Unusual Discrepancy Between S_{pO_2} and S_{aO_2} in a 31-Year-Old Man With Chronic Myelogenous Leukemia

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Introduction

Hyperleukocytosis and thrombocytosis may develop in hematological disorders, including acute myelogenous or lymphoblastic leukemia, chronic leukemias in accelerated phase, and polycythemia vera. In such clinical scenarios, patients are at risk for hypoxemia, either true or spurious.[1] The causes of true hypoxemia may include pulmonary leukostasis, pneumonia, and pulmonary embolism.[1] However, sometimes the bloodstream oxygen saturation of the hemoglobin measured by a pulse oximeter (S_{pO_2}) may be substantially higher than that measured by a laboratory method (S_{aO_2}) in patients with hyperleukocytosis or extreme thrombocytosis.[2-5] These patients are actually not in a hypoxemic status. Spurious hypoxemia or pseudohypoxemia is used to describe this phenomenon.[3-5] Here we report such a condition in a patient with chronic myelogenous leukemia when he was in an accelerated phase.

Case Summary

A 31-year-old man presented to our emergency room with rapidly increased abdominal girth, severe right flank pain, and night sweats for 2 days. He had lost 10 kg in weight in a period of 2 years. Over the year prior to this visit he had had several episodes of self-limited rashes, myalgia, and arthralgia.

On examination he was alert and oriented to person, place, and time, but appeared in distress. His body temperature was 37°C, his pulse was 118 beats/min, his respiratory rate was 22 breaths/min, and his blood pressure was 119/65 mm Hg. His abdomen was distended, and his bowel sounds were hypoactive. In addition to hepatosplenomegaly, he also had unbearable tenderness while the right half of his abdomen was deeply palpated. His S_{pO_2} was 98% while he was breathing ambient air.

The laboratory data included: hemoglobin 61 g/L, red cell count 1.78×10^{12} cells/L, white cell count 589.6×10^9 cells/L (blasts 8.0%, neutrophils 53.0%, monocytes 1.0%, lymphocytes 2.0%), platelet count 1077.0×10^9 cells/L). Chronic myelogenous leukemia in an accelerated phase was diagnosed. The abdominal and pelvic computed tomography scans disclosed a huge hematoma over the right psoas muscle. He underwent a trans-arterial embolization, and the active bleeders from the right superior gluteal artery stopped.

A supine chest radiograph showed neither pneumonia nor pleural effusion (Fig. 1). Unfortunately, progressive tachypnea and increased oxygen demand developed the next day. His S_{pO_2} fell to 90%. He was intubated for mechanical ventilation on the second hospital day, due to respiratory failure, and transferred to our ICU. At an F_{IO_2} of 0.60 and a PEEP level of 8 cm H_2O, his S_{pO_2} was 98%, but the oxygen saturation measured from the blood gas analyzer (S_{aO_2}) was only 82.3%. The arterial blood gases were pH 7.47, P_{aO_2} 43.3 mm Hg, P_{aCO_2} 34.3 mm Hg, bicarbonate 25.2 mEq/L, and base deficit 2.4 mEq/L.

Chemotherapy with low-dose ara-C and mitoxantrone was administered. The sequential laboratory data showed that the S_{pO_2}-S_{aO_2} gap diminished, while leukocyte and thrombocyte counts decreased toward normal (Fig. 2). In our ICU the syringes containing the arterial blood specimens were immediately immersed in crushed ice, and were sent to the blood gas analyzer for analysis within 2–3 min.

His retroperitoneal hemorrhage recurred 4 days after the trans-arterial embolization, and later evolved into an abdominal compartment syndrome. He underwent another trans-arterial embolization and surgical decompression, but in vain. The patient died due to multiple organ failure 18 days after admission.

Discussion

In the settings of marked leukocytosis or thrombocythemia, the leukocytes or platelets may vigorously consume

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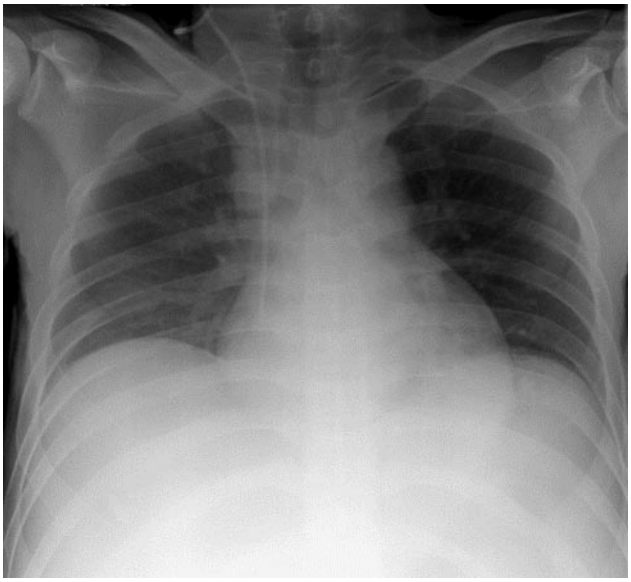

Fig. 1. The supine chest radiograph at the emergency room.

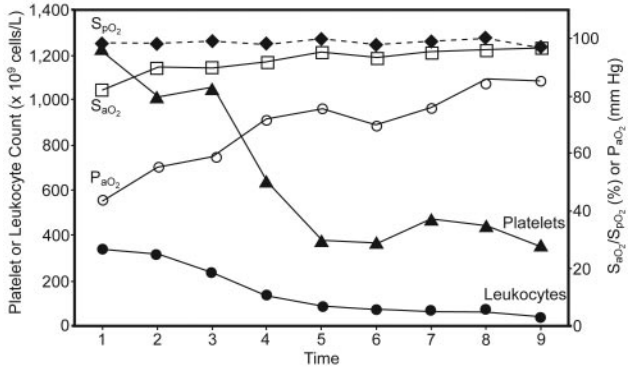

Fig. 2. Sequential data during hospitalization, showing that P_{aO_2} and arterial oxygen saturation measured from an arterial blood sample (S_{aO_2}) increase along with decreasing leukocyte and thrombocyte counts, whereas the S_{pO_2}-S_{aO_2} gap decreases.

the dissolved oxygen from an arterial blood gas specimen. The phenomenon is sometimes referred to as "leukocyte larceny" or "platelet larceny" in the literature.[3,4,6] This occurs immediately after blood is drawn out of patients, and within 5 min the consumption can be large, even if the sample is incubated in ice.[7] There is an inverse correlation between total count of the eliciting cells and P_{aO_2} and S_{aO_2},[1,4,5] which is well illustrated in the present report (see Fig. 2).

In 1911, Onaka was the first to discover the "respiration of blood platelets."[4] Forty years later, DeWardener and Young found that the increased in vitro oxygen utilization affected the estimation of S_{aO_2}.[4] The consumption was directly proportional to the number of circulating leukocytes.[4] In addition to cell count, the type and maturity of proliferating leukocytes were other important determinants in the rate of fall in P_{aO_2}.[7] Among white cells, monocytes were reported to have the highest rate of oxygen consumption, and this diminished with cellular maturation.[1,6] Similarly, cells of the lymphoid series decrease their rate of oxygen consumption as they mature.[8]

If they are prolonged for any reason, several steps during which the blood sample is subjected to elevated temperature are speculated to contribute to increased in vitro oxygen consumption and spurious hypoxemia: from completion of obtaining the blood sample until the syringe containing the blood sample is immersed in ice, while the sample is being agitated before analysis, and while the sample is in the blood gas analyzer, where the temperature rapidly increases to approximately 37°C.[7] Several methods have been suggested to eliminate this effect. The 2 earliest strategies are to immediately cool or add sodium fluoride or potassium cyanide to an arterial blood gas sample, attempting to lower cell metabolism and thus in vitro oxygen usage within the sample.[7,9-11] Some authors believe that it is impossible to completely eliminate in vitro oxygen consumption by leukocytes or thrombocytes with only cooling, and an erroneous measurement may still be made.[10] Moreover, the results of cooling a blood specimen are not reproduced consistently.[12]

In our ICU the arterial blood specimens are bathed immediately in crushed ice and sent for analysis within 2–3 min, which is consistent for every patient and every sampling. This time interval has been as short as possible in our ICU. However, spurious hypoxemia still occurs, as shown in the present case, until the patient's leukocyte and platelet counts normalize. A recent case report proves that the alternative method of incubating a blood specimen with potassium cyanide is reliable.[4] Another strategy is using an intra-arterial monitoring device to provide continuous blood gas analysis.[13] By combining fiberoptic technology with spectrophotometry, this device can display real-time information of blood oxygenation.[13] However, its accuracy and cost-effectiveness remain in question.[13]

Pulse oximetry has been considered as the most convenient and accurate way of reflecting in vivo blood oxygenation in patients with hyperleukocytosis or extreme thrombocytosis.[1,2,4,5] Certain conditions may still predispose to inaccurate S_{pO_2} measurements, such as alkalosis, hypothermia, carboxyhemoglobinemia, or methemoglobinemia.[1,6] In patients with hyperleukocytosis or extreme thrombocytosis, the greater accuracy of pulse oximetry is speculated to originate from the direct measurement of capillary blood oxygen saturation.[14] The discrepancy between S_{pO_2} and spuriously low S_{aO_2} usually decreases along with normalization of the cell count,[1,4,5] as shown by the case reported (see Fig. 2).

There is still another mechanism that is less frequently mentioned in the literature to explain spurious hypoxemia. Leukocytes may coat the membrane of an oxygen elec-

Table. Coexistence of Hyperleukocytosis and Extreme Thrombocytosis Makes Additive Contribution to Pseudohypoxemia*

	S_{pO_2}-S_{aO_2}	
	Pearson's Correlation Coefficient	*P*
Platelet count	0.903	.001
Leukocyte count	0.895	.001
Total count of platelet plus leukocyte	0.906	.001

* All values are calculated from of our patient over the course of his admission.

trode and therefore prevent the movement of the oxygen molecules from plasma into the electrode, interfering with the measurement of blood oxygen tension.[15] Therefore, Charan et al claimed to use plasma rather than whole blood for arterial blood gas analysis in patients with hyperleukocytosis.[15]

The mean leukocyte and platelet counts in our case were 151×10^9 cells/L (range 38–338 $\times 10^9$ cells/L) and 659×10^9 cells/L (range 356–1224 $\times 10^9$ cells/L), respectively. These are higher than those reported in the literature. For example, the mean leukocyte and platelet counts were 17×10^9 cells/L and 622×10^9 cells/L, respectively, in the study by DeWardener and Young, and 117×10^9 cells/L and 331×10^9 cells/L, respectively, in the study by Hess et al.[7,16] Furthermore, the patient reported here presented simultaneously with hyperleukocytosis and extreme thrombocytosis, conditions that were usually observed only in patients with chronic myelogenous leukemia in blast crisis.[7] It is possible that coexistence of hyperleukocytosis and extreme thrombocytosis may enhance the development and severity of pseudohypoxemia (Table).

Teaching Points

Patients with hyperleukocytosis and extreme thrombocytosis may develop spurious hypoxemia before effective cytoreduction therapy. The in vitro oxygen consumption by enormous numbers of leukocytes or thrombocytes may result in the erroneous reading of true blood oxygen saturation, especially if the time delay between sampling and laboratory analysis of the blood specimens is prolonged. In addition to cell count, the type and maturity of proliferating leukocytes may also be important determinants of in vitro oxygen consumption. Furthermore, coexistence of hyperleukocytosis and extreme thrombocytosis may facilitate the development and severity of pseudohypoxemia. Several methods have been proposed to prevent or minimize this phenomenon, such as using a pulse oximeter or using plasma for blood gas analysis. Pulse oximetry is the most convenient and accurate way of reflecting in vivo oxygenation in such a clinical setting. The gap between S_{pO_2} and S_{aO_2} usually decreases along with normalization of the blood cell count. Experience from this case suggests that caution should be exercised in the interpretation of P_{aO_2} in such clinical scenarios. Failure to recognize this phenomenon can lead to unnecessary diagnostic tests and therapeutic interventions.

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