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Acute Hemoglobin Decline with Signs of Hemolysis in Chronically Transfused Beta-thalassemia Patient Post Pfizer-BioNTech COVID-19 (BNT162b2) Vaccine: A Case Report

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Abstract

Thalassemia is an inherited hemoglobinopathy requiring lifelong blood transfusions and iron chelation. Chronic transfusions can lead to alloimmunization and hemolytic reactions. We discuss a patient with a well-established and stable transfusion cycle who showed signs of an acute hemolytic process following administration of the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine. The patient's pre-transfusion hemoglobin over the four weeks around vaccine administration was 1.48 g/dL lower than the pre-transfusion hemoglobin during the three months prior to and after the vaccine administration period. His bilirubin (primarily indirect) was 0.74 mg/dL higher during the vaccine period. Both values returned to baseline within two weeks following the second vaccination. This report signals a novel adverse reaction in the thalassemia population not reported in the study trials. Numerous thalassemia patients have and continue to receive this vaccine (and other vaccines) amidst this pandemic and our goal is to highlight the benefit of closer monitoring and possibly more frequent transfusions during the vaccine administration period.

Keywords: Thalassemia; Pfizer vaccine side effects; Hemolysis from COVID vaccine

Introduction

Thalassemia is an autosomal recessive hereditary chronic hemolytic anemia due to partial or complete deficiency in the synthesis of α-globin chains (α-thal) or β-globin chain (β-thal) which compose the adult hemoglobin (α2β2). A variety of mutations in the corresponding genes can cause these disorders. At the molecular level, mutations generate unstable globin chains that precipitate intracellularly, resulting in hemolysis and premature destruction of RBCs. Chronic life-long blood transfusions are required for patients with severe thalassemia to provide functional RBCs and suppress ineffective erythropoiesis [1]. Cumulative exposure through transfusions increases risk of red cell alloimmunization and subsequent delayed hemolytic transfusion reactions (DHTRs) [2,3].

Antigen-matching can prevent alloimmunization to varying degree. Here we discuss a case of one such chronically transfused patient with a stable transfusion plan using cross-matched compatible units who had an acute decline in baseline pre-transfusion hemoglobin after receiving the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine [4]. This patient received the vaccine few days after nationwide rollout and experienced hemoglobin declines after both the first and second dose. Given the novelty of this vaccine, this is the first documented case of possible hemolysis reported as a side-effect of the Pfizer-BioNTech COVID-19 vaccine [5]. The aim of this report is to encourage more frequent monitoring and possibly more frequent transfusions if hemoglobin decline is noted, especially given the now wider availability of the COVID-19 vaccine and possibility of upcoming booster shots.

Case Presentation

This case report features a 29-year-old male with B-thalassemia major diagnosed at the age of 6 months; he has received blood transfusions every two to three weeks since his diagnosis. The patient has been on iron chelation since age four, was splenectomized at age 11 due to splenomegaly from extramedullary hematopoiesis, and has received antigen matched units since age 15. Pertinent notable results include well-controlled liver iron concertation of 1.3 mg/g and serum ferritin ranging from 100-200 ng/ml.

Antibody identification testing on 12/11/2019 showed a warm autoanti-E. The patient previously had probable cold autoantibodies and warm alloanti-Cw, which were not redemonstrated during this report. Transfusion service recommendations included a conservative transfusion strategy to crossmatch and transfuse units from little c, E, Cw antigen negative donors. The patient had received blood transfusions, as scheduled, every two to three weeks leading up to his first vaccination on December 18th, 2020. For the three months leading up to the vaccine the average pre-transfusion hemoglobin was 8.48 g/dL and average total bilirubin was 1.99 mg/dL. Over the four weeks following the first vaccination (and including the second vaccination on January 8th, 2021), the average hemoglobin was 6.96 g/dL and average total bilirubin was 2.73 mg/dL (predominately indirect). After these findings were observed, the patient was transfused on a two-week interval in anticipation of his second vaccine. He also received hemoglobin checks every three to four days. Despite the more frequent transfusions, his hemoglobin still measured below-average at 7.1 g/dL seven days after the second vaccine. During the three months following the second vaccine, the average hemoglobin had increased to 8.92 g/dL and average total bilirubin was 2.11 mg/dL. To summarize, the main event was a marked hemoglobin drop to 6.9 g/dL noted 10 days after the first vaccine followed by a similar drop to 7.1 g/dL seven days after the second vaccine (Table 1). Figure 1 also shows the trend graphically noting a dip below normal pre-transfusion hemoglobin around the vaccine administration even with frequent transfusions.

Around this period, the patient received frequent hemoglobin checks (every three to four days), extensive hemolysis evaluations, and repeat direct antiglobulin testing. The patient's LDH peaked at 476 U/L around the second vaccine and has since returned to his baseline of 150-200 U/L. Other hemolysis labs were less conclusive: haptoglobin frequently measured <6 mg/dL and the plasma free hemoglobin remained unchanged (<10 mg/dL) during this period, and DAT reactivity was 2+ to 3+ even prior to the vaccines. Extensive blood bank testing did not reveal a new antibody (allo- or auto-).

In regards to his clinical presentation, the patient endorsed a moderate headache that started a few days after the first vaccine which lasted a few weeks, improving once his hemoglobin was back to baseline. This headache was subjectively prolonged and more severe than others he has experienced during periods of low hemoglobin (usually after prolonged interval between transfusions when on vacation, etc). No other symptoms associated with the vaccine were noted. Specifically, the patient did not experience any fevers, myalgias, muscle soreness, or cough in the period leading up to or after the vaccine. No other lifestyle changes, new medications, or other significant life changes were present during this period.

Table 1: Summarizes the frequently checked laboratory studies. Not all timeframes had lab values to report.

	Hgb (g/dL)	Total Bilirubin (mg/dL, predominately direct)	DAT reactivity	LDH (U/L)	Haptoglobin (mg/dL)	Plasma free hemoglobin (mg/dL)
Three-month average prior to vaccine	8.48	1.99	2+/3+	170		
Four weeks after 1st vaccine	6.96	2.73	2+/3+	293.5	<6	<10
Three-month average after the second vaccine	8.92	2.11	2+/3+	190	<6	<10

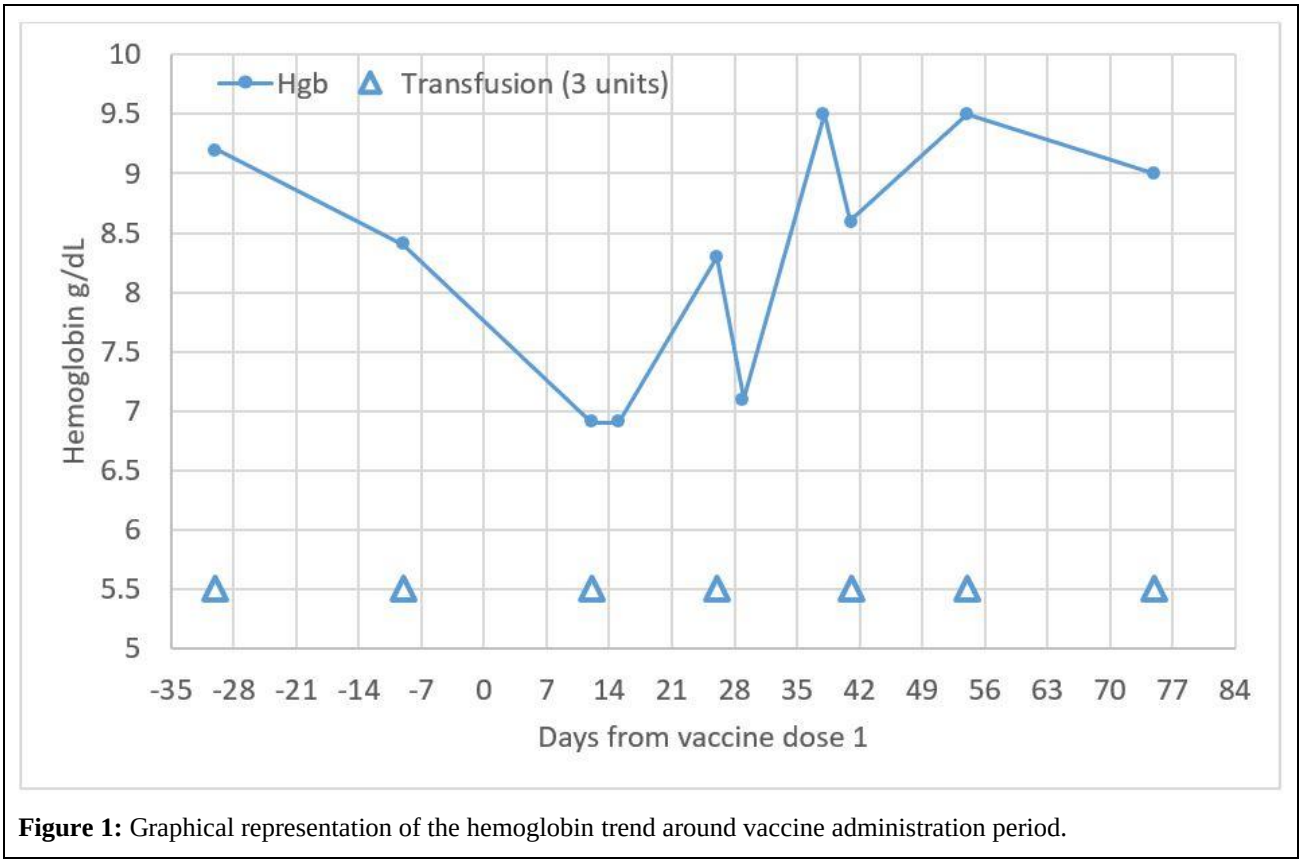

Figure 1: Graphical representation of the hemoglobin trend around vaccine administration period.

Discussion

This case report highlights a novel adverse reaction associated with the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine. Although causality is not proposed by this case report, it does provide some findings associated with an acute hemolytic process in our patient. The average hemoglobin decline to 6.96 g/dL with associated rise in bilirubin (primarily indirect) along with rise in LDH are all supporting signals for hemolysis. Although, as noted above, other measurements were less conclusive (i.e. plasma free hemoglobin). In addition, the return to baseline after the vaccination cycle was complete further supports an associated acute process. Upon investigation of the literature, our highest suspicion is for an antibody-mediated hemolytic reaction, though our testing was not able to identify a new antibody in the patient that developed after the vaccine administration. Still, the likelihood of a transient antibody not specifically detected by the assay is very much possible.

Though we do not have sufficient evidence to suggest causality, our findings support that the novelty of the vaccine allows room for rare adverse reactions in specific populations that were not seen in the study trials. Numerous patients with thalassemia or other transfusion-dependent anemias have and continue to receive this vaccine amidst the pandemic, and we hope this report both highlights the possibility of novel reactions and supports the benefit of closer monitoring and possibly more frequent transfusions during the vaccine administration period.

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