

## Letter to the Editor

# Evan's in a Case of Acute Myeloid Leukemia Post COVID-19 Infection

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## Abstract

The Spectrum of Manifestations of COVID-19, A Pandemic Caused By Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), although emerged as a respiratory tract infection, is now regarded as a multi- system disease including hematological manifestations such as lymphopenia, thrombocytopenia, disseminated intravascular coagulopathy, COVID-19 associated coagulopathy and autoimmune cytopenia. It has been proposed that proinflammatory state induced by COVID-19 can lead to immune dysregulation and hence autoimmune cytopenia. Various case series have reported autoimmune hemolytic anemia (AIHA) post COVID-19 infection. We are reporting an unusual presentation of evan's syndrome (Cold Autoimmune Hemolytic Anemia (CAIHA) with immune thrombocytopenia) secondary to COVID-19 in a case of Acute Myeloid Leukemia (AML) on consolidation chemotherapy with high dose cytarabine at our institute. As steroid did not seem to have any major response in our case, it is imperative to have a better understanding to guide the use of immunosuppression in autoimmune complications of SARS-CoV-2. We emphasize that one needs to be vigilant to look for these rare autoimmune manifestations, particularly in patients with underlying immune aberrancies due to their primary disease.

**Keywords:** Evans syndrome; Cold autoimmune hemolytic anemia; COVID-19; Acute myeloid leukemia

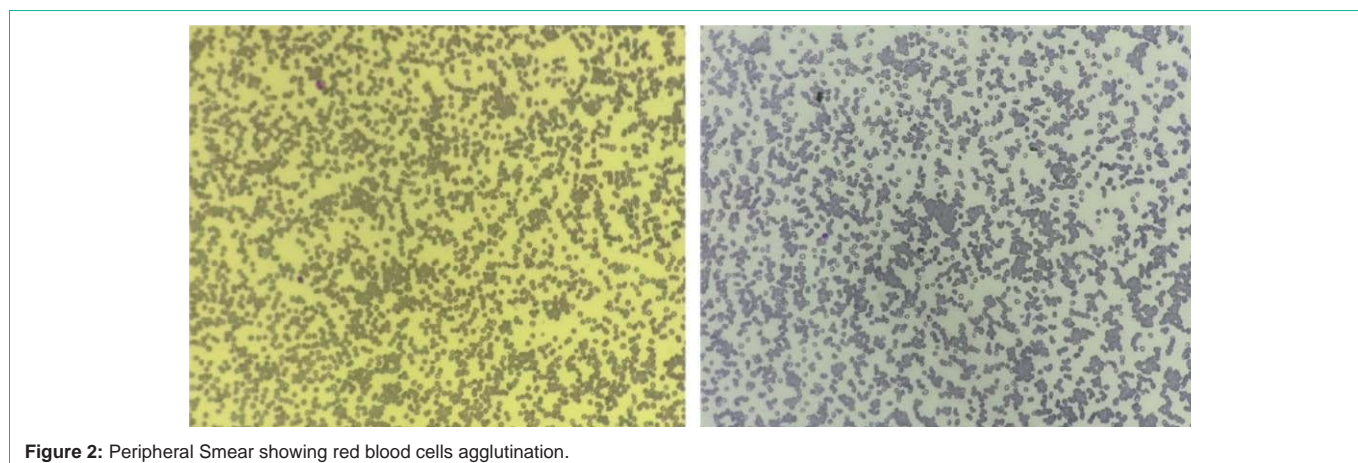
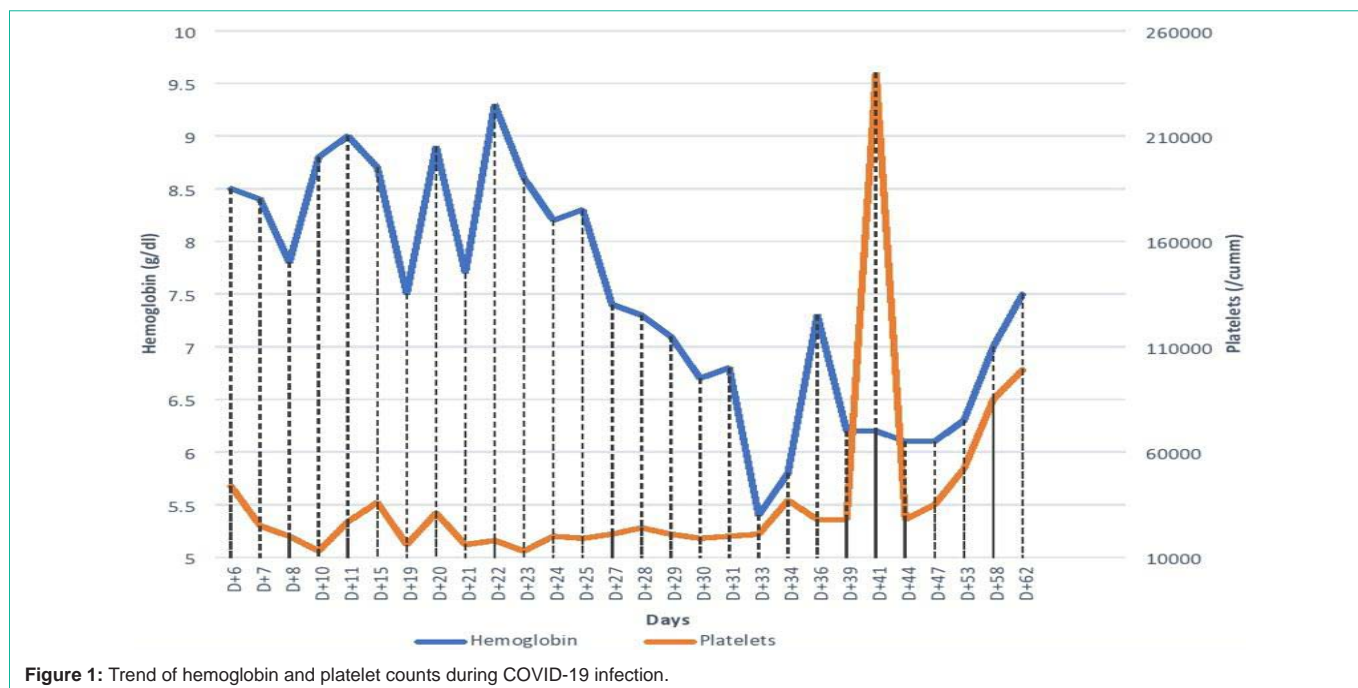
## Dear Editor,

Coronavirus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has rapidly evolved into a pandemic infecting individual all over the world as a multi- system disease [1]. Cardinal hematological manifestations are lymphopenia, thrombocytopenia, disseminated intravascular coagulopathy, COVID-19 associated coagulopathy and autoimmune cytopenia [2]. Various case series have reported Autoimmune Hemolytic Anemia (AIHA) and Evan's Syndrome (ES) post COVID-19 infection [3]. Unusual presentation of ES is Cold Autoimmune Hemolytic Anemia (CAIHA) with immune thrombocytopenia [4]. We, hereby, report a case of ES with this uncommon association in a case of Acute Myeloid Leukemia (AML).

**Case:** A 49-year-old male, AML with t (8:21), was in morphological remission post 3+7 (daunorubicin cytosine) induction chemotherapy and received consolidation with high dose cytarabine. During his 3<sup>rd</sup> consolidation cycle in June 2020, he developed fever, cough and sore throat. Chemotherapy was interrupted and was found to be positive for COVID-19 by RT PCR. He received intravenous dexamethasone 10mg once a day for 10 days as he was hypoxic with ground glass opacities on chest imaging, although did not receive low molecular weight heparin due to thrombocytopenia. Screening for venous thromboembolism was negative. On day+6 post chemotherapy, leucocyte and platelet counts started decreasing probably due to chemotherapy, for which growth factor support was started. His leucocyte and platelet counts recovered by day+13. On day+21, again a fall in hemoglobin and platelets was observed with peripheral smear showing marked agglutination of red blood cells

(rbcs) (Figure 1). Direct coombs test was monospecifically positive for C3b+C3d. Although lactate dehydrogenase (LDH=185U/ml) and reticulocyte count (<0.5%) were not increased, repeated peripheral smear showed agglutination of rbcs (Figure 2). Also, there was gradual drop in hemoglobin and platelet which required transfusions. Hence, an increased dose of steroids were restarted on day+26 (methylprednisolone 1mg/kg/day) in view of autoimmune cytopenia. On day+34, he was still positive for COVID-19. As there was no major improvement with steroid, it was stopped and patient was kept on transfusions as required. Gradually hemoglobin and platelets started improving by day+55. Peripheral smear showed no rbcs agglutination by this time. Repeat COVID-19 test by PCR was negative on day+59. Hemoglobin and platelets became normal by day+63 and bone marrow examination was performed which showed patchy cellular marrow with erythroid prominence and adequate megakaryocytes. He was planned for next cycle of consolidation thereafter.

Although we are aware of our shortcoming that Mycoplasma pneumoniae infection could not be ruled out due to non-availability of test at our institution, dysregulation of the immune system in COVID-19 could have created favorable conditions for the development of ES in our patient. The marked elevation of proinflammatory markers such as interleukins and interferons in severe COVID-19 point to a state of exaggerated immune response to SARS-CoV-2 referred to as cytokine storm [5] which can be monitored in clinical practice by laboratory tests such as LDH, ferritin, C-Reactive Protein (CRP), fibrinogen and procalcitonin. Understanding the link of cytokine storm and autoimmune cytopenia



is a crucial step to remodel the therapies of COVID-19, still very less is known about the marked difference between immune responses amongst the patients.

To conclude, in accordance to above mentioned case reports and our experience of CAIHA with immune thrombocytopenia, autoimmune cytopenia is not so uncommon hematological manifestation of this disease. As steroid appears to have no major role in treatment of these cytopenia, further data are needed to guide the use of immunosuppression in autoimmune complications of SARS-CoV-2. We emphasize that one needs to be vigilant to look for these rare autoimmune manifestations, particularly in patients with underlying immune aberrancies due to their primary disease.

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