Journal of Community Medicine & Public Health
Kharaba A, et al. J Community Med Public Health 6: 264.
www.doi.org/10.29011/2577-2228.100264
www.gavinpublishers.com



Case Report

# Methemoglobinemia and Hemolytic Anemia after AstraZeneca COVID-19 Vaccine: A Case-Report

**Ayman Kharaba[1*], Amal Albeihany[2], Reham Kharabah[3]**

[1]Department of Pulmonary and Critical Care, King Fahad Hospital, Madinah, Saudi Arabia

[2]Department of Medicine, King Faisal Specialist Hospital, Madinah, Saudi Arabia

[3]Department of Family Medicine, King Fahad Hospital, Madinah, Saudi Arabia

[*]**Corresponding author:** Ayman Kharaba, Consultant, Department of Pulmonary and Critical Care, King Fahad Hospital, Madinah, Saudi Arabia

**Citation:** Kharaba A, Albeihany A, Kharabah R (2022) Methemoglobinemia and Hemolytic Anemia after AstraZeneca COVID-19 Vaccine: A Case-Report. J Community Med Public Health 6: 264. DOI: 10.29011/2577-2228.100264

**Received Date:** 25 October, 2022; **Accepted Date:** 31 October, 2022; **Published Date:** 04 November, 2022

## Abstract

**Background:** We are reporting a rare case of methemoglobinemia and non-autoimmune hemolytic anemia after AstraZeneca COVID-19 vaccination in the absence of an identifiable precipitating drug. **Case presentation:** A 33-year old male was admitted with jaundice and hypoxemia after AstraZeneca COVID19 vaccination. Upon admission, he was hypoxic and had normal other vital signs without any signs of respiratory distress. An arterial blood gas revealed a normal partial pressure of oxygen and a high methemoglobin level confirming a methemoglobinemia diagnosis. Hemolysis was diagnosed with decreased levels of hemoglobin, increased levels of indirect bilirubin, increased reticulocyte count, and lactate dehydrogenase level. A hemolytic anemia investigation panel came back normal, including the glucose-6-phosphate dehydrogenase level (G6PD). COVID 19 PCR was negative. A second G6PD test was done in six weeks' follow up, revealing a low level and establishing a G6PD diagnosis. **Conclusion:** This is the first case to be reported with methemoglobenima and non-autoimmune hemolytic anemia post AstraZeneca vaccine in a patient with G6PD deficiency.

**Keywords:** COVID19; Hemolysis; Methemoglobinemia; AstraZeneca; Vaccines

## Introduction

Since WHO declared COVID19 a pandemic on March 11, 2020, more than 200 million people have been infected worldwide [1].

Four different types of vaccines were evaluated for the necessary criteria of safety and efficacy. The AstraZeneca/Oxford vaccine was among the first to be recognized. As per WHO, many side effects have been reported post AstraZeneca covid19 vaccine, including pain, swelling, tenderness, redness at the injection site, headache, muscle pain, nausea, chills, and fever. Anaphylactic reaction and thromboemolic complications are uncommon side effects [2].We are reporting a rare concurrence of methemoglobinemia and hemolytic anemia post AstraZeneca vaccine.

## Case Study

A 33-yearold man without previous medical illness presented to the emergency department with a 6-hour history of body aches, fever associated with yellow sclera, and dark red urine. His symptoms started two hours after the COVID-19 vaccine (Astra Zeneca). He denied any respiratory symptoms. He gave a history of nausea but no vomiting. He has no history of any medication in this period, except for the vaccine. His initial vital signs included a blood pressure of 110/90 mmHg, heart rate of 80, temperature of 37.5 degrees Celsius and respiratory rate of 25/min. His peripheral oximetry showed an 80% saturation in room air. The physical exam was unremarkable, without any signs of respiratory distress. His peripheral oximetry remains at 80% in spite of the 15L non-rebreather facemask oxygen. Initial laboratory exams showed an elevation in lecucytosis, anemia, and elevated total bilirubin, which was mainly indirect at 89%. The chest x-ray was normal (Figure 1) and the CT scan anigo of the chest showed a normal lung field and no evidence of pulmonary embolism (Figure 2).

An ABG was done on a non-rebreather mask at a rate of 15 L/ min, which showed pH 7.44, $pCO_2$ of 30 mmHg, $pO_2$ of 374, and oxygen saturation of 99.4% while peripheral oxygen saturation of 82% (Figure 3).

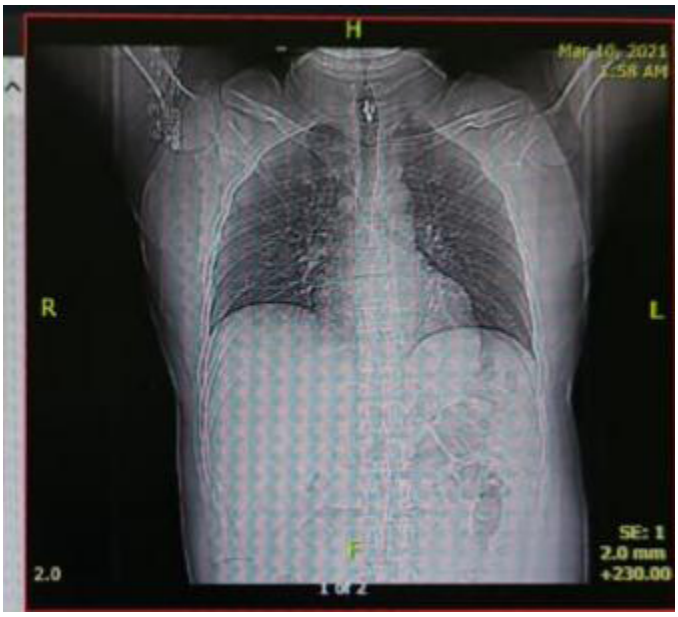


**Figure 1:** Chest X-ray of the patient on day of admission.

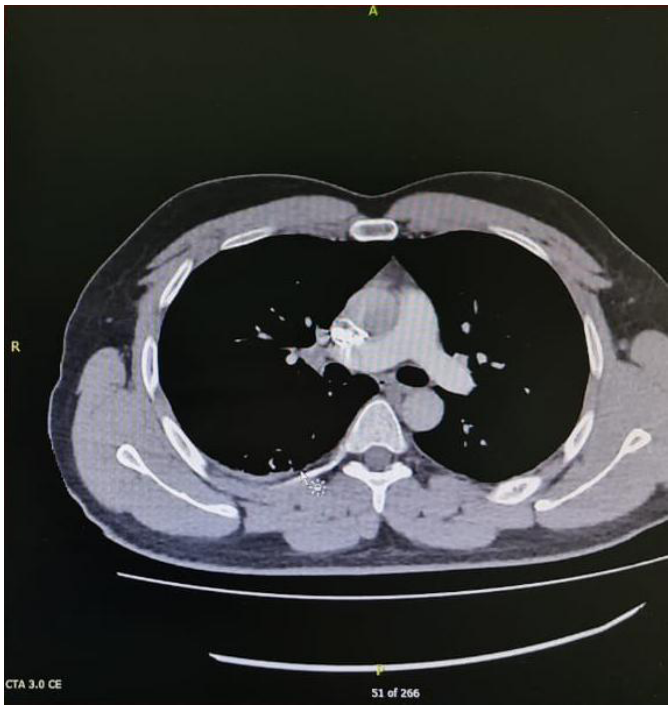


**Figure 2:** CT Angiography showing no evidence of pulmonary embolism.

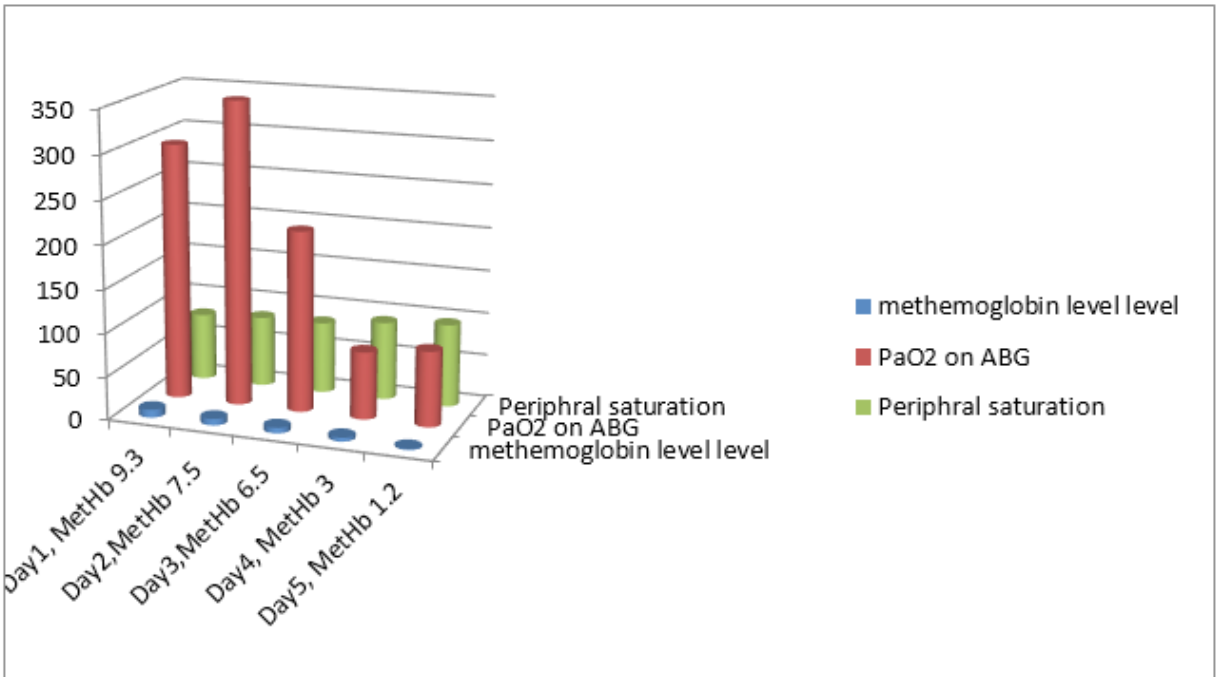


**Figure 3:** Relationship between Methemoglobin level, $PaO_2$ on ABG and peripheral Saturation Day 1 to Day 3 patient was on 15L NRFM, Day 4, Day 5 on room air.

A patient was admitted to the critical care unit. The anemia investigation showed Hb of 7g/dl, which dropped to the lowest 5.5 g/dl with normal MCV and MCH. The reticulocytic count was 8.1%. His comb's tests, direct and indirect, were negative and his LDH was 1862 (Table 1). Hemoglobin electrophoresis was normal with HbA1 97.3% and HbA2 2.7%. COVID19 and hepatitis serology A, B and C were negative. His biochemistry, including BUN and creatinine, was normal and his G6PD level was normal. In the first two days, his Hb dropped to the lowest 5 g/dl with normal renal function and with the same oxygen saturation in spite of high oxygen flow. The patient was managed with intravenous fluid and blood transfusions of a total of 4 units of PRBC. As regards methemoglobinemia, it was mild and managed conservatively without methylene blue. His condition gradually improved, his bilirubin level returned to normal, his Hb level improved with blood transfusion, and his methemoglobinemia level returned to normal. As his methemoglobin level was reduced, his oxygen saturation improved and returned to normal (Figure 3). The patient's condition was monitored in the clinic and remained stable. A repeat G6PD level in six weeks was low (35 mU/109RBCs), which confirms the diagnosis of G6PD anemia.

| Lab/ date | Day 1 | Day 2 | Day 3 | Day 4 | Day5 | Day 6 | Day 15 |
|---|---|---|---|---|---|---|---|
| WBC | 25 | 32 | 31 | 21.5 | 17.4 | 12.6 | 8 |
| Hb | 11.4 | 7.2 | 5.5 | 8.6 | 10.2 | 11.2 | 14.5 |
| PLT | 331 | 264 | 224 | 197 | 198 | 240 | 383 |
| PTT | 29 | 1 | | 24.9 | 26 | | |
| INR | 0.95 | 30 | | 0.92 | 1 | | |
| Reticulocyte count | | | 8.1 | 7.6 | | | |
| BUN | 6.6 | 7.9 | 8 | 4.7 | 5 | | 4.4 |
| Creatinine | 85 | 97 | 89 | 63 | 77 | | 90 |
| ALT | | | | 53 | 39 | 40 | 60 |
| AST | 85 | | | 66 | 41 | 60 | 29 |
| Total Bilirubin | 187 | | 149.8 | 73 | 22.5 | 14 | 12.5 |
| Direct bilirubin | 20 | | 20.2 | 15 | 8 | 5 | 3.5 |
| LDH | | 1862 | | 1756 | 1000 | 900 | 200 |

**Table 1:** Patient laboratory results.

We believe a methemoglobenima and non-autoimmune hemolytic anemia is a potential complication post AstraZeneca vaccination in a patient with G6PD deficiency.

## Discussion

Methemoglobinemia is a rare condition characterized by tissue hypoxia with normal partial pressure of oxygen in the blood due to increased methemoglin levels [3]. Patients usually present with cyanosis and dyspnea that may progress to coma and severe respiratory failure [4]. Oxidizing agents are the most common cause of acquired methemoglobinemia [5].

The oxidation of hemoglobin's iron to its ferric state leads to a failure of oxygen carriage by the hemoglobin. Medications and toxins are the major triggers of the oxidation burst. Patients with genetic defects in anti-oxidation are more liable to this condition [3]. Drugs like nitrate derivatives nitroglycerin, nitrite derivatives (nitric oxide and nitroprusside), sulfonamides, dapsone and some local and topical anesthetics (lidocaine, prilocaine) have been reported to cause methemoglobinemia [6].

Methemoglobinemia and non-immune hemolytic anemia have been well documented in patients with an inherited G6PD defect [7]. Oxidative stress damage plays an important role in infections [8]. However, whether infection-related ROS insults are enough to promote both methemoglobin and hemolysis is still unknown. [9] With respect to COVID-19, there is increasing evidence that oxidative stress worsens lung injury during infection: an imbalance between high ROS production and a weak anti-oxidation system is thought to explain disease progression

and severity in preclinical studies [10]. During the COVID19 pandemic, many reports described the concurrence of hemolysis and methemoglobinemia in a COVID-19 infected patient with a G6PD deficiency [9,11]. Triggering factors were identified in some of these cases and remain unclear in others [11,12].

## Conclusion

This is the first case of concurrence of non-autoimmune hemolysis and methemoglobinemia in a patient with a G6PD deficiency post-AstraZeneca vaccine without clear precipitating factors.

## Declaration

### Ethics approval and consent to participate

The case report was approved by local Ethics Committees in the hospital and informed consent was obtained from the patient.

**Consent for Publication:** Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Availability of the supporting data:** All supporting data are available.

**Author contributions:** AK collected the data; AK, AA and RK analyzed the data. All authors read and approved the manuscript.

## References

1. Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, et al. (2020) Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med 288: 335-344.
2. World Health Organization (2021) Interim statement of the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety on Astrazeneca COVID-19 Vaccine.
3. Mansouri A, Lurie AA (1993) Concise review: methemoglobinemia. Am J Hematol 42: 7-12.
4. Cortazzo JA, Lichtman AD (2014) Methemoglobinemia: a review and recommendations for management. J Cardiothorac Vasc Anesth 28: 1043-1047.
5. Skold A, Cosco DL, Klein R (2011) Methemoglobinemia: pathogenesis,diagnosis, and management. South Med J 104: 757-761.
6. Alanazi MQ (2017) Drugs may be induced methemoglobinemia. J Hematol Thrombo Dis 6: 270.
7. Schuurman M, van Waardenburg D, Da Costa J, Niemarkt H, Leroy P (2009) Severe hemolysis and methemoglobinemia following fava beans ingestion in glucose- 6-phosphatase dehydrogenase deficiency: case report and literature review. Eur J Pediatr 168: 779-782.
8. Liu M, Chen F, Liu T, Chen F, Liu S, et al. (2017) The role of oxidative stress in influenza virus infection. Microbes Infect 19: 580-586.
9. Au WY, Ngai CW, Chan WM, Leung RY, Chan SC (2011) Hemolysis and methemoglobinemia due to hepatitis E virus infection in patient with G6PD deficiency. Ann Hematol 90: 1237-1238.
10. Delgado-Roche L, Mesta F (2020) Oxidative stress as key player in severe acute respiratory syndrome coronavirus (SARS-CoV) infection. Arch Med Res 51: 384-387.
11. Palmer K, Dick J, French W, Floro L, Ford M (2020) Methemoglobinemia in patient with G6PD deficiency and SARS-CoV-2 infection. Emerg Infect Dis 26: 2279-2281.
12. Scholkmann F, Restin T, Ferrari M, Quaresima V (2021) The Role of Methemoglobin and Carboxyhemoglobin in COVID-19: A Review. J Clin Med 10: 50.