

The Role of Point-of-Care Testing in the Early Diagnosis of Pseudo-Hypoxemia in Myeloproliferative Disorders

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Introduction

The diagnosis and management of hypoxemic respiratory failure is part of the daily routine of anesthesiologists, intensivists, and respiratory therapists. However, identification of some pathological states can be challenging, and failure to rapidly diagnose them can lead to inappropriate therapeutic decisions with expensive and potentially severe adverse consequences. These decisions can range from unnecessary intubation and mechanical ventilation to inappropriate administration of bicarbonate for false acidosis and consequent worsening of any existing metabolic abnormality. Additionally, performing unnecessary tests, such as computerized tomographic angiography to rule out pulmonary embolism, may negatively affect the kidneys, due to the intravenous iodine contrast. We report the case of a patient with hyperleukocytosis secondary to myelofibrosis who presented with altered mental status and pseudo-hypoxemia. We discuss the differential diagnoses of hypoxemia in this setting and the role of point-of-care arterial blood gas (ABG) analysis in diagnosing pseudo-hypoxemia.

Case Summary

A 61-year-old white male with a 3-year history of myelofibrosis was brought to the emergency center of our institution with an altered mental status presumed to be secondary to an opiate overdose. Over the past 2 years his

condition had progressively deteriorated; he developed anemia unresponsive to darbepoetin alfa and prednisone, thus ultimately requiring splenic radiation. Recently his primary care physician had prescribed methadone (40 mg twice a day) for severe bone pain. On the morning of admission, while at home, the patient became unresponsive and had pinpoint pupils. He was intubated for airway protection by emergency medical services and transported to MD Anderson Cancer Center. On arrival to the emergency center he was treated with opioid reversal, stabilized hemodynamically, and transferred to the intensive care unit for further management.

Upon admission to the intensive care unit his blood pressure was 99/33 mm Hg, heart rate 110 beats/min, and S_{pO_2} was 90% on F_{IO_2} of 1.0. White-blood-cell count was 348,000/UL, hemoglobin was 7.1 g/dL, and platelet count was 294,000/UL. After placing a double-lumen central venous catheter for apheresis, and an intra-arterial cannula for invasive blood pressure monitoring, the patient was treated with hydroxyurea, cytarabine, and leukapheresis. An arterial blood sample was taken from a radial artery cannula and transported to the laboratory for analysis (model 865 blood gas analyzer, Bayer Chiron), which showed severe acidosis and hypoxemia: pH 7.15, P_{aCO_2} 47 mm Hg, P_{aO_2} 49 mm Hg, bicarbonate 16 mEq/L, base excess -13 mEq/L, and S_{pO_2} 90% on F_{IO_2} 1.0. The chest radiograph showed a normal cardiac silhouette and full expansion of all lung fields, without alveolar or interstitial pulmonary infiltrates, signs of flash pulmonary edema, pneumothorax, or pneumonia (Fig. 1). Resuscitation and treatment of hypoxemia and acidosis were continued and a second arterial blood sample was drawn, while still on F_{IO_2} 1.0, with an S_{pO_2} of 97%, and yielded similar results: pH 7.22, P_{aCO_2} 50 mm Hg, P_{aO_2} 58 mm Hg, bicarbonate 20 mEq/L, base excess -8 mEq/L, and calculated oxygen saturation 98%. Concurrently we tested an arterial blood sample with a portable bedside ABG analyzer (i-STAT, Abbott Point of Care, Princeton, New Jersey) and found completely different results: pH 7.39, P_{aCO_2} 56 mm Hg, P_{aO_2} 225 mm Hg, bicarbonate 34 mEq/L,

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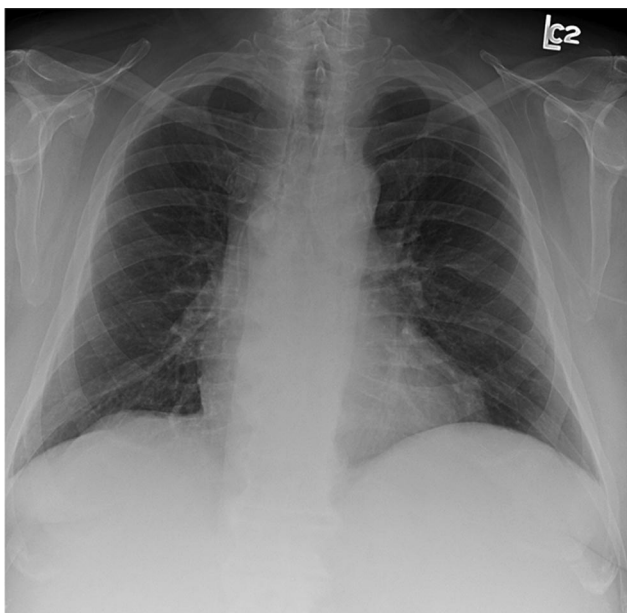


Fig. 1. Chest radiograph.

base excess 7 mEq/L, and calculated oxygen saturation 100%.

Pseudo-hypoxemia was determined to be the main cause of the discrepancies between the laboratory versus bedside-analyzer ABG results. Subsequently, the F_{IO_2} was decreased to 0.50, and all ABG samples were analyzed with the bedside ABG analyzer. Unfortunately, despite aggressive intensive oncological and critical care, multiple organ failure, including renal, liver and uncontrollable blast crisis, resulted in death 4 days after initial treatment.

Discussion

Pseudo-hypoxemia occurs when P_{aO_2} is reduced by increased oxygen demand and consumption by markedly elevated white blood cells in the arterial blood sample. This is further aggravated by the delayed laboratory analysis of the blood sample or incorrect sampling.¹ Pseudo-hypoxemia occurs not only in hyperleukocytosis; it has also been reported in thrombocytosis associated with polycythemia vera.² A few cases of pseudo-hypoxemia have been published under the names of “spurious hypoxemia” and “leukocyte larceny.”

Opportunistic infections associated with pneumonia, lung edema, and pulmonary hemorrhage are the leading causes of acute respiratory failure in patients with myeloproliferative disorders, such as acute myeloid leukemia and chronic myeloid leukemia in blast crisis.³ In the absence of radiographic evidence of pulmonary infiltrates or pneumothorax, leukostasis along with pulmonary embolism must also be considered in any tachypneic leukemic patient.⁴ Pseudo-hypoxemia could coexist with the above

pathologies or even precede the signs of respiratory failure.

Patients with hyperleukocytosis develop leukostasis, an abnormal intravascular leukocyte aggregation and clumping often seen in patients with myeloproliferative disorders. Symptoms associated with leukostasis are primarily due to the congestion and sludging in the microvascular beds. Although the brain and lungs are most commonly involved in hyperleukocytosis, every organ system can be affected, as illustrated by the present case. In patients with diseases associated with hyperleukocytosis, the pulmonary complications arising from leukostasis in the pulmonary capillary vessels substantially increase morbidity and mortality.⁵ Treatment regimens and supportive care have shown little improvement in outcomes over the years, with a one-week mortality rate as high as 26%.^{6,7}

A recently published algorithm to diagnose the etiology of hypoxemia in these settings fails initially to identify pseudo-hypoxemia as the cause of the low P_{aO_2} value in the laboratory ABG analysis in our patient.¹ The algorithm suggests that the etiology of $P_{aO_2} < 60$ mm Hg associated with an $S_{pO_2} > 95\%$ is pseudo-hypoxemia, and when P_{aO_2} is associated with $S_{pO_2} < 90\%$, it should be considered true hypoxemia (eg, pulmonary leukostasis, pulmonary embolism, or pneumonia). Our case demonstrates pseudo-hypoxemia in both scenarios described in the algorithm. In addition, the point-of-care blood-gas analyzer also showed that P_{aO_2}/F_{IO_2} was below 300 mm Hg. Considering that the patient had neurological signs of leukostasis, it is clear that his abnormal oxygenation was also associated with pulmonary leukostasis, which makes this case a unique example of combined hypoxemia and misleading pseudo-hypoxemia.

Inaccurate or delayed diagnosis of pseudo-hypoxemia could lead to inappropriate medical interventions, such as unnecessary hyperventilation, which pose risks such as brain ischemia in patients with altered microcirculatory blood flow. Increasing the respiratory rate or airway pressure to “treat” pseudo-hypoxemia or pseudo-acidosis could result in gas trapping and barotrauma. Increased costs, risk of infections, and oxygen toxicity are among many other undesirable consequences of misdiagnosing pseudo-hypoxemia.

Hyperleukocytosis is a medical emergency requiring prompt identification with immediate leukocyte reduction utilizing leukapheresis, hydroxyurea, and induction chemotherapy. Newer chemotherapy and leukapheresis techniques are being developed in many cancer centers. However, because of the multi-organ involvement and aggressive nature of hyperleukocytosis, therapy must focus on early identification and rapid intervention to minimize mortality.⁸

Teaching Points

Respiratory management of patients with myeloproliferative disorders can be challenging, as illustrated in this case. Pulse oximetry and standard laboratory ABG measurements are not sufficient to make an accurate and early diagnosis of pseudo-hypoxemia. The role of point-of-care measurements for respiratory or metabolic assessment and management should be considered the standard of care in patients with myeloproliferative disorders such as hyperleukocytosis or thrombocytosis.

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