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High Altitude Brain Swelling

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Introduction

The high-altitude (HA) environment generally refers to elevations over 1500 m (4800 feet) above sea level. High-altitude illnesses is the term given collectively to Acute Mountain Sickness (AMS), High-Altitude Cerebral Edema (HACE) and High-Altitude Pulmonary Edema (HAPE), the latter two being potentially fatal conditions. The complete pathophysiological mechanisms of these maladies are not completely known and their incidences are highly variable amongst different ethnic populations. Some individuals are able to acclimatize better and are genetically more resistant to HA conditions compare to others. The occurrence and severity of the disease is highly dependent on the rate of ascent, the altitude attained and individual susceptibility.

AMS is characterized by non-specific symptoms such as headache, anorexia, nausea, vomiting, fatigue, dizziness, and sleep disturbance, but not all need to be present at one time. HACE has a relatively lower incidence rate and is widely viewed as an extension of AMS and is normally preceded by symptoms of AMS. Thus HACE is a potentially fatal form of AMS, wherein the brain swells and functions in an abnormal manner. It is caused by complex pathophysiological mechanisms with serious neurological manifestations [1]. However, it can even occur in the absence of symptoms of AMS.

HACE is characterized by neurological changes of varying degree including confusion, ataxia and altered consciousness, which may progress to coma and even death. HACE occurs in un-acclimatized lowlanders at altitudes above 2000 m. Being very less common than AMS, the exact incidence of HACE is not known. Its incidence is reported to be approximately 1.0% of all trekkers between 4243 m and 5500 m in Nepal, but increased to 3.4% in those who suffered AMS [2]. Its incidence is much more common in individuals suffering from HAPE, occurring in 13-20% of people suffering from HAPE [2]. There have been a few landmark studies which describe the characteristic features and pathophysiological mechanism of HACE besides several individual case reports.

The most common neurological features of HACE are disturbance of consciousness, ataxia, papilledema, urinary retention or incontinence and abnormal plantar reflexes [3]. Abnormal limb tone and power, pupil difference, visual field loss, speech difficulty and hearing loss are amongst the some uncommon features [3]. Autopsy studies of HACE patients [4,5] reveal edematous brain with flattening of gyri and

obliteration of sulci with evidence of uncal and tonsillar herniation commonly associated with petechial hemorrhages. Researchers have proposed a model to explain the pathophysiology of AMS and HACE in which hypoxaemia elicits various neurohumoral and haemodynamic responses lead to raised cerebral blood flow, altered permeability of the blood-brain barrier (BBB), and eventually cerebral edema [6,7]. These changes cause swelling in brain swelling and raised intracranial pressure. Patients of AMS do not show raised intracranial tension. At HA, there is a generalized increase in sympathetic nervous activity that may aggravate the condition by increasing the levels of the anti-diuretic hormone (ADH) and aldosterone, resulting in salt and water retention in the body. Fluid accumulation in the brain is a result of cytotoxic edema i.e., cell swelling due to increased intracellular osmolarity and vasogenic edema i.e., leak of the BBB with extravasation protein rich fluid into the interstitial space or both. Thus all the above conditions result in vasogenic edema and the brain swelling.

Cerebral edema is diagnosed in neuroimaging and at autopsy in patients with severe AMS [8,9]. MRI scans reveal reversible vasogenic brain edema, with characteristic increase in T2 signal in the splenium of the corpus callosum and subcortical white matter indicating increased BBB permeability [10]. Increased gene expression of vascular endothelial growth factor, a potent promoter of capillary leakage by hypoxia is believed to play an important role in the development of AMS and HACE [11]. Thus biochemical factors (e.g. VEGF, nitric oxide, and cytokines) may also play a role by altering endothelial permeability [12]. Onset of illness after 3 days at a stable altitude, abrupt onset, trauma, focal neurological signs, high fever, stiff neck, and lack of response to treatment are certain pathologies which should not be confused with HACE and may require different treatments.

Slow ascent and allowing time for acclimatization, is the best strategy for preventing HA illness. Determining an ideal rate of ascent is however difficult and varies from person to person. In some situations, pharmacological prophylaxis may be warranted. These situations include rapid ascent to altitudes higher than 3000 m and for people with increased susceptibility to AMS. Early recognitions of symptoms, diagnosis and confirmation in case of HACE with imaging studies such as MRI is very essential as it can rapidly progress to cause death. Some case reports have revealed incorrect diagnosis of HACE, wherein it mimics symptoms of stroke [13]. All cases of cerebral edema must be evacuated to a lower

altitude as an emergency. In case where the descent is not possible, a simulated descent to lower altitude by use of pressurized chambers is a solution. Portable recompression chambers which are capable of generating up to 130 mmHg pressure, which is equivalent to a reduction of altitude of 1800 m to 2400 m can be lifesaving at remote posts [14].

Treatment of HACE is similar to that for other altitude illnesses, with emphasis on oxygen and descent. According to Lake Luis scoring system [15], HACE can be diagnosed when patient of AMS show changes in mental status and or ataxia. Acetazolamide is the preferred drug, although the ideal dose varies (250 mg twice daily) [14]. Dexamethasone is also effective for more severe cases of AMS prophylaxis (4 mg every 6 hourly) and is frequently the alternative if acetazolamide cannot be prescribed. The recovery time in HACE has been reported to be 3-14 days [16].

With the increase in number of people visiting high altitudes and engaging in high altitude activities, it becomes essential that the signs and symptoms of HACE and other forms of high altitude illness are effectively communicated. Awareness regarding HA problems can help in reducing the incidences and mortality associated with HACE.

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