A DANGEROUS DIAMINODIPHENYL DIFFERENTIAL
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1. INTRODUCTION

Dapsone, a sulfone antibiotic, is used for Pneumocystis jirovecii pneumonia (PJP) prophylaxis in patients who cannot tolerate trimethoprim-sulfamethoxazole (TMP-SMX). Dapsone-induced methemoglobinemia (methHb) is a rare and potentially life-threatening adverse effect. Our case illustrates the importance of identifying methemoglobinemia as a differential in patients recently treated with immunosuppressives and PJP prophylaxis who have persistent hypoxia and peripheral cyanosis.

2. CASE DESCRIPTION

77-year-old female with a PMH of COPD and rheumatoid arthritis, who presented with worsening shortness of breath.

Patient Hospital Course
- Admitted for COPD exacerbation and acute kidney injury (AKI)
- Switched to dapsone due to concerns of nephrotoxicity. A G6PD deficiency screen is negative.
- Develops worsening hypoxia and peripheral cyanosis
- Decomposes and transferred to the ICU due to respiratory failure and worsening kidney function
- Initially began on TMP-SMX for PJP prophylaxis
- ARB reveals methHb of 12%. Saturation gap is present. Started on methylene blue
- AKI found to be secondary to crescentic IgA nephropathy
- Started on immunosuppressive therapy
- Resolution of peripheral cyanosis and returns to baseline O2

3. CLINICAL MANIFESTATIONS OF METHB

<table>
<thead>
<tr>
<th>MethHb levels (%)</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>&lt;15</td>
<td>None</td>
</tr>
<tr>
<td>15-30</td>
<td>Peripheral cyanosis, chocolate-brown blood</td>
</tr>
<tr>
<td>30-50</td>
<td>Headache, dizziness</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Arrhythmias, coma, death</td>
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</tbody>
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4. DISCUSSION

- Methemoglobinemia is based on clinical symptoms according to serum methHb levels. Symptoms may arise even at lower levels like with our patient (see Table above).
- Helpful to the diagnosis is the classic oxygen “saturation gap”, i.e. discordance between arterial blood gas analysis (paO2) and pulse oximetry readings (peripheral O2 sat).
- Clinical symptoms and severity depend on the serum methHb present and, at high levels (>50%), can cause arrhythmias, coma and death.
- Removing the inciting agent alongside the use of IV methylene blue is the mainstay therapy.

5. TAKE HOME POINTS

- Dapsone is contraindicated in patients with G6PD deficiency, therefore screening is important prior to starting dapsone.
- Methemoglobinemia can occur even with a negative G6PD deficiency screen and with therapeutic doses.
- Removal of the inciting agent and IV methylene blue is the mainstay of therapy. There is paucity of data for incidence of dapsone-induced methemoglobinemia but is estimated at 3% for transplant recipients on dapsone for PJP prophylaxis.
- A review of medications should be performed to evaluate for methemoglobinemia despite an initial negative screen of G6PD deficiency in similar clinical scenarios.

6. REFERENCES