Hypoxemia From Multiple Causes in a Patient With Acquired Immunodeficiency Syndrome

To the editor: Hypoxia is defined as the decrease of PaO_2 below 80 mm Hg breathing normal air at sea level.[1] There are 4 main causes of hypoxia: alterations in the ventilation/perfusion ratio (V/Q), alveolar hypoventilation, presence of an anatomical shunt, and alterations in diffusion.[2] Frequently one cause predominates over the others or is the sole cause of hypoxia. The simultaneous presence of several causes is rare. We present the case of a patient with acquired immunodeficiency syndrome (AIDS) diagnosed with acute respiratory insufficiency with hypoxia from multiple causes.

A 44-year-old woman was admitted to our hospital with progressive dyspnea developing over a period of 4 days, accompanied by sweating, cough with purulent expectoration, and right-sided pleuritic pain. The patient had been smoking two packs per day since she was 14 years old, had been addicted to parenteral drugs, was receiving methadone treatment, and was infected with hepatitis B and C, Child-Pugh class A. The patient had been diagnosed with infection by human immunodeficiency virus (HIV) 9 years earlier and had been receiving treatment with antiretroviral drugs for the past 5 years. She had not suffered opportunistic infections. Physical examination revealed acrocyanosis, painless hepatomegalia 2 cm below the last rib, generalized hypophonia, and inspiratory crepitations in the lower right third of the thorax. Blood tests showed hemoglobin, 9 g/L; white cell count, 2400/mL (segmented neutrophil count 1580/mL); CD4 cell count, 70/mL; platelets, 7700/mL; lactate dehydrogenase, 459 U/L; and normal ionogram and renal parameters. Arterial gasometry revealed pH to be 7.39, $PaCO_2$ 56 mm Hg, and PaO_2 46 mm Hg; bicarbonate, 15 mEq/L; alkaline phosphatase, 167 IU/L; total bilirubin, 16 µmol/L; alanine aminotransferase, 26 U/L; aspartate aminotransferase, 57 U/L.

The chest x-ray showed an alveolar infiltrate at the right base. Although a computed tomography scan of the chest showed absence of alveolar opacities, the patient remained acrocyanotic and hemoglobin oxygen saturation by pulse oximetry ranged from 84% to 88%. This situation was reversed with oxygen therapy through a nasal mask at 2 L/min. A contrast echocardiogram showed clearly that the contrast medium arrived at the left chambers after more than three heart beats. This indicated the presence of a right-left pulmonary shunt, as well as the absence of atrial or ventricular septal defects or other cardiac abnormalities that might account for the passage of contrast medium between the left chambers. Pulmonary hypertension was not detected. A perfusion scan clearly indicated the presence of a pulmonary arteriovenous shunt.

Lung function testing indicated the existence of a moderate anatomical shunt (14% of ejection fraction) while breathing 100% oxygen for 20 minutes. The patient presented severe reduced carbon monoxide (CO) transfer (CO diffusing capacity, 36%; and a CO transfer coefficient 40% of predicted). Mild airflow limitation was detected by spirometry: forced expired volume in 1 second (FEV_1), 1.98 L (70%); forced vital capacity (FVC), 3.29 L (90%); and the ratio of FEV_1/FVC, 60%. Carboxyhemoglobin was 1.8%.

In summary, the patient, who had been diagnosed with AIDS, presented severe

hypoxia and mild hypercapnia at rest, severely altered CO diffusing capacity, moderate airflow limitation, and intrapulmonary shunt, probably related to her liver disease.

Lung diseases are among the most frequent illnesses suffered by patients in the later stages of HIV infection, in keeping with the decrease in CD4 cell count. Among opportunistic pathogens, *Pneumocystis carinii* is the one mainly responsible for disease in patients with AIDS. It is followed by *Mycobacterium tuberculosis*, cytomegalovirus, idiopathic diseases such as lymphoid interstitial pneumonia, and oncologic diseases such as lymphoma or Kaposi's sarcoma.[3] In our patient, none of the above diseases was identified as the cause of symptoms. For this reason, we believe that hypoxia was caused by the coexistence in this patient of several pulmonary alterations, which were different from more commonly observed presentations.

Hypoxia is a common manifestation of a variety of diseases which involve the lung or other parts of the organism.[4] The 4 main causes of hypoxia should be considered, V/Q alteration being the most common one. All pulmonary diseases present with more or less severe alteration in regional V/Q homogeneity.[5] Hypoxia may have more than one pathogenic mechanism, although usually one predominates. Intrapulmonary shunt has been shown to be the main cause of hypoxia in a variety of diseases, and this has considerable practical interest because it determines the treatment approach to be taken. The alveolar-arterial oxygen gradient—called the alveolar-arterial oxygen difference or $P(A\text{-}a)O_2$—is often used to determine the cause of hypoxia along with the measurement of PaO_2 and the response to supplementary oxygen. To quantify the existence of an increased anatomical shunt, 100% oxygen is administered for 20 minutes, after which arterial gases are sampled. The increase in $P(A\text{-}a)O_2$ indicates the presence of an anatomical shunt, which can be expressed as the percentage of cardiac output that does not participate in gas exchange. In this case, the hemodynamic and echocardiographic study proved the existence of a right-left anatomical shunt that was quantified by the previously described method to be 14% of cardiac output. The considerable decrease in CO transfer, even though pulmonary hypertension was not detected, suggested a reduction in the exchange surface area, contributing to hypoxia. The more than likely existence of anomalies in V/Q in a smoker with airflow limitation must be added to the causes of hypoxia. The last of the causes was the presence of mild hypoventilation, contributing to the decrease in $PaCO_2$ (46 mm Hg), although this condition was of less importance than the previous ones. Furthermore, the coexistence of a high carboxyhemoglobin concentration meant that the presence of significant tissue hypoxia must be added to the other multiple causes of hypoxia in this case.

In conclusion, the patient presented severe hypoxia from multiple causes. The most relevant ones were an anatomical shunt (arteriovenous fistulae, a possible hepatopulmonary syndrome), severely altered CO transfer caused by a diminished pulmonary vascular bed, mild V/Q alteration, and very slight alveolar hypoventilation. To all of this the harmful presence of carboxyhemoglobin must be added. All possible causes of hypoxia developed in this patient simultaneously, although each one of them had contributed to the pathogenesis to a different degree.

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