection. Ann Hematol 2020;99:1951-2.

Therapy-related myeloid neoplasms after transcatheter arterial chemoembolization for hepatocellular carcinoma

TO THE EDITOR: Patients who are exposed to DNA-damaging agents, such as the chemicals used in cytotoxic chemotherapy and radiation therapy, are at risk of developing therapy-related myeloid neoplasms (t-MNs). Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths, especially in East Asia. Transarterial chemoembolization (TACE) is widely used in patients with HCC, wherein anthracycline or platinum-based agents are infused into the liver. Herein, we describe 8 cases of t-MNs that occurred after TACE in 2 tertiary institutes in Korea. A retrospective medical record review was performed for 8 patients: all were male; 4 had acute myeloid leukemia (AML), 1 had acute promyelocytic leukemia, and 3 had myelodysplastic syndromes (MDS). The TACE procedure was performed 2–14 times, and the cumulative dose of doxorubicin ranged from 60 to 700 mg. The median time for t-MN development after TACE was 36.4 months (range, 16.8–64.1 mo). Two patients were treated with sorafenib and 1 patient received radiation therapy. Patients who developed t-MNs after TACE for HCC generally showed a dismal prognosis; no patient with AML survived for more than 6 months and only 1 patient with MDS survived for 29 months after showing a good response to decitabine. We describe a new entity of t-MNs in patients who received TACE for HCC, an under-evaluated and under-reported disease that warrants further investigation. Considering its poor prognosis, early detection and optimal management are needed to improve treatment outcomes.

INTRODUCTION

Therapy-related myeloid neoplasms (t-MNs) are a subgroup of acute myeloid leukemia (AML) in the revised 2017 World Health Organization (WHO) classification. The neoplasms include therapy-related myelodysplastic syndrome (t-MDS), therapy-related myelodysplastic syndrome/myeloproliferative neoplasm (t-MDS/MPN), and therapy-related acute myeloid leukemia (t-AML) in patients who are exposed to cytotoxic or radiation therapy for an unrelated malignancy or autoimmune disease [1]. The pathogenesis of t-MN has not been completely elucidated. Historically, t-MN development has been considered a consequence of DNA damage induced by cytotoxic therapy or the induction of genome instability in normal hematopoietic stem cells. Recently, it has been argued that intrinsic factors, including preexisting hematopoietic cell clones or inherited mutations in cancer-associated genes, may play an important role in the pathogenesis of t-MNs [2].

There are several clinical subsets of t-MNs that correlate with the nature of prior therapy. The most common subtype (in ~70% of patients) develops after treatment with alkylating agents, such as cyclophosphamide, melphalan, platinum agents, or radiotherapy, for which the latency period (the interval between treatment and disease development) is 5–10 years. It is characterized by unbalanced aberrations of chromosomes 5 and 7 and/or a complex karyotype and is often preceded by MDS. The second-most common subtype develops after the use of topoisomerase II (TOP II) inhibitors such as anthracycline drugs or etoposide. This subtype has a shorter latency period (2–3 yr) without any preceding MDS and is frequently associated with *KMT2A/MLL* gene rearrangements [3].

T-MNs account for approximately 7–10% of all AML cases [4, 5], and the incidence is expected to increase because of increasing cancer survivorship. The most common preceding malignancies are breast cancer, lymphoma, and prostate cancer [2]. Hepatocellular carcinoma (HCC) is one of the most frequently diagnosed cancers and is a leading cause of cancer-related deaths, especially in East Asia; however, its implication has not been studied in t-MN. Transarterial chemoembolization (TACE) is a widely used therapeutic modality in HCC patients, and during this procedure, anthracycline or platinum-based agents are infused into the liver. Given the high incidence of HCC and the frequent use of TACE, we examined 8 cases of t-MNs that developed after TACE for HCC in two tertiary institutes in Korea.