Immune thrombocytopenia flare with mild COVID-19 infection in pregnancy: A case report

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the third zoonotic coronavirus to be identified in humans during the twenty-first century, after severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). The resultant disease, Coronavirus Disease 2019 (COVID-19), was first identified in December 2019 in Wuhan, Hubei province, China and rapidly evolved into a pandemic within months. In the UK, the first confirmed case was identified in late January 2020 and the first COVID-19-related death was recorded in March 2020. The clinical picture of COVID-19 ranges from asymptomatic infection to fatal pneumonia, with the latter caused by the ‘cytokine storm’ and the consequent acute respiratory distress syndrome (ARDS). Although SARS-CoV-2 affects the respiratory system primarily, gastrointestinal, genitourinary, nervous and cardiovascular systems’ affection was reported. The haematopoietic system is affected both quantitatively and qualitatively, with some of these changes, namely lymphocyte and platelet counts, bearing prognostic significance in the disease course.

Immune thrombocytopenia (ITP) is an autoimmune disease characterized by an isolated low platelet count (<100 × 10^9/l). The pathophysiology of ITP is complicated, with some aspects yet to be elucidated. Autoantibodies against platelet glycoproteins increase their destruction by macrophages and dendritic cells in the spleen and liver, and decrease their production by megakaryocytes. The initial trigger for the production of autoantibodies remains unknown and about 50% of patients lack these autoantibodies. An abnormal Th1/Th2 ratio, with skew towards the Th1 phenotype, and higher levels of Th17, Th22 and splenic follicular Th cells contribute to the autoimmunity. In addition, increased numbers of CD8+ T cells and reduced numbers of Treg cells also play a role. Herein, we present a case of a pregnant patient known to have ITP, who sustained a flare after being diagnosed with COVID-19.

A 34-year-old lady, pregnant in the second trimester (20/40 weeks; gravida 2 para 1), and known to have ITP since 2013, presented to the A & E department in our hospital with a one-day history of dry cough, fever, petechiae and gum bleeding. The patient had no other comorbidities and reported no recent change in her medications. Physical examination showed no other bleeding manifestations or respiratory symptoms, with no cardiacological or abdominal findings, apart from the known gestation. An initial full blood count (FBC) was remarkable for a platelet count of 13 × 10^9/l (normal range 150–450 × 10^9/l). The rest of her blood analyses, including renal and hepatic profiles, C-reactive protein, D-dimer and clotting screen (prothrombin and activated partial thromboplastin times, and fibrinogen level) were all unremarkable. A blood film did not show red cell fragments. A nasopharyngeal swab for SARS-CoV-2 PCR was taken on admission, and was later found to be positive. A working diagnosis of ITP flare was instated. Given the active bleeding, she was admitted and started on intravenous immunoglobulins (IVIG, 1 g/kg of body weight) and oral prednisolone (1 mg/kg of body weight). Respiratory symptoms and fever were managed conservatively, without the need for supplemental oxygen. On the next day of her admission (Day 1), the patient reported improvement in bleeding from her gums and no new petechiae. A drop in lymphocyte count to 1.2 × 10^9/l (normal range 1.5–4 × 10^9/l) was also noted. Day 2 showed further improvement in platelet count to 64 × 10^9/l. Based on the clinical improvement and the
recovering platelet count, the patient was deemed medically fit for discharge with outpatient follow-up. Figure 1 shows the platelet and lymphocyte count before, during and after the admission.

Dysregulated immune response is pivotal in the pathophysiology of ITP and is thought to contribute to the thrombocytopenia seen with COVID-19. Mechanisms suggested for the latter include:

1. Decreased platelet production through direct infection of the bone marrow cells, as part of secondary haemophagocytic lymphohistiocytosis in patients with severe COVID-19, or due to the disruption of platelet release in the pulmonary circulation.
2. Increased platelet clearance by the immune system, non-specifically through coating by immune complexes produced as a part of the immune response against SARS-CoV-2, or specifically by platelet antibodies produced through molecular mimicry to SARS-CoV-2.
3. Increased consumption secondary to low-grade coagulopathy.

Our patient had mild COVID-19 with no coagulopathy, and hence most of the above mechanisms are unlikely to be applicable. The platelet nadir and the response to IVIG and steroids makes a diagnosis of gestational thrombocytopenia unlikely. The normal kidney and liver functions, and absence of red cell fragments, excluded thrombotic microangiopathies. Taking this into consideration, and based on the chronology of events, COVID-19 is likely to be the precipitating factor for the disease flare. One mechanistic explanation, in the context of pre-existing ITP, would be the overactivation of T cells, manifested by an increase of Th17 and high cytotoxicity of CD8 T cells as reported by Xu et al., albeit the fact that their patient developed ARDS and hence had severe COVID-19.

Of relevance to our current report is the publication by Zulfiqar et al. wherein they presented a patient with ‘de-novo’ ITP developing after infection with SARS-CoV-2. It is to be highlighted that the patient in their report had autoimmune hypothyroidism and received low-molecular-weight heparin, which might have contributed to the thrombocytopenia. Likewise, ‘de-novo’ ITP with COVID-19 infection was diagnosed in recently published case reports, one of which was on a pregnant lady in her third trimester. To the best of our knowledge, our report is the first of ITP flare in a patient with COVID-19.

To conclude, we reported a case of a pregnant patient known to have ITP who developed a flare of her disease in the context of mild COVID-19 infection. Although, COVID-19 remains a primarily respiratory disease, extra-pulmonary manifestations are increasingly recognized and vigilance is needed to detect these in an effort to mitigate complications.

**Conflicts of interest**

The authors declare to have no potential conflicts of interest regarding the present work.

**Author contributions**

GN collected the data and wrote the manuscript. CG, CB and SA critically reviewed the manuscript.

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**Fig 1.** Line chart showing the platelet and lymphocyte counts before, during and after admission. The grey-shaded part highlights the inpatient admission period. D0 denotes the admission day. The patient had frequent full blood counts before and after admission given her pregnancy.
I read with interest the recent article by Li et al., detailing the risk for COVID-19 pneumonia and for the different ABO blood groups.

After demonstrating that group O healthcare workers were less likely to become infected with SARS-CoV-2, a research group proved that anti-A blood group natural isoagglutinins inhibit SARS-CoV entry into competent cells and could opsonize viral particles leading to complement-mediated neutralization. Since SARS-CoV-2 uses the same receptor as SARS-CoV, anti-A isoagglutinins are expected to have similar effects against SARS-CoV-2, accordingly, clusters of glycosylation sites exist proximal to the receptor-binding motif of the SARS-CoV and SARS-CoV-2 S protein.

Several recent publications from China, the USA, Turkey, Spain and Italy have shown that the odd ratio for acquiring COVID-19 is higher in blood group A than in blood group O when compared to healthy controls (Table I), while no statistically significant difference was found for groups B and AB. Most importantly, the Italian–Spanish genome-wide association study identified the rs657152 polymorphism in the ABO locus on chromosome 9q34 (and only one other polymorphism in chromosome 3p21-31) as the only susceptibility locus for respiratory failure in COVID-19, suggesting that, in addition to disease acquisition, ABO blood group could also affect disease severity.

Blood group A and ABO polymorphisms (rs495828, gene promoter, and rs817674, exon 7) predispose to COVID-19 severity via increased ACE activity and cardiovascular disorders. In a multivariate regression analysis for predicting COVID-19 prevalence, C3 and ACE1 polymorphisms were more important confounders in the spread and outcome of COVID-19 in comparison with the A allele. But an alternative explanation should be considered.

Enveloped viruses show ABO antigens on the virion’s surface and isoagglutinins act as neutralizing antibodies. Under this model, transmission from group O individuals and between individuals of the same group will always be maximal. High titre isoagglutinins can prevent transmission, while low-titre isoagglutinin could lead to milder disease presentations.

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