

Spurious Hypoxemia in an Intensive Care Patient with Hyperleukocytosis Secondary to Acute Leukemia

Akut lösemiye Sekonder Hiperlökositozlu Yoğun Bakım Hastasında Sahte Hipoksemi

Muhammet Faruk Hekimoğlu¹, Sevil Ayaydın Mürtezoğlu², Mehtap Pehlivanlar Küçük³

Abstract

A rare phenomenon that can occur in intensive care patients with hyperleukocytosis has been identified that is known as "spurious hypoxemia" in arterial blood gas analyses. Hyperleukocytosis is a common cause of spurious hypoxemia. A 53-year-old male patient who was newly diagnosed with acute myeloid leukemia, and who had no known chronic disease or drug use, presented with complaints of weakness, swelling of the hands and blood spitting, and is reported on here in the light of the literature due to the inconsistency between the peripheral oxygen saturation and arterial blood gas values. The aim in presenting this case report is to emphasize the importance of spurious hypoxemia in patients in which hypoxemia may be expected, but who are not actually hypoxemic, for the determination of a treatment procedure.

Key words: Hyperleukocytosis, spurious hypoxemia, intensive care.

Özet

Hiperlökositozlu yoğun bakım hastalarında ortaya çıkabilen ve arteriyel kan gazı analizlerinde "sahte hipoksemi" olarak adlandırılan nadir bir fenomen tanımlanmıştır. Hiperlökositoz, sahte hipoksemimin yaygın bir nedenidir. Bilinen kronik hastalığı ve ilaç kullanımı olmayan, halsizlik, ellerde şişme, kan tükürme şikayetiyle başvuran 53 yaşında, yeni tanı akut myeloid lösemili erkek hasta, periferik oksijen satürasyonu ile arteriyel kan gazı değerleri arasındaki uyumsuzluk nedeniyle literatür ışığında sunulmuştur. Bu olgu sunumunun amacı, hipoksemimin gerçekten beklenebileceği ancak gerçekte hipoksemik olmayan hastalarda tedavi prosedürünü belirlemede, sahte hipoksemimin önemini vurgulamaktır.

Anahtar Sözcükler: Hiperlökositoz, sahte hipoksemi, yoğun bakım.

¹Department of Internal Medicine, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

²Department of Chest Disease, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

³Department of Chest Disease, Division of Intensive Care, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

¹Karadeniz Teknik Üniversitesi, Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Trabzon

²Karadeniz Teknik Üniversitesi, Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Trabzon

³Karadeniz Teknik Üniversitesi, Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Yoğun Bakım Bilim Dalı, Trabzon

Submitted (Başvuru tarihi): 30.01.2021 **Accepted (Kabul tarihi):** 25.03.2021

Correspondence (İletişim): Mehtap Pehlivanlar Küçük, Department of Chest Disease, Division of Intensive Care, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey

e-mail: mehtap_phlvnlr@hotmail.com



Intensive care patients often experience hypoxemic respiratory failure. Hypoxemia is diagnosed based on arterial blood gas values. A rare phenomenon that can occur in intensive care patients with hyperleukocytosis has been identified that has been termed “spurious hypoxemia” in arterial blood gas analyses. Hyperleukocytosis is a condition in which the number of leukocytes is $>50,000 \text{ mm}^3$, and it is often associated with acute leukemia and myeloproliferative disease. While the saturation of patients measured by pulse oximeter is $>90\%$, SaO_2 examined in arterial blood gas is $<90\%$, though no correlation may be established. Pulmonary symptoms include dyspnea and hypoxia with or without common interstitial or alveolar infiltrates (1). Arterial PaO_2 measurement is incorrectly found to be low in patients with hyperleukocytosis because white blood cells (WBC) in the test tube use oxygen. A pulse oximeter allows a more accurate assessment of O_2 saturation under these conditions known as “spurious hypoxemia”. If this is not taken into account, it can lead to an incorrect interpretation of the patient's condition, as well as aggressive and potentially harmful treatments (2).

CASE

A 53-year-old male patient without chronic disease applied to a physician complaining of weakness, rapid fatigue, throat and abdominal right lower quadrant pain for 15 days. The patient reapplied to the doctor with complaints of swelling in the hands, bruising around the eyes, tenderness, bleeding in the gums and spitting blood on the third day of treatment. The patient was followed up by hematology with acute leucosis and bicytopenia. The measured laboratory parameters were white blood cell count (WBC); $289 \times 10^3/\mu\text{l}$ (4.8-10.8); hemoglobin, 7.2 g/dl (12-17); platelets, $29 \times 10^3/\mu\text{l}$ (130-400); total protein, 67.2 g/l (66-83); albumin, 36.1 (35-52) g/l; creatinine, 1.24 mg/dl (0.67-1.17); ALT, 137 μl (0-45); AST, 60 μl (0-35); ALP, 582 μl (30-120); GGT, 693 μl (0-55); total bilirubin, 7.07 mg/dl (0.3-1.2); direct bilirubin, 4.14 mg/dl (0-0.2); LDH, 1458 μl (<248); calcium, 9 mg/dl (8.8-10.6); sodium, 129 meq/l (136-146); potassium, 4.5 meq/l (3.5-5.1); aptt, 31 sec (22-35); pt, 13 sec (10-15); inr, 1.16 (0.85-1.15); fibrinogen, 332 mg/dl (180-350); D-dimer, 5.65 mg/dl (0-0.55); arterial blood gas parameters, pH 7.36 (7.35-7.45); pCO_2 , 33.5 mmHg (32-48); pO_2 , 31.7 mmHg (83-108); SaO_2 , 54.6% (95-99); HCO_3 , 19.3 mmol/L (22.2-28.3); and SpO_2 measured with pulse oximetry, 89%. The bone marrow aspiration was found to be compatible with acute myeloid leu-

kemia (MPO+, CD13+ CD33+ CD117+). The patient, whose dyspnea and clinical condition deteriorated, was taken into the intensive care unit. A bilateral interstitial infiltration on a lung X-ray was thought to be related to leukocyte migration and interstitial edema (Figure 1). Upon physical examination, the patient was conscious, somnolence, his Glasgow coma score was 14, and he had a bilateral periorbital swelling, left periorbital ecchymosis, scleral icteric, left submandibular painful lymph node and tenderness in the right upper quadrant of the abdomen; his fever was 37°C , heart rate was 128 beat/min, blood pressure was 150/90 mmHg, respiratory rate was 40/min and peripheral oxygen saturation was 88% (oronasal 14 L/min O_2). Hydroxyurea and empirical piperacillin-tazobactam were started, and noninvasive mechanical ventilation (IPAP, 12mmHg; EPAP, 8mmHg) and intermittent high frequency nasal cannula was administered. The patient's clinical findings deteriorated and he was intubated during follow-up. The patient had clonus-like movements in the face and arms that lasted for about 5 minutes. A suspected hyperdense lesion measuring 9x7 mm was observed in the right capsula interna crus posterior on a brain tomography of the patient. The patient was started to be followed up with the SIMV+PC+PS mode, FiO_2 , 0.6; frequency, 16/min; PEEP, 8 cmH_2O ; and Pins, 16 cmH_2O settings. While the SpO_2 measured with a pulse oximeter after intubation was $>90\%$, and the hypoxemia persevered in the radial arterial catheter and in the blood gas were studied repeatedly. The patient's blood gas follow-up data is presented in the table below (Table 1).



Figure 1: Chest radiography at the time of admission to the intensive care unit

Table 1: Arterial blood gas and peripheral saturation values of the patient

	07.05.20 -02:58	07.05.20-05:32	07.05.20-18:36
WBC ($\times 10^3$ cell/mm ³)	394	455	333
PaO ₂ (mmhg)	31.7	47	43
SaO ₂ (%)	54.6	62.8	56.8
PaCO ₂ (mmhg)	33.5	62	52.4
HCO ₃	19.3	15.5	6.4
ph	7.36	7.09	6.80
sPO ₂ (%)	94	95	92

Inotropic/vasopressor support was initiated for the patient, who could not achieve normotension, despite adequate fluid support. The patient was also scheduled for dialysis due to a deepening metabolic acidosis and anuria, and for plasmapheresis due to acute leucosis, but only underwent dialysis, as they developed sudden cardiac arrest prior to the plasmapheresis treatment.

DISCUSSION

Spurious hypoxemia is a rare phenomenon, the incidence of which is unknown (2), but that usually occurs due to technical failure (hemolysis, proper temperature, late access to the laboratory) (3,4), although spurious hypoxemia induced by hyperleukocytosis can also occur. Although spurious hypoxemia is a rare phenomenon, it can direct the clinician to aggressive and potentially harmful invasive attempts (2). The aim in presenting this case report is to emphasize the importance of spurious hypoxemia in patients at risk of hypoxemia, but that are not actually hypoxemic, when determining treatment. Clinicians often turn to arterial blood gas examination results for accurate information about the patient's oxygenation, being more reliable than the saturation examined using a fingertip pulse oximeter, especially in cases where peripheral tissue perfusion is impaired. In cases of hyperleukocytosis, however, as was the case in our patient, arterial blood gas parameters lose their accuracy and can present the physician with problems in deciding upon the most appropriate oxygen support therapy. According to etiopathogenesis identified by Chillar et al. (5), oxygen is consumed due to the increase in the number of hematological cells and the high metabolism of these neoplastic cells. Spurious hypoxemia can be seen in the arterial blood due to the increased O₂ consumption.

Arterial blood gas examinations are carried out using blood gas measurement devices for the measurement of pH, partial carbon dioxide pressure (PaCO₂), and partial oxygen pressure (PaO₂) through the use of sensitive electrodes, while bicarbonate (HCO₃) is calculated from oxygen saturation (SaO₂) and base deficit (BE). PaO₂ and SaO₂ are used to evaluate oxygenation, with a decrease in PaO₂ in the arterial blood being hypoxemia, and a decrease in tissue oxygenation due to hypoxemia being hypoxia. PaO₂ values decrease with age, although PaO₂ ≥ 60 mmHg and SaO₂ $\geq 90\%$ are preserved in a healthy person (6).

Additionally, the greater the time between the collection and analysis of the sample in the laboratory, the lower the oxygen content. For example, the oxygen level in the tissue will be higher in the absence of certain pathologies (pneumonia, sepsis, ventilation/pulmonary perfusion disorder), since the time of transfer to the laboratory will be longer than the time of oxygenation. However, this decrease in oxygen (PaO₂) in blood gas is more severe than hypoxia (SaO₂) in plasma. The described phenomenon explains the absence of signs and hypoxia symptoms in patients who are being monitored (7).

In a study by Angulo et al. (8), the blood gas values of a patient with discordance between PaO₂ in arterial blood gas due to hyperleukocytosis and SpO₂ measured by pulse oximetry was tested for 30 minutes at room temperature, and kept on ice to reduce metabolism-related consumption. While the levels of PaO₂ and SaO₂ were maintained significantly in the ice, they dropped significantly at room temperature (Figure 2). In subsequent follow-ups, the margin of error was minimized through both rapid processing and the protection of the blood in ice.

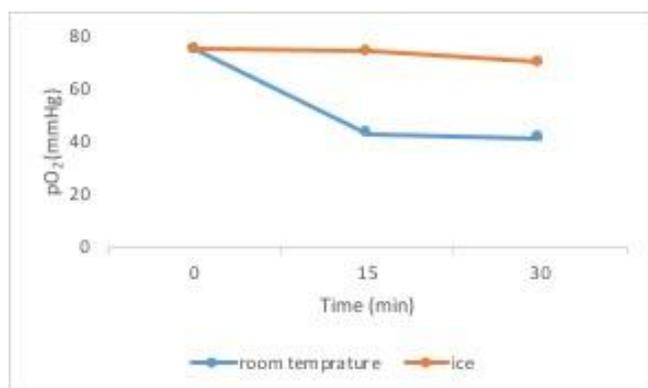


Figure 2: pO_2 levels of two blood gas samples taken simultaneously at ice and room temperature at the 15th and 30th minutes

Hypoglycemia, hyperkalemia, and metabolic or respiratory acidosis may also be observed due to the hypermetabolism of neoplastic cells in patients with hyperleukocytosis. Blood gas should be examined next to the patient's bed to identify spurious hypoxemia. If it is not possible, measures should be taken to ensure that it is analyzed as soon as possible.

Lele et al. (9) proposed an algorithm for dealing with hypoxemia in patients with hyperleukocytosis. Clinical and laboratory correlations should be investigated in patients with hyperleukocytosis who show hypoxemia ($PaO_2 < 60$ mmHg), acidosis, hypoglycemia, or hyperkalemia following this algorithm.

The following procedures are recommended; 1- Using the pulse oximeter, if hypoxemia is suspected, 2- Measurement by strip from the fingertip in case of hypoglycemia, and 3- Electrocardiography if hyperkalemia is suspected.

If no abnormality that is consistent with the laboratory tests is found in such patients, a spurious abnormality should be suspected, and these results should not be considered in clinical decision making. Lastly, after chemotherapy is started and the white blood cell count has decreased, blood gas tests should be evaluated immediately to confirm normalization due to the decrease in the number of white blood cells. In our case, while the initial WBC was 394×10^3 cell/mm³, SpO_2 measured from the fingertip was 94%, while the SaO_2 in the blood gas was 54%. Although the evidence of pathological leukocytosis can be found in most organs in patients whose WBC numbers are found to be high, the main clinical symptoms of leukocytosis and the causes of death have also been found to be associated with the central nervous system (approximately 40%) and lung involvement (30%), as in our patient (10,11).

CONCLUSION

"Spurious hypoxemia" identified in arterial gas analyses is a rare phenomenon that occurs with hyperleukocytosis, and especially in hematological intensive care patients. The clinic outcomes, arterial blood gas parameters and fingertip saturation values measured with a pulse oximeter may be incompatible in such patients. It is important to recognize such patients in clinical practice. While some improvement can be achieved by analyzing the sample next to the patient, or transporting it on ice, PaO_2 may be completely normalized with cytoreductive therapy. If spurious hypoxemia cannot be detected, it may lead the clinician to perform unnecessary and potentially dangerous treatments on patients.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - M.F.H., S.A.M., M.P.K.; Planning and Design - M.F.H., S.A.M., M.P.K.; Supervision - M.F.H., S.A.M., M.P.K.; Funding - M.F.H., M.P.K.; Materials - M.F.H., M.P.K.; Data Collection and/or Processing - M.F.H., M.P.K.; Analysis and/or Interpretation - M.F.H., M.P.K.; Literature Review - M.F.H.; Writing - M.F.H., M.P.K.; Critical Review - M.P.K.

YAZAR KATKILARI

Fikir - M.F.H., S.A.M., M.P.K.; Tasarım ve Dizayn - N.Ç., M.F.H., S.A.M., M.P.K.; Denetleme - M.F.H., S.A.M., M.P.K.; Kaynaklar - M.F.H., M.P.K.; Malzemeler - M.F.H., M.P.K.; Veri Toplama ve/veya İşleme - M.F.H., M.P.K.; Analiz ve/veya Yorum - M.F.H., M.P.K.; Literatür Taraması - M.F.H.; Yazıyı Yazan - M.F.H., M.P.K.; Eleştirel İnceleme - M.P.K.

REFERENCES

1. Würthner JU, Köhler G, Behringer D, Lindemann A, Mertelsmann R, Lübbert M. Leukostasis followed by hemorrhage complicating the initiation of chemotherapy in patients with acute myeloid leukemia and hyperleukocytosis: a clinicopathologic report of four cases. *Cancer* 1999; 85:368-74. [\[CrossRef\]](#)
2. Khoo SM, Lee KH, Notley M. Spurious hypoxaemia in a patient with leukaemia and extreme leucocytosis. *Singapore Med J* 2003; 44:208-10.
3. Gorski TF, Ajemian M, Hussain E, Talhouk A, Ruskin G, Hanna A, et al. Correlation of pseudohypoxemia and le-

- ukocytosis in chronic lymphocytic leukemia. *South Med J* 1999; 92:817-9. [\[CrossRef\]](#)
4. Mizock BA, Franklin C, Lindesmith P, Shah PC. Confirmation of spurious hypoxemia using continuous blood gas analysis in a patient with chronic myelogenous leukemia. *Leuk Res* 1995; 19:1001-4. [\[CrossRef\]](#)
 5. Chillar RK, Belman MJ, Farbstein M. Explanation for apparent hypoxemia associated with extreme leukocytosis: leukocytic oxygen consumption. *Blood* 1980; 55: 922-4. [\[CrossRef\]](#)
 6. Aygencel G. Interpretation of arterial blood gases *Arch Turk Soc Cardiol* 2014; 42:194-202. [\[CrossRef\]](#)
 7. Gartrell K, Rosenstrauch W. Hypoxaemia in patients with hyperleukocytosis: true or spurious, and clinical implications. *Leuk Res* 1993; 17:915-9. [\[CrossRef\]](#)
 8. Angulo M, Machado D, Larrosa L, Biestro A. Real and spurious hypoxemia in a patient with extreme hyperleukocytosis. *Med Intensiva* 2019; 43:435-6. [\[CrossRef\]](#)
 9. Lele AV, Marek A Mirski, Robert D Stevens. Spurious hypoxemia *Crit Care Med* 2005; 33:1854-6. [\[CrossRef\]](#)
 10. Porcu P, Cripe LD, Ng EW, Bhatia S, Danielson CM, Orazi A, et al. Hyperleukocytic leukemias and leukostasis: a review of pathophysiology, clinical presentation and management. *Leuk Lymphoma* 2000; 39:1-18. [\[CrossRef\]](#)
 11. Lester TJ, Johnson JW, Cuttner J. Pulmonary leukostasis as the single worst prognostic factor in patients with acute myelocytic leukemia and hyperleukocytosis. *Am J Med* 1985; 79:43-8. [\[CrossRef\]](#)