Sinus Vein Thrombosis Following Exposure to Simulated High Altitude

Refael Torgovicky, Bela Azaria, Alon Grossman, Uri Eliyahu, and Liav Goldstein

A relation exists between high altitude exposure and a hypercoagulable state, the nature of which is not entirely clear. This has been mostly reported in mountain climbers. We describe the first reported case in the literature of sinus vein thrombosis after high altitude chamber training. Possible mechanisms and prevention methods are discussed.

CASE REPORT

The patient was a 19-yr-old woman working as a high-altitude chamber instructor for 2 mo prior to the event, during which she participated in six training sessions. She was in a generally good health and was using oral contraceptives for 3 yr prior to the event. There was no history of smoking. Her family history was not contributory.

During a routine high altitude chamber training of simulated gradual ascent to 43,000 ft, the patient complained of dyspnea at 33,000 ft, attributing this to an oxygen mask malfunction (she claimed it was not receiving pressurized oxygen). Due to her symptoms, chamber height was adjusted to 25,000 ft, and the patient received a new oxygen mask. Another attempt was made to ascend to 43,000 ft, but the same symptoms recurred, leading to termination of the training session. Fellow instructors observing the patient described a hyperventilation state.

Immediately following this training the patient was examined by a flight surgeon. The patient’s complaint was of dyspnea and general malaise. Her oxygen saturation, as measured by a pulse-oxygenimeter, was 92%. Physical examination revealed acrocyanosis in her hands and tachypnea. The rest of the physical examination was within normal limits. The clinical diagnosis was recorded as hyperventilation combined with hypoxia.

Following a quick symptomatic improvement, the patient was discharged to 1 d of bed rest. Then, 3 d after the above event, while feeling completely well, the patient was approved by a flight surgeon to participate in another high altitude training which involved ascent to 43,000 ft. This time she felt well during the training, and no special events were noted. This was her last high altitude chamber exposure.

A few days after her last high altitude chamber training, the patient started complaining of frontal headaches, gradually increasing in severity over a month. Due to the unremitting nature of the symptoms, the patient was admitted to the neurology department, and a series of imaging studies (CT, MRI) were performed. Sinus vein thrombosis was diagnosed (sagittal and transverse sinus), and anticoagulant therapy was initiated (low molecular weight heparin followed by warfarin). Following treatment, a slow symptomatic improvement was observed, and the patient was discharged. On discharge, it was recommended she continue oral anticoagulant therapy. Literature review and detailed recommendations for prevention are provided.

Keywords: hypoxia, hypobaric, thrombosis.
plete coagulation screening panel was performed (anti-cardiolipin antibody; antithrombin III, protein C, S activity; activated protein C resistance; homocysteine level; genetic testing for factor V Leiden and prothrombin mutation), which was normal. Following the incident, all oxygen masks were inspected. No malfunctions were found.

DISCUSSION

Review of the literature shows conflicting data on the effect of hypoxic/hypobaric conditions on the coagulation system, and the mechanisms of thrombosis remain not entirely clear. Cerebral thrombosis is a well-known complication of mountain sickness. In their article, Boulos et al. (3) describe a case of superior sagittal sinus thrombosis in a mountain climber ascending to an approximate altitude of 3000 m, which eventually was found to be associated with familial protein C deficiency. This patient was heterozygous for protein C deficiency, a condition usually asymptomatic. However, in previous studies, protein C levels were shown to drop, even in mountain climbers with normal baseline levels, when ascending to height. Therefore, a first thrombotic event in a patient with low baseline levels of protein C could easily be explained even at the relatively low altitude of 3000 m.

Song et al. (7) provided 4 case reports of high altitude cerebral thrombosis, and another 10 cases of mountain sickness with CNS lesions other than cerebral thrombosis, after ascent to heights as low as 5200 m. Past and family history of the patients in this article was not contributory, and no other risk factors for development of thrombosis were found. All thrombi were of venous origin. It was postulated that hemoconcentration due to secondary polycythemia during the relatively long stay at altitude was an important factor in the development of cerebral thrombosis. Dehydration due to insufficient intake of water and increase in respiration at altitude are factors that aggravate hemoconcentration. However, it is doubtful whether hemoconcentration at altitude alone can cause cerebral thrombosis. It seems that a disturbance of cerebral circulation, in addition to hemoconcentration, is important to the development of high altitude cerebral thrombosis. It is advised by the authors for women not to use oral contraceptives while at altitude in order to prevent cerebral venous thrombosis.

Bendz et al. (2) studied 20 healthy male volunteers who were suddenly exposed to a hypoxic-hypobaric environment (8 h at a simulated altitude of 2400 m). Markers of activated coagulation (thrombin-antithrombin complex and prothrombin fragments 1 + 2) transiently increased by 2–8 fold. The authors concluded that hypobaric hypoxia combined with sedentariness and dehydration may cause increased risk of venous thrombosis. This study did not include a control group. The findings of Bendz et al. (2) have been criticized by Bartsch et al. (1), who studied a group of healthy mountaineers ascending over 22 h to a height of 4559 m, starting on foot at 3200 m. Surprisingly, in this group markers of activated coagulation did not increase following the ascent.

The contradiction between the findings of the two above studies can probably be explained by the differences in study design. Bendz et al. (2) exposed the subjects to rapid decompression (440 m to 2400 m over 10 min), while Bartsch et al. (1) studied the results of a gradual ascent to altitude (3200 m to 4559 m over 22 h). It appears that activation of the coagulation system on ascent to altitude is rate dependent. A rapid decompression poses a much higher risk than a gradual ascent.

Hodkinson et al. (4) tested whether mild normobaric hypoxia alone causes activation of coagulation. Six healthy male volunteers were exposed for 3 h to a hypoxic gas mixture. Examination of markers of activated coagulation did not support the suggestion that mild hypoxia alone causes activation of coagulation in vivo without additional factors involved. This study included a control group. However, it should be mentioned here that in vitro hypoxia is well known to promote local thrombosis.

Other studies provide further data regarding the mechanism by which high altitude exposure may contribute to a greater risk of thrombosis. Hudson et al. (5) studied the effect of high altitude exposure on platelet count in a group of volunteers that were examined after ascent from 600 m to 3600 m. A significant elevation of platelet count was found within 48 h of ascent to high altitude. This difference was sustained as a permanent feature in long-term residents. Singh and Chohan (6) described increased coagulation factors with elevated platelet adhesiveness and aggregation on ascent to altitude.

Although the patient complained of an oxygen mask malfunction, this is highly unlikely, as the symptoms recurred after the mask was changed and no malfunction was detected in a careful inspection of the masks. Also, none of the other trainees complained of any problem. The patient was initially diagnosed with hypoxia and hyperventilation. However, the diagnosis of hypoxia is doubtful, as there was no unequivocal evidence to support it clinically, and no proved causes for hypoxia could be found. It is possible that her initial symptoms resulted entirely from hyperventilation, which might cause vasoconstriction, acro-cyanosis, and following that, a wrongful pulse-oxymeter reading.

The literature review presented above shows an association between exposures to high altitude, whether real or simulated, and a hypercoagulable state. This association may change with different altitudes and acute or chronic exposures, and is ascent rate dependent. Nevertheless, the exact mechanism is not entirely clear. It is clear however, that exposure to altitude may combine with other risk factors to increase the likelihood of thrombosis; therefore, people with known risk factors, including use of oral contraceptives, should consider their risks before deciding to undertake exposure to simulated altitude in chambers. In our patient, it appears that a combination of oral contraceptive use, a tight training schedule (possible cause of hemoconcentration and coagulation system activation), hyperventilation (which may cause disturbance of cerebral circulation due to alkalosis and vasoconstriction), and maybe some yet-unknown defect in coagulation or ce-
rebral circulation, may have caused the unfortunate event of sinus vein thrombosis.

Following this event, we provide recommendations for managing people frequently exposed to simulated high altitude:

1. Careful medical history for candidates regarding coagulopathies, and closely monitored medical follow-up by a flight surgeon.
2. Women using oral contraceptives should consider their risks before deciding to undertake exposure to simulated altitude in chambers.
3. Perform coagulation-screening tests for candidates.
4. Periodic CBC examination to R/O polycythemia, thrombocytosis.
5. Emphasis on sufficient drinking before training to prevent dehydration.
6. Avoidance of exposure to simulated altitude while not feeling well (even mildly).
7. Education of flight surgeons and high altitude chamber staff that any kind of neurological complaint in a relevant setting should be addressed very seriously, investigated, and treated appropriately.
8. Further research is indicated in order to define the exact recommended exposure regimen to simulated altitude. Until exact data will be available, it is recommended to minimize unnecessary exposure.

CONCLUSION

Although the relation between exposure to high altitude and a hypercouagulable state is well known, this is the first time a case of sinus vein thrombosis has been reported after high altitude chamber training. The changes occurring in the coagulation system and risk for thromboembolic disease with ascent to high altitude deserve further study. Careful history and tight medical follow-up should be performed on designated staff exposed to simulated high altitude.

REFERENCES