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Case Report Open Access

Extreme Altitude Chronic Mountain Sickness Misdiagnosed as High Altitude Cerebral Edema

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Abstract

Introduction: Chronic mountain sickness (CMS) represents a syndrome of secondary polycythemia along with thrombocytopenia, altered hemorheology, pulmonary and systemic hypertension, and congestive heart failure, occurring due to hypobaric hypoxia-anoxia-induced erythropoiesis reported in both native mountain residents and new climbers after prolonged stays at high and extreme altitudes.

Case Presentation: A healthy non-smoker non-drinker reported occipital headache, breathlessness, and insomnia after an uneventful stay of 70 days at 6400 m/21000 ft. His hemoglobin was 21 gm/dL. The patient was diagnosed as having a case of CMS with a Qinghai CMS score >6. Therapeutic phlebotomy was performed; 350 mL was drained on two occasions, reducing his hemoglobin to 14.6 gm/dL.

Conclusion: The altered presentation, difficult diagnosis, evacuation, and long-term management highlighted in this case occurring at 6400 m/21 000 ft in the Karakoram Himalayas represents the insidious nature of altitude sickness in acclimatized subjects.

Keywords: Chronic mountain sickness, Excessive erythrocytosis, Stress polycythemia, Gaisböck syndrome, Cerebral edema, Extreme altitude, Triple hypoxia syndrome

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Introduction

Chronic mountain sickness (CMS) represents a variably reversible asynchronous syndrome of secondary polycythemia along with erythrocytosis, erythrocyte aggregation, hemoglobinemia, hemoconcentration, thrombocytopenia, increased whole blood viscosity, fibrinogenemia, prothrombotic state, pulmonary and systemic hypertension, and congestive heart failure, occurring due to hypobaric hypoxia-anoxia-induced erythropoiesis reported in both native mountain residents and new climbers after prolonged stays at high altitudes. CMS can be accelerated by smoking-induced carboxyhemoglobinemia at high altitudes. The core pathology of polycythemia is both a boon to mountain adaptation and athletic training as well as a bane towards high altitude deterioration (HAD) leading to CMS.[1,2]

A large number of explorers and adventurers along with 140 million people residing at altitudes above 3000 m/9800 ft are at risk of contracting altitude illness. CMS along with hypoxia, cold, and other physiological extreme altitude stressors can contribute to lassitude, cyanosis, thromboembolic phenomena, right ventricular enlargement, myocardial infarction, cerebral infarction, stroke, and frostbite. CMS can be asymptomatic or oligosymptomatic at extreme altitudes above 5500 m/18 000 ft and may be confused with high altitude cerebral edema (HACE). The case being discussed highlights some important aspects of an insidious presentation of CMS which was confused with HACE at an extreme altitude of 6400 m/21 000 ft in the Karakoram Himalayas.

Case Presentation

A 26-year-old healthy non-smoking, non-drinking explorer from plains country underwent an extended staged-graded acclimatization schedule before reaching 6400 m/21 000 ft. After an uneventful stay of 70 days at that altitude, he reported moderate to severe occipital headache, breathlessness, and two episodes of vomiting to the medical doctor staying at 5790 m/19 000 ft in November. Though there was no history of gain in altitude or exertion, altitude illness was suspected. Rest, plenty of fluids, acetaminophen 500 mg, acetazolamide 250 mg and intravenous dexamethasone 8 mg were initiated following which the patient reported mild improvement. He continued to have headache, breathlessness, and nausea the

next day along with insomnia. His condition deteriorated with disorientation reported by other people around him the following day. He was descended from 6400 m/21 000 ft to 5790 m/19000 ft, crossing an ice wall on foot supported by climbing ropes and two assistants. Preliminary examination revealed a conscious, oriented, but flushed individual with a heart rate of 144 beats per minute, blood pressure of 160/110 mm Hg, respiratory rate of 24 breaths/min, a normal temperature, and 90% oxygen saturation. Cyanosis, clubbing, and pedal edema were not present. Seeing his condition as critical, an immediate air evacuation was requisitioned, but the helicopter could not land at 6400 m/21 000 ft due to heavy winds. The explorer was towed behind a snow scooter in a supine position inside a sleeping bag and transported approximately 50 km over glaciated terrain to 4570 m/15 000 ft from where he was evacuated by air to a secondary care facility. His hemoglobin was 21 gm/dL on two occasions without any other changes in routine hematological or clinical chemistry parameters. His electrocardiogram (ECG) was normal. No evidence of congestive heart failure was seen. He was diagnosed as a case of CMS with a Qinghai CMS score >6[1] and swiftly transferred to a tertiary care facility where the findings were confirmed. Other intuitive investigations such as echocardiography, pulmonary function tests, contrast enhanced computed tomography-venography, and magnetic resonance venography were not contributory. No evidence of pre-existing or co-existing risk factors for secondary polycythemia were found. V617F mutation in exon 14 of *JAK2* gene was not detected in leuocytes excluding chronic myeloproliferative disorders, especially polycythemia vera and idiopathic myelofibrosis. Therapeutic phlebotomy was performed and 350 mL was drained on each of two occasions, reducing his hemoglobin to 14.6 gm/dL. A 6-month follow up revealed symptomatic improvement and a hemoglobin of 17 gm/dL. A 6-month retrospective and prospective surveillance of fellow climbers having undergone a similar staged-graded acclimatization schedule and having stayed at a similar altitude of 6400 m/21 000 ft for 70 days or more did not reveal the development of CMS.

Discussion

The patient reported here, who was developing CMS, presented with headache, vomiting, tachycardia, tachypnea, and hypertension despite acclimatization and being a nonsmoker. This case represents the insidious nature of altitude sickness in acclimatized subjects.[2-5] The presentation of headache and vomiting could have been caused by specific altitude illness, fatigue, dehydration, or hypoglycemia. HACE can only be diagnosed clinically with Lake Louis criteria in a setting of recent gain in altitude, which was not the case with this patient.[2-4] However, altitude illness has been reported to occur in acclimatized subjects at extreme altitudes with no history of recent elevation gains.[2-4] Fatigue, dehydration, and hypoglycemia can independently present with such symptoms or coexist with altitude illness. Any uncompensated physiological state can present with altered vitals. Both altitude illness and movement of patient on the mountains can lead to altered vitals. Irrespective of the diagnosis, it is pertinent to descend and/or evacuate the patient for investigations and definitive management, as was done in this case.[2,3,5]

Mountain Sickness

Three different syndromes are described under the ambit of mountain sickness. The first is acute mountain sickness (AMS). It presents with a history of ascent, headache, nausea, vomiting, fever, and lassitude and resolves on rest, fluids, oxygen, paracetamol, and antiemetics; it rarely requires descent or evacuation. The second syndrome, subacute mountain sickness (SMS), presents with congestive cardiac failure, exertional dyspnea, bilateral pedal edema, salt and water retention, ascites, and polycythemia with underlying pulmonary hypertension, cardiomegaly, and right ventricular enlargement after a history of prolonged stay at altitude. It is managed with diuretics, oxygen, descent, and evacuation to plains. The third syndrome, CMS, may have a syndromic presentation including headache, dizziness, tinnitus, asthenia, nausea, vomiting, dyspnea, palpitations, insomnia, visual disturbances, a sense of fullness in the head and left upper abdomen, flushing of the face, erythromelalgia, dilated veins, and hypertension. However, the most common presentation is oligosymptomatic or even asymptomatic. Altered, muted, and overlapping presentation can be possible at extreme altitudes.[2-5] CMS with a hemoglobin of >24 g/dL, hematocrit of >70%, and 6 000 000 RBC/dL has been reported.[6]

Diagnosis of Chronic Mountain Sickness

Diagnosis is based on clinico-laboratory findings. Hyperuricemia and proteinuria may be associated with CMS. Even basic investigations are not available at extreme altitudes. Other causes of secondary polycythemia such as chronic lung and heart conditions, pulmonary hypertension, renal hypoxia, erythropoietin releasing renal, adrenal, hepatic and uterine malignancies, renal cysts, sleep apnea, testosterone, and steroid and erythropoietin abuse need to be excluded along with causes of stress and relative and primary polycythemia. Stress polycythemia, also known as stress erythrocytosis, pseudopolycythemia, or Gaisböck syndrome, may also contribute to CMS in mountaineers because of prolonged dehydration-induced low plasma volume. Triple hypoxia syndrome comprising altitude hypoxia, CMS hypoxia, and respiratory infection-induced hypoxia is reversible (with oxygen administration), transitory, and treatable.[2,3,7]

Treatment of Chronic Mountain Sickness

CMS is treated by therapeutic phlebotomy after de-induction from altitude. Adjunct therapy with oxygen, antiplatelet agents, pentoxifylline, acetazolamide, and cytostasis may be helpful. Most patients reach normal levels of hemoglobin three months after de-induction from altitude and therapeutic phlebotomy. However, some patients continue to reach higher levels of hemoglobin even after repeated phlebotomies. Treated CMS patients have a good prognosis, although they are likely to develop CMS on re-ascent.[8]

The Physiology of Chronic Mountain Sickness

CMS patients hypoventilate, have smaller tidal volume, smaller mean pulmonary acceleration time, lower cardiac output, increased minute ventilation with 100% oxygen, and increased ratio of dead space to tidal volume compared with normal subjects. This suggests hypoxic ventilatory depression.[1,8] Free erythroprotoporphyrins reach a peak after eight weeks of stay

at a high altitude followed by a gradual decline, while they are always higher in native mountain residents. Iron metabolism comprises three-fold increased intestinal iron absorption and plasma and erythrocyte turnover along with marrow hyperplasia around 4570 m/15 000 ft compared with sea-level residents. Reciprocal changes are known in native mountain residents upon reaching sea level. The *SENP1* gene encoded protein regulates the hypoxia inducible factor, and GATA leads to the down-regulation of plasma soluble erythropoietin receptor and the up-regulation of erythropoietin production.[9] While erythrocytosis and increased hemoglobin enable oxygen carriage capacity, erythrocytosis increases whole blood viscosity and reduces velocity, leading to decreased cardiac output and consequent arterial hypoxemia.[10] A plethora of effects consequent to CMS can contribute to aging, obesity, metabolic syndrome, hypertension, diabetes as well.

Chronic Mountain Sickness: An Enigma

CMS as an entity is an enigma. First, excessive erythrocytosis and polycythemia are considered beneficial for high altitude adaptation. Athletic training at high altitude beneficially employs polycythemia for performance enhancement at sea level. Mountaineers are altitude endurance athletes who endure extremes of hypoxia, physical exertion, physiological stress, and cold by virtue of erythrocytosis. Native residents with CMS are better adapted to altitude. Notwithstanding all these benefits, CMS that leads to altered hemorheology is known to cause HAD and CMS.[11] Furthermore, while CMS has been found in 4%-28% of native mountain residents on the South American Andean Altiplano, Central Asia, and Indian Himalayas, the prevalence of CMS is extremely low or absent in Tibetans and East Africans who are better adapted to hypoxia.[12,13] A prevalence of 36.5% has been reported in the military.[14] Moreover, certain polycythemic mountain residents may not be prone to thrombotic events. Clinical research coupled with systems biology may help discern pathogenesis, identify specific susceptibility, and provide insights into the diagnosis and management of high altitude diseases.

The threshold altitude for human dwelling is 4500 m/14 700 ft, as most humans can never acclimatize beyond that altitude.[2-4,8] Nevertheless, man has successfully defied physiological limits through altitude acclimatization, respiratory capacity exercise, cold acclimatization, and psychological self-regulation, and this is best evident at extreme altitudes.[2-4]

Conclusion

CMS at extreme altitudes may have an altered insidious presentation leading to difficulty in diagnosis, management, and evacuation. A high index of suspicion based on ongoing screening programs for acclimatized subjects may facilitate early diagnosis. Long-term management and follow-up may be required for prognosticating CMS.

Authors' Contributions

The author served as the medical officer at 5790 m/19 000 ft and attended the patient in secondary care.

Conflict of Interest Disclosures

None declared.

Ethical Approval

Patient consent and ethical approval were covered by the institutional committee.

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References

1. León-Velarde F, Villafuerte FC, Richalet JF. Chronic mountain sickness and the heart. Prog Cardiovasc Dis. 2010 ;52(6):540-549. doi:10.1016/j.pcad.2010.02.012.
2. Khan ID. Extreme Altitude Pulmonary Oedema in Acclimatized Soldiers. Med J Armed Forces India. 2012;68(4):339-345. doi:10.1016/j.mjafi.2012.04.018.
3. Khan ID. Comorbid cerebral and pulmonary edema at 7010 m/23000 ft: an extreme altitude perspective. J Med. 2013;14(2): 153-155. doi:10.3329/jom.v14i2.19668.
4. Khan ID. Cerebral venous sinus thrombosis (CVST) masquerading as high altitude cerebral edema (HACE) at extreme altitude (6700 m/22000 ft). Int J Travel Med Glob Health. 2016;4(3):96-98. doi: 10.21859/ijtmgh-040306.
5. Khan ID, Sahni AK. Possession syndrome at high altitude (4575 m/15000 ft). Kathmandu Univ Med J (KUMJ). 2013;43(3):247-249.
6. Fujimaki T, Matsutani M, Asai A, Kohno T, Koike M. Cerebral venous thrombosis due to high altitude polycythemia. J Neurosurg. 1986;64:148-1450.
7. Zubieta-Castillo G, Zubieta-Callaja G, Arano E, Zubieta-alleja L. Respiratory disease, chronic mountain sickness and gender differences at high altitude. In: Ohno H, Kobayashi T, Masuyama S, Nakashima M, eds. Press Committee of the 3rd World Congress on Mountain Medicine and High Altitude Physiology, Matsumoto, Japan; 1998:132-137.
8. Kryger M, McCullough R, Doekel R, et al. Excessive polycythemia of high altitude: role of ventilatory drive and lung disease. Am Rev Respir Dis. 1978;118(4):659-66.
9. Villafuerte FC. New genetic and physiological factors for excessive erythrocytosis and Chronic Mountain Sickness. J Appl Physiol (1985). 2015;119(12):1481-1486. doi:10.1152/japplphysiol.00271.2015.
10. Jiang C, Chen J, Liu F, et al. Chronic mountain sickness in Chinese Han males who migrated to the Qinghai-Tibetan plateau: application and evaluation of diagnostic criteria for chronic mountain sickness. BMC Public Health. 2014;14:701. doi:10.1186/1471-2458-14-701.
11. Xie SW, Liu C, Gao YX, et al. The study of prevalence rate, and clinical characteristics of high altitude deterioration.Eur Rev Med Pharmacol Sci. 2015;19(18):3444-3449.
12. Lorenzo FR, Huff C, Myllymäki M, et al. A genetic mechanism for Tibetan high-altitude adaptation. Nat Genet. 2014;46(9):951-956. doi:10.1038/ng.3067.
13. Sahota IS, Panwar NS. Prevalence of chronic mountain sickness in high altitude districts of Himachal Pradesh. Indian J Occup Environ Med. 2013;17(3):94-100. doi:10.4103/0019-5278.130839.
14. Li X, Pei T, Xu H, et al. Ecological study of community-level factors associated with chronic mountain sickness in the young male chinese immigrant population in Tibet. J Epidemiol. 2012;22(2):136-143. doi:10.2188/jea.JE20110058.