Introduction

Recently, the five year survival rate for Acute Lymphoblastic Lymphoma (ALL), the most common childhood cancer patients, drastically increased to more than 90%. With these increasing survival rates, anesthesiologists now, more than ever before, care for pediatric oncology patients in the operating room who present for diagnostic and therapeutic procedures like lumbar punctures, bone marrow aspirates and chemo port insertions and removals. Children with primary or acquired immunodeficiency like those with hematologic malignancy, are at risk for Pneumocystis pneumonia (PCP). Dapsone is currently the best alternative for PCP prophylaxis to those who are intolerant to Trimethoprim–sulfamethoxazole (TMP–SMX), the first line agent.

Case Report

A 9-year-old male with a past medical history significant for Langerhan Cell Histiocytosis (LCH), presented to the emergency room with flu like symptoms including fever, fatigue, dizziness and seizures. As part of the diagnostic workup, the patient was scheduled to undergo a lumbar puncture in the operating room. Anesthesia preoperative evaluation was unremarkable except for central and peripheral cyanosis with an oxygen saturation of 88% on room air and minimal improvement to 90% after supplementation with 2 liters of oxygen via nasal cannula. Laboratory results, chest X-ray and echo were unremarkable. Upon further questioning, the parents reported the patient’s biweekly use of dapsone with the most recent usage the night before presenting to the ED. Methemoglobinemia was then suspected and blood level of met-Hb was checked and found to be 19%. The patient was treated with 2 doses of 1 mg/kg methylene blue over 10 minutes with improvement of his clinical symptoms. Lumbar puncture was no longer indicated as patient improved clinically, dapsone was discontinued and patient was discharged home the following day.

Discussion

Methemoglobin is normally produced when iron is oxidized from a ferrous (Fe$^{2+}$) to a ferric (Fe$^{3+}$) form leading to decrease in the oxygen carrying capacity of blood, left shift of the oxygen-hemoglobin dissociation curve and increase in the affinity of Hb for oxygen limiting the unloading of oxygen to tissue. The cytochrome b5-MetHb reductase pathway (95%) and the NADPH-MetHb reductase pathway (5%) are responsible for physiologically reducing the ferric back to ferrous and maintaining the levels of met-Hb close to 1-2% that is well tolerated in normal population. Methemoglobinemia is a preventable and treatable life-threatening hemoglobinopathy that occurs in almost 20% of pediatric oncology patients receiving Dapsone for PCP prophylaxis. Though the prevalence and associated risk factors for Dapsone-associated methemoglobinemia has not been well studied, there seems to be a strong correlation with Dapsone doses higher than 2mg/kg/day. Clinical presentation depends on blood level of methemoglobin. Levels greater than 15% are associated with cyanosis and levels between 20 and 45% present with signs and symptoms of headache, lethargy, tachycardia, weakness, and mental status changes. Dyspnea, acidosis, cardiac dysrhythmias, heart failure, seizures, and coma may occur at levels above 45% while levels more than 70% are associated with a high mortality rate. Co-oximetry which uses multiple wavelengths of light is the gold standard for diagnosis and Intravenous Methylene blue 1-2 mg/kg/day is the only effective treatment available for methemoglobinemia.

Conclusion

• This case illustrates the increasing occurrence of perioperative methemoglobinemia in pediatric oncology patients who are on PCP prophylaxis with Dapsone and highlights the importance of good history taking, knowledge of drugs likely to induce methemoglobinemia.
• Anesthesiologists must be aware of this increasingly occurring and potentially fatal condition.
• Immunocompromised pediatric patients presenting with equivocal flu-like symptoms, unexplained cyanosis and low oxygen saturation should be evaluated for elevated MetHb levels in the presence of offending agent.