Take My Breath Away: The Case of Mrs. Blue

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The Case

- Patient: Mrs. Blue
- 55-year-old female admitted to hospital September 2011
- Admitted due to shortness of breath, tingling on toes, fingers, and lips, as well as lightheadedness and fatigue

Previous Medical History

- 1965: Rheumatic Fever
- 1985-2001: Hepatitis, Essential Hypertension, Mitral Valve Prolapse, Hyperlipidemia, Hypothyroidism, Osteoporosis

Medical History continued

- Of special note regarding patient's symptoms:
- Asthma 1993
- Pulmonary fibrosis 2008
- Sleep apnea 2009
- Patent foramen ovale 2010
- Methemoglobinemia

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Worsening Symptoms

- Patient had noted shortness of breath increasing in frequency since diagnosis of pulmonary fibrosis
  - Previously only occurred during exertion but now occurring even while at rest
- Lab tests were then ordered
  - BMP, LFT, CBC, Coag, and AbGs

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Lab Results of Note

- 51% oxygen saturation at time of admission
  - Up to 64% four hours later
  - Normal range is >90%
- Potassium was 3.4 (low)
- Glucose 141 (high)
- Arterial oxygen partial pressure 171 (high)

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Clinical Assessment

- Chronic hypoxemic, hypercapnic respiratory failure
  - Caused by combination methemoglobinemia, desquamitive interstitial lung pneumonitis, chronic interstitial lung disease, sleep apnea, asthma, patent foramen ovale, and pulmonary hypertension
  - Despite medical therapy increased shortness of breath occurring
  - Plan: Mrs. Blue will begin to receive partial exchange transfusions

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Methemoglobinemia

- Disorder in which higher amounts of methemoglobin (metHb) are found in the blood
  - Methemoglobin: form of hemoglobin where ferric iron is present instead of ferrous iron
- Those with it experience headaches, fatigue, shortness of breath, cyanosis
  - In severe cases, where metHb is more than 50% of Hgb is present dysrhythmias, seizures, coma, and even death can occur

Methemoglobin

- Methemoglobin contains a ferric form, Fe^{3+} of iron unlike hemoglobin which has ferrous iron, Fe^{2+}
- Ferric iron has a decreased affinity for binding oxygen than ferrous iron
  - Ferric iron also has a greater affinity for oxygen already bound
- Result: hemoglobin that doesn't bind well and once it does bind, doesn't want to release it

Causes of Methemoglobinemia

- Congenital: due to a deficiency of NADH methemoglobin reductase, which leads to buildup of metHb is very rare.
    - What Mrs. Blue has
- Acquired: certain antibiotics and more commonly inadvertent exposure to chemicals causing an increase in metHb by nearly a thousand-fold

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Congenital Methemoglobinemia

- Autosomal recessive pattern of heredity
  - 2 carrier parents leading to affected child
- Due to mutations in the gene that codes for NADH-cytochrome b5 reductase (metHb reductase)
- 2 types of congenital methemoglobinemia

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Type 1 (erythrocyte reductase deficiency)

- Most common/least harmful form of congenital methemoglobinemia
- Only the red blood cells in the body lack functioning enzyme
- Patients experience the milder symptoms of the disease, most notably cyanosis of skin
  - Asymptomatic till >25% of hemoglobin is metHb

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Type 2 (generalized reductase deficiency)

- Less common but more harmful
  - Roughly 10% of all cases
- Those with type 2 lack functioning enzyme throughout entire body
- Prognosis for those with type 2 very poor
  - Most experience developmental delay, intellectual disability, seizures, and failure to thrive
  - Generally, causes death within the first few years

Diagnosis

- Methemoglobinemia initially suspected by presence of cyanosis while arterial pO2 is normal in ABG testing
- Can be diagnosed in-lab by co-oximetry
- Identifying the cause involves enzyme assays for methemoglobin reductase and evaluation of the patient's family pedigree

Treatment and Management of Methemoglobinemia

- Intravenous injection of methylene blue to reduce methemoglobin back to hemoglobin
  - The treatment of choice for those suffering from methemoglobinemia
  - Has toxic potential that can cause dyspnea and chest pain
- High does ascorbic acid can be used alongside methylene blue as treatment
  - Directly reduces methemoglobin, but much slower rate

Treatment and Management of Methemoglobinemia

- In certain patients who don't respond to methylene blue or have conditions contraindicated for use
  - i.e. those with G6PD
- As an alternative these patients can receive blood through transfusion exchange as well as hyperbaric treatment
- In general, all patients will receive supplemental oxygen

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Back to Mrs. Blue

- January 2012
  - Mrs. Blue went to for surgery to have a hemodialysis catheter implanted into left internal jugular vein for access during exchange transfusions
    - Surgery went successfully
- May 2014
  - Mrs. Blue has received red cell exchanges every 3 months
  - 5-7 units transfused each time
  - Treatment appears to be sufficient

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Preparation for Exchange

- The volume of blood is determined by a pre-hematocrit, a target ending hematocrit and the patient's total blood volume.
- An order is placed for a type and screen and packed red blood cells with a total volume in the comments
- The weight and hematocrit is obtained for each unit.
- The average HCT of all the units should be between 58 and 62.
- The total weight is converted to mls.
- The units are electronically crossmatched and issued.

One Decade Update

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The Case of Mrs. Blue

- Mrs. Blue has still been receiving red cell exchanges every 3 months
  - O positive, antibody screen negative
  - Phenotype: C+c+, E+e+, K= k+, Fy(a+b+), Jk(a+b=), S+s+, M=N+ (6/2023)
  - 5-7 units exchanged each time
  - 3/2024 receiving HgbS= (due to low O2 sats) and K=
  - Methyl blue is administered with exchanges, as needed
  - Ascorbic acid has been ordered multiple times but is discontinued
  - Hgb as low as 6.9 but usually well above transfusion threshold
    - Most recent exchange 11.8 before and 13.9 after
- Treatment still appears to be sufficient

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Thank you!

We do make a difference in our patient's lives.

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