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SARS-COV-2 infection in a patient with Evans syndrome: a silent enemy or an ally?

SARS-COV-2 infekcija kod bolesnika sa Evansovim sindromom: nevidljivi neprijatelj ili saveznik?

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Abstract

Introduction. During the current outbreak of Coronavirus disease 2019 (COVID-19), the way to manage patients with autoimmune diseases remains elusive due to limited data available. **Case report.** We presented a case of a COVID-19 positive 20-year-old female with prior history of Evans syndrome. The patients remained asymptomatic even though she had been treated with immunosuppressants (prednisolone and azathioprine) together with romiplostim. Moreover, her course of infection was accompanied by thrombocytosis, although her platelet count was mostly below the reference range before the infection. The patient was monitored vigilantly, with special regard to platelet count and signs of thrombotic events. **Conclusion.** Platelet count monitoring and romiplostim administration should be performed more cautiously in chronic immune thrombocytopenic patients infected by SARS-CoV-2.

Key words:
covid-19; evans syndrome; purpura, thrombocytopenic, idiopathic; romiplostim; thrombocytosis.

Apstrakt

Uvod. Tokom pandemije COVID-19 lečenje bolesnika sa autoimunskim bolestima veoma je izazovno, pre svega zbog nedostatka pouzdanih podataka. **Prikaz bolesnika.** Prikazana je dvadesetogodišnja COVID-19 pozitivna bolesnica koja se prethodno lečila od Evansovog sindroma. I pored činjenice da je bila lečena imunosupresivima (prednizon, azatioprin), zajedno sa romiplostimom, tokom celog toka infekcije kod bolesnice se nisu ispoljili simptomi. U krvnoj slici bolesnice uočena je trombocitoza tokom SARS-CoV-2 pozitivnosti, dok je broj trombocita pre infekcije bio ispod referentnog opsega. Bolesnica je praćena vrlo pažljivo, sa posebnim osvrtom na broj trombocita i eventualnu pojavu znakova tromboznih događaja. **Zaključak.** Neophodno je opreznije praćenje broja trombocita i doziranje romiplostima tokom SARS-CoV-2 infekcije kod bolesnika sa autoimunom trombocitopenijom.

Ključne reči:
covid-19; evansov sindrom; purpura, trombocitopenijska, idiopatska; romiplostim; trombocitoza.

Introduction

Patients with certain underlying medical conditions are (or might be) at increased risk for severe forms of Coronavirus disease 2019 (COVID-19). Addressing this issue, experts in different medical fields have provided guidelines on how to treat such patients during the pandemic. Thus, some recommendations regarding chronic primary immune thrombocytopenia (ITP) advise no changes in therapy because of the pandemic, even if it includes steroids and immunosuppressants [1]. Additionally, if a patient shows platelet count (PC) decrease and already uses a thrombopoietin receptor agonist (TPO-RA), a dose could be increased or a second one started. Short-term steroids (1–5 days) could be considered to increase PC, or intravenous immunoglobulins could be administered. Since low molecular weight heparin (LMWH) or heparin are widely employed for thromboprophylaxis in all hospitalized COVID-19 patients, its use is recommended even in patients with ITP. However, the potential benefits vs. risk of LMWH/heparin and the most beneficial dosage and schedule must be evaluated carefully for each ITP patient individually [2]. Herein, we presented a case of

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a SARS-CoV-2 positive patient with Evans syndrome (ES) treated with romiplostim, prednisolone and azathioprine who experienced transient thrombocytosis during the infection.

Case report

A 16-year-old female was diagnosed with primary ITP in October 2016. Corticosteroid therapy resulted in partial remission and corticosteroid-dependence. Afterwards, the patient was treated with azathioprine, vinblastine and eltrombopag without response. Moreover, at week 8 of eltrombopag usage, the patient developed autoimmune hemolytic anemia (AIHA) and a diagnosis of ES was made. At that point, azathioprine (2.5 mg/kg) and prednisolone (1 mg/kg) were initiated and the hemolysis parameters were normalized after 2 weeks of the therapy. Romiplostim was introduced in December 2019 and given once weekly at the average dose of 6.5 μg/week. Before the SARS-CoV-2 infection, PC had fluctuated (PC_{min} 4×10^9/L; PC_{max} 143×10^9/L; normal range is from 150×10^9/L to 400×10^9/L, Figure 1) but the patient showed no signs of hemorrhage. Azathioprine was continued due to AIHA. Namely, hemolysis occurred each time a reduction in immunosuppressant dose was attempted. In March 2020, a new episode of AIHA was registered. Therefore, prednisolone was reintroduced, which led an increase in hemoglobin level from 56 g/L to 99 g/L (normal range for women is 120 g/L to 150 g/L).

After contact with a SARS-CoV-2 positive person, a nasopharyngeal swab was taken on April 11, and proved negative. The test was repeated 10 days later with a positive result (Figure 1). The patient had an asymptomatic course of COVID-19, with normal serum levels of C-reactive protein (CRP) and interleukin (IL)-6. D-dimer was slightly elevated initially (1.23 mg/L; normal value: < 0.5 mg/L) and then manifested a declining trend. The chest X-ray was normal. At the next check-up (April 14) her hemoglobin and PC were 99 g/L and 160×10^9/L, respectively. Romiplostim was applied in a dose of 6 μg/week. One week later, PC was 768×10^9/L, so romiplostim was omitted and the need for anticoagulant prophylaxis was considered. While white blood cells, neutrophil to lymphocyte ratio and D-dimer levels were low, anticoagulant therapy was not administered. In the forthcoming period, for the first time since the patient was diagnosed with ITP, her PC remained above 100×10^9/L for more than a month. Romiplostim was given once when PC was 144×10^9/L. The first negative polymerase chain reaction (PCR) test was taken on May 21, and at the check-up on May 27, her PC was 7×10^9/L. Afterwards, the patient's PC continued to fluctuate as prior to the infection (Figure 1).

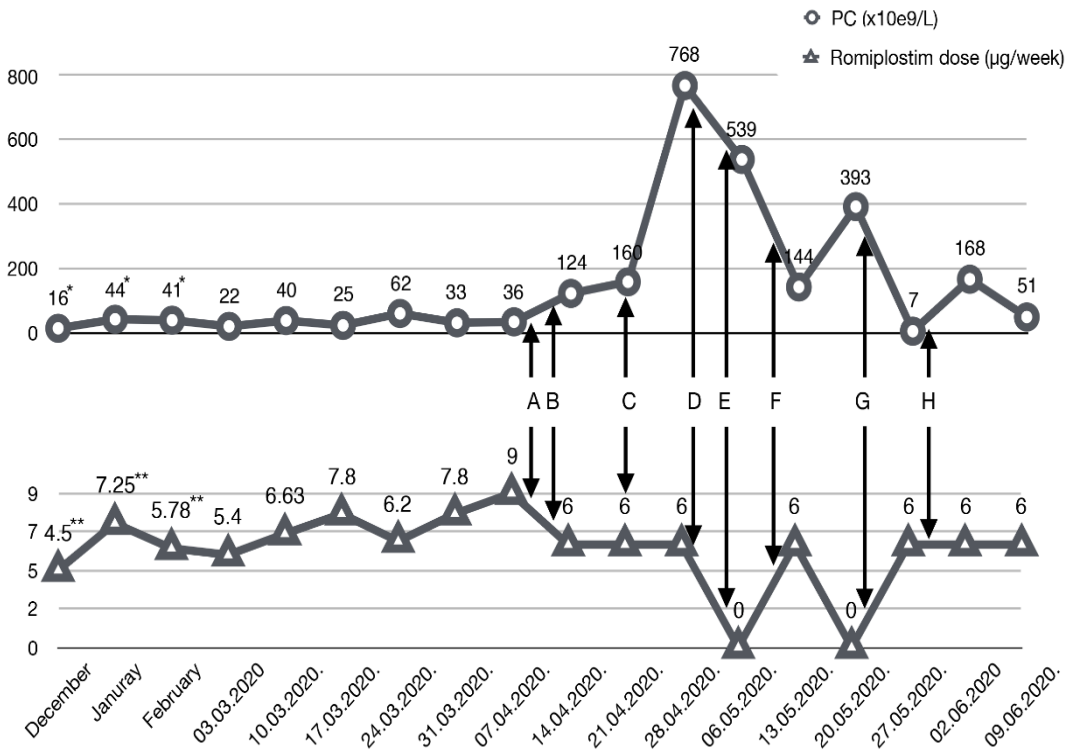

Fig. 1 – Platelet count (PC) and romiplostim dose dynamics before and during the SARS-CoV-2 infection. A – probable exposure date (April 4); B – the first swab test: negative (April 11); C – the first positive test (April 21); D – the second positive test (April 23); E – the third positive test (May 5); F – the fourth positive test (May 12); G – the first negative test (May 21); H – the second negative test (May 28).
***Average PC (× 10^9/L) for the month.**
****Average romiplostim dose applied (μg/week) for the month.**

Discussion

The majority of COVID-19 patients, especially those with nonsevere disease, have normal PC. However, thrombocytopenia has been registered among 20.7% of SARS-CoV-2 positive patients and it has been associated with more severe disease [3]. Moreover, several cases of COVID-19 associated acute ITP or even ES have been recorded [4, 5]. However, to our knowledge, this is the first case of thrombocytosis in a COVID-19 positive patient with chronic ITP.

Although the WHO [6] advised avoidance of corticosteroids in SARS-CoV-2 patients, the systematic reviews by Gao et al. [7] and Minotti et al. [8] showed that immunosuppression and immunodeficiency were not significantly associated with an increased risk of severe COVID-19. Having all this in mind, we decided to continue corticosteroids. Moreover, COVID-19 leads to systemic coagulation activation resulting in thromboembolic (TE) events in up to 40% of critically ill patients. On the other hand, the incidence of TE in ward patients varied between 3–5% [9]. Consequently, a prophylactic dose of LMWH should be introduced in all patients who require hospital admission [10]. However, there are no data regarding TE incidence and thromboprophylaxis in outpatients. Previous studies showed that PC $> 450 \times 10^9$/L, elevated D-dimer, CRP and erythrocyte sedimentation rate at initial presentation, stay in intensive care units, high white blood cells and high neutrophil-to-lymphocyte ratio were predictive of TE events [9, 11]. Additionally, ITP itself is considered a thrombophilic condition, with prevalence of thrombotic events up to 3–4 times greater than for the average control subject [12]. Moreover, the risk of thrombosis could be enhanced by TPO-RA [1, 13]. In addition, our patient had active hemolysis during the infection, which was a supplementary risk factor for venous thromboembolism [14]. Despite several thrombophilic factors, but considering that our patient was asymptomatic, not hospitalized, mobile, with low levels of inflammation parameters and D-dimer, we abandoned the idea of anticoagulant prophylaxis. However, her physical and biochemical status were regularly monitored.

Conclusion

The presented case indicated that PC monitoring and romiplostim administration should be performed more cautiously in ITP patients infected by SARS-CoV-2. Further studies are needed to provide us with information about TE risk factors and anticoagulant prophylaxis in ITP patients with SARS-CoV-2 infection.

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