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HYPERTENSION

CASE REPORT: CLINICAL CASE

Nicardipine-Induced Acute Hypoxia in a Patient With Type B Aortic Dissection

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A 53-year-old man admitted for type B aortic dissection developed worsening hypoxia on initiation of nicardipine. Workup revealed only trace pleural effusions with associated atelectasis. Hypoxia resolved with the cessation of nicardipine. This case highlights nicardipine as a potential underlying cause of hypoxia in patients without known lung disease.

HISTORY OF PRESENTATION

A 53-year-old man presented to the emergency department with several hours of lightheadedness and severe, acute abdominal pain radiating to his back. This was preceded by fevers and chills the previous evening. Vital signs on presentation were a temperature of 37.6 °C, heart rate of 95 beats/min, blood pressure of 208/125 mm Hg, and oxygen saturation of 100% on room air. On physical examination, cardiac auscultation demonstrated regular rate and rhythm, normal heart sounds, and a soft diastolic murmur. The jugular venous pulse was not elevated. Pulses in bilateral radial, posterior tibial, and dorsal pedal were symmetrical and 2+ on palpation. No peripheral edema was present. The patient had normal respiratory effort, and pulmonary auscultation was clear bilaterally. A chest x-ray demonstrated severe enlargement of the thoracic aorta, and a computed tomography (CT) angiogram of the chest demonstrated a type B aortic dissection extending from his aortic arch to bilateral iliac arteries. There was no evidence of pulmonary disease.

He was admitted to the cardiac intensive care unit for further management. He was started on a continuous esmolol infusion for impulse control and blood pressure management. On the second day of admission, he was transitioned to a continuous nicardipine infusion at 2 mg/h due to a third-degree atrioventricular block believed to be secondary to the esmolol infusion. Within 1 hour of initiation of the nicardipine infusion, he became hypoxic, requiring 2 L/min of oxygen by nasal cannula, and within 3 hours he required high-flow oxygen at 20 L/min to maintain an oxygen saturation >92%. That evening, his nicardipine infusion was further increased to 15 mg/h because of inadequate blood pressure control. He had a concurrent increase in his oxygen requirements, requiring maximal high flow with 100% fraction of inspired oxygen (Fio_2) at 40 L/min to maintain an oxygen saturation above 92%.

TAKE-HOME MESSAGES

- Nicardipine can cause acute hypoxia in patients with underlying lung pathology because of inhibition of hypoxic pulmonary vasoconstriction, which is a physiological response to reduce shunting.
- Acute hypoxemia related to nicardipine should be considered when using it in the setting of aortic dissection and related pleural effusions.

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ABBREVIATIONS AND ACRONYMS

ABG = arterial blood gas

CT = computed tomography

Fio_2 = fraction of inspired oxygen

HPV = hypoxic pulmonary vasoconstriction

V/Q = ventilation-perfusion

PAST MEDICAL HISTORY

The patient had a history of hypertension and hyperlipidemia. He was prescribed lisinopril for hypertension but did not take it. He was compliant with atorvastatin 20 mg for hyperlipidemia. He was a former smoker and had occasional alcohol consumption.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for our patient's worsening hypoxic respiratory failure included pulmonary embolism, extension of his dissection to the coronary arteries leading to flash pulmonary edema, pneumothorax, aspiration, pneumonia, pulmonary arteriovenous malformation, congestive heart failure, and intracardiac or extracardiac shunt.

INVESTIGATIONS

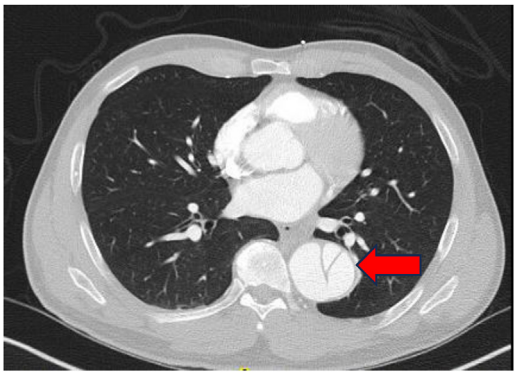
After the onset of hypoxia, an arterial blood gas (ABG) was performed, which showed a P_{CO_2} of 28 mm Hg and P_{O_2} of 45 mm Hg. A chest x-ray demonstrated basilar linear opacities, consistent with atelectasis. A CT angiogram of the chest revealed an unchanged aortic dissection, trace pleural effusions with associated atelectasis, and no evidence of pulmonary embolism, pneumothorax, or pneumonia. An electrocardiogram again demonstrated a third-degree atrioventricular block with a junctional escape rhythm without evidence of ischemia.

A repeat ABG after initiation of high-flow oxygen to 20 L/min with an Fio_2 of 60% demonstrated a P_{CO_2} of 31 mm Hg and P_{O_2} of 73 mm Hg. After the nicardipine was titrated up to 15 mg/h, high flow was escalated to 35 L/min with an Fio_2 of 80%, and a repeat ABG revealed a P_{CO_2} of 29 mm Hg and P_{O_2} of 67 mm Hg. A repeat electrocardiogram demonstrated sinus rhythm. On transthoracic echocardiogram, the left ventricular ejection fraction was normal at 65% to 70% with no regional wall motion abnormalities, right ventricular size and function were normal, and there was no significant valvular disease and no intra- or extracardiac shunt detected on saline injection.

MANAGEMENT

Because of his persistent hypoxia without an identifiable cause, a broader differential diagnosis for his clinical syndrome was considered by the clinical team. There is a risk of nicardipine-induced hypoxia for patients with lung pathology because of inhibition of physiological shunting that would normally reduce the ventilation-perfusion (V/Q) mismatch. To determine if this was a contributing factor, the rate of the nicardipine infusion was decreased at 9 AM on hospital day 3, which had remained at 15 mg/h overnight the night before. Within 8 hours the infusion had been discontinued. The patient's oxygen requirements decreased over this time period, and by 9 AM the following day he was back on room air. The only additional intervention performed during this time was diuresis, although the patient had a total fluid balance of positive 400 mL despite 3 doses of 40-mg intravenous furosemide.

FIGURE 1 Computed Tomography Findings on Presentation



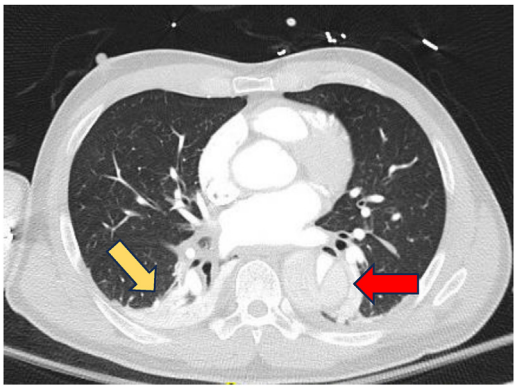
The red arrow shows the aortic dissection.

DISCUSSION

Nicardipine is known to induce hypoxia because of the inhibition of hypoxic pulmonary vasoconstriction (HPV) (Figure 1).[1] HPV is the physiological process of vasoconstriction of the pulmonary vasculature in response to low regional partial pressure of oxygen in the lungs, effectively reducing the V/Q mismatch by reducing blood flow to the hypoxemic lung.[2] This process is particularly important for patients with underlying lung disease, including chronic obstructive pulmonary disease and pneumonia, by reducing the V/Q mismatch.

Intravenous calcium channel blockers, including nicardipine, have been shown to decrease HPV, which can be clinically deleterious among patients with lung disease.[3] For instance, nifedipine has been found to decrease systemic oxygen concentration due to an

FIGURE 2 Computed Tomography Findings on Day 2



The red arrow shows the aortic dissection, and the yellow arrow shows pleural effusions with associated atelectasis.

increased V/Q mismatch in patents with cor pulmonale.[4] In 1 case report, a 55-year-old man admitted for hypoxia due to pneumonia experienced worsening hypoxia after receiving nicardipine.[5] In this case, discontinuation of the nicardipine resulted in rapid improvement of hypoxia. In another case report, a 63-year-old woman who underwent bilateral lung transplant for idiopathic pulmonary fibrosis developed hypoxia postoperatively when nicardipine was initiated for blood pressure management. Her hypoxia resolved after discontinuation of nicardipine.[1] Similar case reports have been published regarding clevidipine-induced hypoxia, with rapid improvement of hypoxia after cessation of the infusion.[6]

To our knowledge, our case report is the first to describe clinically significant hypoxia in the setting of continuous nicardipine infusion in a patient without previously known pulmonary disease. He was found to have small bilateral pleural effusions and associated atelectasis (**Figure 2**), but no other parenchymal lung pathology was visualized on CT. Of note, prior studies have identified an association between pleural effusion and aortic dissection.[7] It is possible that the pleural effusions our patient developed exacerbated pulmonary shunting and activation of HPV, causing intolerance of the nicardipine infusion.[8] The elevated risk of pulmonary pathology in aortic dissection may highlight the need for increased suspicion of nicardipine intolerance in this patient population. Regardless, the dose-dependent effect of the nicardipine infusion on the patient's hypoxia as well as the "dechallenge" test, with rapid resolution in oxygen requirements with discontinuation of the nicardipine, supports our hypothesis that his hypoxia was driven by medication side-effect. Our case highlights the importance of including nicardipine-related reduction in HPV on the differential diagnosis for patients with worsening hypoxia who are being treated with a continuous infusion of calcium channel blocking medications, regardless of underlying lung pathology.

FOLLOW-UP

The patient's oxygen requirement resolved, and he ultimately underwent surgical management of his type B aortic dissection with open descending thoracic aortic aneurysm repair on cardiopulmonary bypass. His postoperative course was uncomplicated. He was discharged home, and at his first outpatient follow-up visit, an interval CT angiogram of the chest demonstrated no residual aneurysm.

CONCLUSIONS

Continuous nicardipine infusion has previously been found to cause clinically significant hypoxia among patients with known lung pathology. Our case demonstrates that it may also induce hypoxia in patients without clinically significant lung pathology.

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