# TRIPLE THREAT: SULFA ALLERGY, DAPSONE-INDUCED METHEMOGLOBINEMIA AND ATOVAQUONE-ASSOCIATED ANEMIA

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## CASE PRESENTATION

**A 68-year-old woman with PMHx of stage IIB small cell neuroendocrine carcinoma of the right lung status post chemoradiotherapy, complicated by radiation pneumonitis requiring long-term prednisone and pneumocystis pneumonia (PCP) prophylaxis.**

**Pre-admission**

- **Dapsone** 100mg po daily initiated
- CBC, LFTs and **G6PD levels were normal**

**E.R.**

- 3 days later, she presented with **dyspnea, lightheadedness, hypoxia (80% on room air)** and no other systemic symptoms
- Unremarkable workup; placed on O2 and **dapsone continued**

**Hospital Course**

- ABG with co-oximetry (Figure 1) showed **persistent MHb** and a **"saturation gap"** requiring escalation to high-flow nasal cannula
- Dapsone was switched to **atovaquone** 1500mg po daily
- Discharged on atovaquone, prednisone, and home O2

**Post-discharge**

- O2 weaned in the Pulmonology clinic
- 3 weeks later, developed **exertional dyspnea, fatigue, lightheadedness** and **palpitations**

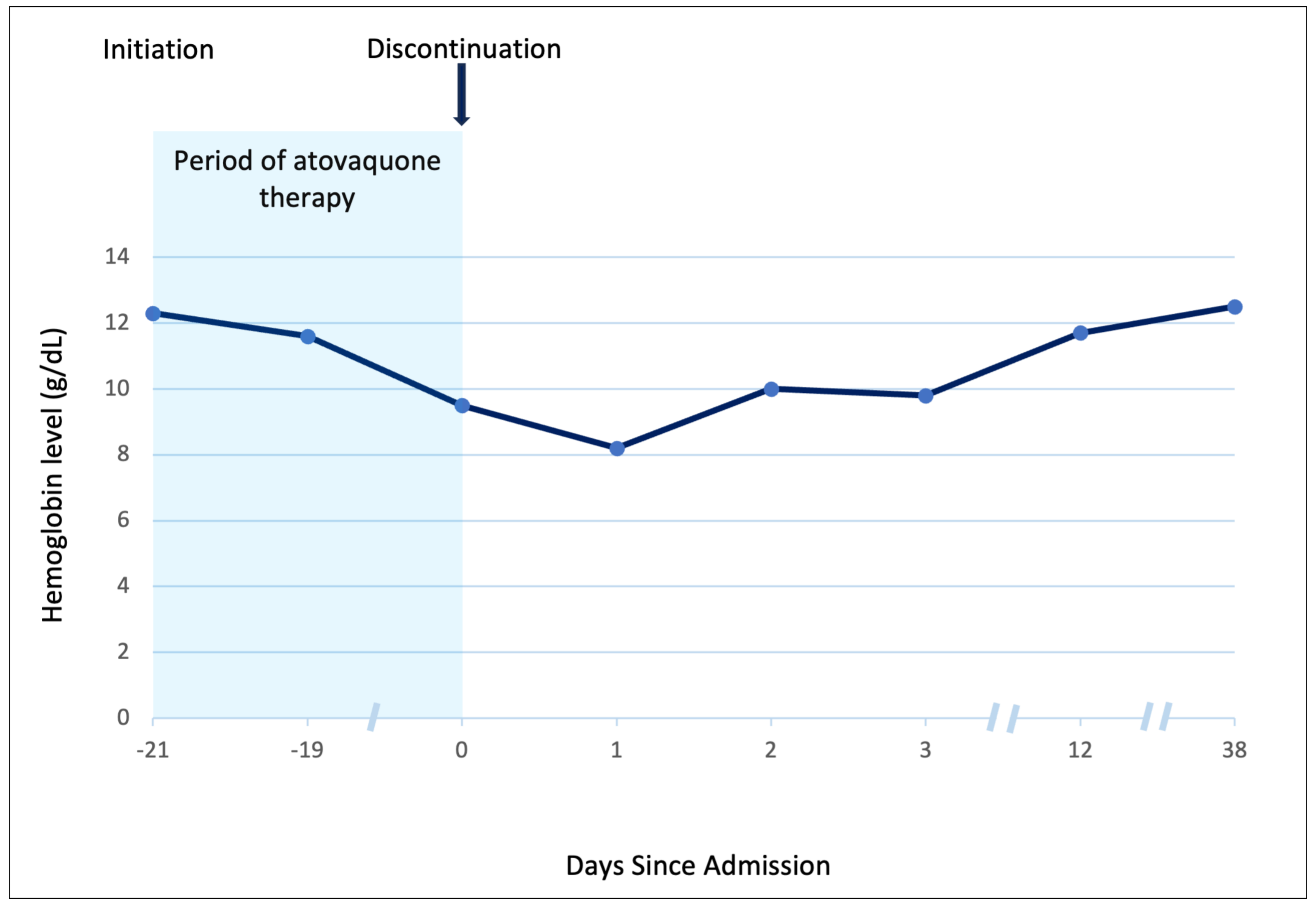
**Re-admission**

- Found to have **hypoproliferative macrocytic anemia of 9.5g/dL,** but extensive anemia workup was **unrevealing**
- Atovaquone was stopped and the **anemia resolved spontaneously** (Figure 2)

## FIGURE 1


**Photograph of the arterial blood sample with presence of MHb showing: (A) the characteristic "chocolate-brown" color, (B) no color change with exposure to oxygen.**

## FIGURE 2




**Line graph showing the hemoglobin trend with initiation and discontinuation of atovaquone therapy.**

## DISCUSSION

- PCP prophylaxis in adults is preferably treated with the sulfa drug TMP-SMX. Alternatively, in patients with adverse reactions or contraindications, the main second-line agents with good tolerability are dapsone or atovaquone.
- **Dapsone**-induced MHb is typically seen in G6PD deficiency. However, our patient with sulfa allergy developed MHb **despite normal G6PD levels** then atovaquone-associated anemia when therapy for PCP prophylaxis was changed.
- MHb is a potential risk with dapsone at **prophylactic doses**,[1] even in patients **without G6PD deficiency**.
- Since MHb can be fatal (>50%), prompt recognition of signs and symptoms like dyspnea, cyanosis, refractory hypoxia and chocolate-brown-colored arterial blood with a "saturation gap" is crucial.[2-3]
- Management of MHb involves co-oximetry, supportive oxygen, selective methylene blue use, or ascorbic acid alongside drug cessation.[2-3]
- Though a diagnosis of exclusion, **cytopenias** can rarely occur with **atovaquone**.[4] In particular, **anemia occurs in 4-6% of cases.**
- Patients on atovaquone should be monitored and given alternatives if clinically significant cytopenias ensue.

## CONCLUSION

- Dapsone can induce MHb even at prophylactic doses in patients without G6PD deficiency.
- Hematological monitoring for cytopenias should be considered with atovaquone.
- Prompt recognition of these rare associations, drug cessation and directed therapies are key steps in optimizing hospital outcomes.

## REFERENCES

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