A Case of Chronic Mountain Sickness Diagnosed by Routine Pulmonary Function Tests*

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Chronic mountain sickness is a syndrome seen in high altitude natives and consists of relative hypoventilation, hypoxemia, polycythemia and cor pulmonale. The patient described herein demonstrated these abnormalities in addition to the typical pattern of sleep-disordered breathing. This diagnosis was made using standard laboratory and blood gas data, pulmonary function testing and polysomnography.

CASE REPORT

The patient is a 64-year-old lifelong resident of Mexico City (altitude of approximately 2,300 meters or 7,500 feet) presenting with progressive dyspnea on exertion, hypersomnolence and pedal edema. The family reported loud snoring, frequent arousal, and cyanosis during sleep. He had seen a local physician who treated him for “heart failure,” but no diagnostic studies were available. He had never smoked and denied any history of asthma, organic, or inorganic dust exposure. His medications were aspirin, atenolol, digoxin, allopurinol, indomethacin and a combination diuretic (furosemide and amiloride). Physical examination revealed: heart rate, 54 bpm; blood pressure, 110/76 mm Hg; respiratory rate, 12 bpm. His height was 6’1” (185 cm) and weight was 274 lb (124.6 kg). Mild circumoral cyanosis was present. No jugular venous distention was noted. Chest examination showed decreased breath sounds. No murmur or gallop was present. The abdomen was protuberant and 2+ pitting edema was present in the lower extremities. The electrocardiogram showed sinus bradyarrhythmia at a heart rate of 56 bpm, an axis of +120o, right ventricular hypertrophy, and an incomplete right bundle branch block. Chest x-ray film revealed mild hyperinflation, right ventricular prominence, and enlarged pulmonary arteries consistent with air trapping and pulmonary hypertension. Echocardiogram showed concentric left ventricular hypertrophy (left ventricular ejection fraction of 60-69 percent), mildly enlarged right atrium and left atrium, enlarged right ventricle with diffuse hypokinesis and an estimated pulmonary artery systolic pressure of 50-55 mm Hg. These findings are consistent with pulmonary hypertension and cor pulmonale. A nuclear medicine ventilation/perfusion lung scan was interpreted as being low probability for the presence of pulmonary emboli. The measured bicarbonate was 28 mEq/L (normal 24-28 mEq/L). Hemoglobin and hematocrit were markedly elevated at 21.4 g/dl and 75.6 percent respectively.

Arterial blood gas determinations on arrival at sea level and one week later are shown in Table 1. These results reveal respiratory acidosis and severe hypoxemia with a relatively normal A-a gradient (approximately 20 mm Hg) when adjusted for the patient’s age. Results of pulmonary function tests are also shown in Table 1. There was air trapping, as suggested by the elevated RV, but minimal airways obstruction, as reflected by the normal FEV1/FVC and airways resistance.

In addition, complete nocturnal polysomnography was performed on two occasions (four days after arrival and one week later following tracheostomy). The initial study four days after arrival at sea level showed nine apneas per hour. He had a low oxygen saturation while awake (75-80 percent) which dropped during the periods of apnea and hypopnea (avg 29% sleep). The CPAP and BIPAP titrated as high as 14 cm H2O and varying combinations of inspiratory and expiratory pressures did not affect the sleep architecture or magnitude of desaturation. Oxygen was not administered during this test. The follow-up study performed after tracheostomy showed minimal improvement in sleep architecture, but revealed continued episodic desaturation and CO2 retention.

DISCUSSION

The patient in this case study demonstrates alveolar hypoventilation with hypoxemia, polycythemia, signs of pulmonary hypertension and cor pulmonale with marked desaturation during sleep apnea, and hypopnea. This case represents the complex interaction between ventilatory drive, sleep-disordered breathing, and dwelling at high altitude. At sea level, one of

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the physiologic parameters that affects ventilatory drive is the partial pressure of carbon dioxide. Increasing the carbon dioxide tension in the blood leads to a linear rise in minute ventilation usually reported as the slope of \( V_{E}/PaCO_2 \) (normal range 1.5–5.9 L/min/mm Hg). Hypoxemia also stimulates ventilation, but in a hyperbolic pattern when plotted against \( P_{a}O_2 \). The increase in minute ventilation to hypoxemia becomes steep at 50–60 mm Hg \( P_{a}O_2 \) and increases rapidly at \( P_{a}O_2 \) 30–40 mm Hg. The ventilatory response to hypercapnia and hypoxemia are interactive. The slope of \( V_{E}/PaCO_2 \) increases in the setting of hypoxemia. On ascent to altitude, hyperventilation occurs as a result of the increased drive to ventilation from hypoxemia (due to the lowering of the barometric pressure and the \( P_{a}O_2 \) with a resulting decrease in arterial \( PaCO_2 \). Over time, the body compensates for the hypoxemia by increasing hemoglobin, shifting the oxyhemoglobin affinity curve to the right, and increasing cardiac output. The kidney excretes excess bicarbonate in an attempt to maintain a near normal pH. It is reported that high altitude natives will have a slightly higher \( PaCO_2 \) and lower \( PaO_2 \) than newcomers.2,3

Respiratory drive to hypercapnia or hypoxemia is slightly increased or unchanged in acutely acclimatized sea level natives.4,5 However, many investigators have demonstrated depression of hypoxic and hypercapnic ventilatory drive in chronic altitude dwellers and loss of the interactive effect of combined hypoxemia and hypercapnia.3,5-10 Whether this loss of ventilatory drive is genetic or acquired, reversible or irreversible, is a matter of controversy.4,6,10,11 Severinghaus3 has postulated that a desensitization of peripheral chemoreceptors occurs due to chronic hypoxemia. Indeed, structural changes in the carotid body have been demonstrated in autopsy studies.12,13 Administration of high inspired oxygen concentrations to high altitude natives results in unpredictable changes in \( V_{E} \) ranging from increased \( V_{E} \) (thought secondary to removal of hypoxic medullary chemoreceptor depression) to no change or slight decrease.3,5,14 Severe hypoxemia (\( PaO_2 \) <50 mm Hg) has been shown to suppress ventilation in native highlanders both at altitude and sea level in a fashion similar to that seen in chemodenerveated dogs.5,15 In fact, Lahiri et al6 showed a negative interactive effect of hypoxemia and hypercapnia in native highlanders, which probably reflects loss of peripheral chemoreceptor function. Relocation of a high altitude native to sea level results in no improvement of depressed hypoxic or hypercapnic ventilatory responses.3,5,10

At the altitude in Mexico City (approximately 2,300 meters), the barometric pressure of 578 mm Hg results in a \( P_{a}O_2 \) of 111 mm Hg. If we assume that the patient’s A-a gradient was the same in Mexico City as at sea level and his \( PaCO_2 \) was 40–44 mm Hg (given a measured \( HCO_3^- \) of 28 mEq/L and assuming near normal pH), then his \( PaO_2 \) in Mexico City would have been 36–41 mm Hg. Of course, at the altitude of Mexico City, a normal \( PaCO_2 \) would be approximately 30–34 mm Hg depending on the degree of acclimatization.5,6,7 Our patient demonstrates relative hypventilation at his native altitude with severe hypoxemia and worsening of this hypventilation upon descent to sea level.

An unusual clinical syndrome associated with relative hypoventilation at altitude is chronic mountain polycythemia or chronic mountain sickness (CMS) described first by Monge in 1928.16 CMS occurs in native altitude dwellers or sojourners of any age and at any time after arriving at altitude and is characterized by relative hypoventilation resulting in hypoxemia, polycythemia and cor pulmonale.3,4,8 Whereas high altitude natives may have depressed hypoxemia and hypercapnic ventilatory drives, those patients with CMS exhibit an extreme of this depression with profoundly blunted responses to both hypoxemia3,4,8 and hypercapnia.14 Although measurements of ventilatory sensitivity to carbon dioxide and oxygen can be made in patients with CMS, this case report demonstrates that the diagnosis can be made without such specialized studies.

Hurtado14 reported that oxygen administration in subjects with CMS produced no change in ventilatory effects of \( CO_2 \) rebreathing. Since hypoxic drive is the major stimulus for breathing at altitude, breathing higher inspired oxygen concentrations at sea level may depress minute ventilation. The patient we describe fits all of the clinical criteria for CMS (relative hypoventilation at altitude resulting in hypoxemia, polycythemia and cor pulmonale). The etiology or precipitating factors for the development of CMS are unknown. CMS may represent a form of alveolar hypoventilation in altitude dwellers or simply one end of the spectrum of abnormal ventilatory response to hypoxia and hypercapnia. Altered lung function, obesity, or sleep-disordered breathing alone or in combination may precipitate or contribute to development of CMS.

Patients with CMS have abnormal sleep physiology. In normal subjects at sea level, sleep depresses the ventilatory response to hypercapnia. In a study by Reed and Kellogg,17 three healthy sea level natives were found to have similar decreases in \( CO_2 \) response curves at sea level and at altitude (3–5 mm Hg shift to right) while overall \( CO_2 \) responsiveness was increased on ascent to altitude (waking curve shifted 10–12 mm Hg to left). Weil et al18 studied ten long-term high altitude (3,100 meters) residents during sleep (five patients had CMS and five normal natives). Three types of respiratory sleep patterns were noted: (1)
undulating respirations without true apnea, (2) periodic breathing with 10-12 s apneas, and (3) periods of grossly irregular breathing. The amount, time and number of episodes was similar for the two groups of patients with the undulant pattern most common. The striking difference was the profound oxygen desaturation noted in the five patients with CMS (mean time of 201 minutes below 80 percent saturation). This degree of desaturation was noted for the patient in this case report during the initial sleep study. In addition, Weil et al17 showed a marked improvement in nocturnal desaturation with administration of medroxyprogesterone acetate (MPA), although no apparent improvement in hypoxic or hypercapnic ventilatory response nor abnormal sleep breathing pattern was noted.

**Summary**

In summary, this is a patient who presented with respiratory acidosis and cor pulmonale. The major diagnostic challenge was in differentiating primary cardiopulmonary disease from a central abnormality of ventilatory drive. The arterial blood gases showed a normal A-a gradient suggesting hypoventilation as the etiology of his hypoxemia. Pulmonary function testing showed air trapping, but a relatively normal FEV1/FVC and airways resistance. The literature suggests that most altitude natives have depressed hypoxicemic and hypercapnic drives with a distinct subset demonstrating a profoundly depressed drive to ventilation. This latter group has been labeled as having chronic mountain sickness or Monge's disease. As one might expect, ventilatory control during sleep is also abnormal in these patients with CMS. Our patient indeed showed typical frequent severe desaturations with hypopnea. The diagnosis of CMS in our patient was made with routine arterial blood gases and standard pulmonary function tests. Additional tests of ventilatory responsiveness to oxygen and carbon dioxide could have been performed, but are not necessary to make the diagnosis.

**References**

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