Autoimmune hemolytic anemia following COVID-19 vaccination
Meredith Ryan, M.D. Patricia Louis, M.D., Hyma Polimera, M.D., Shavini Athukorala
Penn State Milton S. Hershey Medical Center

Introduction
Vaccination against COVID-19 has been proven to be the safest and most effective method of protecting against the devastating respiratory virus. Mostly mild and moderate adverse events were reported in vaccine trials. Following widespread vaccination, there have been case reports of severe hematologic complications. Here, we report a case of autoimmune hemolytic anemia one day following administration of the first dose of the Pfizer-BioNTech COVID-19 vaccine.

Patient Presentation
A 26 year old man with a history of limb-girdle muscular dystrophy, scoliosis, rhabdomyolysis, migraines, and chronic back pain presented after a fall preceded by lightheadedness, progressive extremity weakness, myalgias, and dark urine. Vital signs were notable for heart rate of 124bpm but were otherwise within normal limits.

Physical exam was notable for scleral icterus and lower extremity weakness. Abdominal ultrasound revealed mild hepatosplenomegaly.

Labwork on admission was remarkable for a hemoglobin 7.1 g/dL (baseline 8 months earlier, 15.0), MCV 83, WBCs 6,400/µL, platelets 173,000/µL, total bilirubin 5.7 (direct, 0.6), LDH 514 u/L, haptoglobin <10, and CPK 3346u/L. He was admitted to the medicine service at Penn State Milton S. Hershey Medical Center.

Hospital Course
Two days after admission, his hemoglobin dropped to 4.5 g/dL. This was accompanied by a severe headache. He was transfused a total of 11 units of packed red blood cells over five days for hemoglobin <8 g/dL. He noted that the severity of his headaches corresponded with need for transfusion.

Direct antiglobulin test (DAT) was negative for both anti-IgG and anti-C3.

Peripheral smear was normal and notable for no increase in schistocytes nor spherocytes.

A bone marrow biopsy was performed and revealed hypercellular marrow with adequate megakaryopoiesis, markedly increased dysplastic erythropoiesis and adequate myelopoiesis. Flow cytometry revealed no immunophenotypic evidence of non-Hodgkin’s lymphoma.

Hematology was consulted and despite the negative DAT, his presentation was felt to be consistent with an autoimmune process and he was started on oral prednisone 1mg/kg on hospital day 6. The day following the initiation of prednisone, his blood counts had stabilized and he required no further transfusions. A micro/super Coombs test was sent. Incidentally, the patient noted that he had received the initial dose of the Pfizer-BioNTech COVID-19 vaccine the day prior to admission.

On hospital day 10, he was discharged with a hemoglobin of 11.1 and a prednisone taper over the next month. By the time of his followup visit with his PCP one month later, he had no complaints and his hemoglobin had recovered to 13.8 g/dL.

Discussion
Based on the clinical presentation, and despite the negative DAT, this patient was felt to have an autoimmune hemolytic anemia. He responded promptly to corticosteroid therapy. The patient’s antibody screen from the micro/super Coombs test which resulted several weeks later did reveal a low affinity IgG warm auto-antibody reactive by 4c LISS wash IAT. This was felt to be suggestive of a warm autoimmune hemolytic anemia.

The diagnosis of hemolytic anemia may be challenging to make given the incomplete understanding of the pathophysiology and the vast range of possible provoking factors. Additionally, about 3–11% of hemolytic anemia cases may be DAT negative. In our patient, despite transfusion support, the hemoglobin dropped to dangerous levels despite the negative DAT, this patient may be DAT negative. In our patient, despite transfusion support, the hemoglobin dropped to dangerous levels and his clinical trajectory may have ultimately proven fatal had steroid therapy not been initiated promptly on the suspicion of a hemolytic anemia.

The role of the COVID-19 vaccine that leads to autoimmune response is not well understood. One theory is an autoimmune response via molecular mimicry of host antigens by viral-derived peptides that cause cross-activation of autoreactive T or B cells. The vaccine-induced host response leads to the destruction of erythrocytes and hemolysis. In this case, the reaction occurred after receiving the first dose.

Conclusions
We present a rare case of DAT-negative severe AIHA following the first dose of the mRNA COVID-19 vaccine, which was successfully treated with corticosteroids. This case highlights the importance of maintaining a high clinical suspicion of AIHA in the setting of unexplained hemolytic anemia, and a super Coombs or micro-Coombs test should be considered. Given effective treatment options that significantly improve survival, it is essential for physicians to identify the mRNA COVID-19 vaccine-related AIHA and to entertain this uncommon diagnostic test with atypical presentations such as unexplained hemolytic anemia.

References