

Case Report

A case of thrombosis at high altitude

In November 2003, a 33-year-old nurse presented herself in a Dutch hospital with a painful and warm left leg. She had just returned from a hiking trip in Nepal where she had stayed for a month at a maximum altitude of 5400 meters. The trip included two transcontinental flights of 12 hours and two bus trips of 6 and 12 hours (Fig. 1). As an obligatory carrier of the Factor V Leiden mutation (confirmed by DNA analysis) – her father has the homozygous genotype of the mutation – she took thrombosis precautions for the flight by using nadroparin 2850 E once, and wearing elastic stockings.

After a gradual ascent to 3500 meters in seven days, she used acetazolamide 125 mg once daily for prevention of High Altitude Disease. Other medication used was 1 mg lynestrenol (Orgametril®; a first generation progestin-only pill) for birth control. She was used to regular exercise and the physical effort was not excessive. After reaching an altitude of 4450 m, she developed a painful and warm left leg. A local doctor prescribed aspirin after physical examination and she was reassured that deep vein thrombosis was not very likely. Since her complaints persisted, she sought medical help back in the Netherlands. The duplex ultrasound confirmed the diagnosis deep vein thrombosis (extending from the popliteal vein to the distal femoral vein), after which treatment with nadroparin

and phenprocoumon was administered for six months. Eleven months later, she developed a superficial thrombosis of the right leg after a long haul flight to Sydney. For future journeys she was advised to use a prophylactic dosage of nadroparin (2850 IE) until two days after arrival.

Recently, the role of air travel in the pathogenesis of thrombosis has received ample attention. As underlying mechanism, apart from the obvious immobilisation, effects of dehydration and hypobaric hypoxia (inherent to the cabin altitude) on the clotting system have been suggested. The latter has been studied at high altitude, in hypobaric chambers and during actual air travel. In a study by Mannucci et al., 8 healthy volunteers flew to Kathmandu (1200m), and later by helicopter to 5060 m. A transient prothrombotic imbalance was found, expressed by increased thrombin formation and fibrinolysis inhibition (1). These results were not confirmed in a similar study in which healthy mountaineers ascended from 3200 m to 4559 m within 22 hours (2). Bendz et al. exposed 20 volunteers in a hypobaric chamber to a hypoxic and hypobaric environment similar to the altitude in airplane cabins of 2400 m. Markers of activated coagulation were found to be transiently increased by two- to eight-fold (3). During actual air travel, Schobersberger et al. measured markers for coagulation and fibrinolysis in 20 volunteers. An increased activity of FVII and FVIII was found as well as suppressed fibrinolysis (4). A recent French study did not show an increase in haemostasis parameters (and even found a reduction in F1+2 and TAT) in young healthy men after a long-haul flight to la Réunion (5). Several studies with various designs have shown a positive relation between air-travel and thrombosis and its relative risk is now estimated to lie between 2 and 4 (6–8). In addition to these studies a number of case reports have been published that describe the occurrence of venous thrombosis at high altitude, or as part of mountain sickness (9, 10). In a case-series of 7 altitude-related deaths in the Himalayas, pulmonary embolism was prominent in four of the seven cases. The authors warned of a possible

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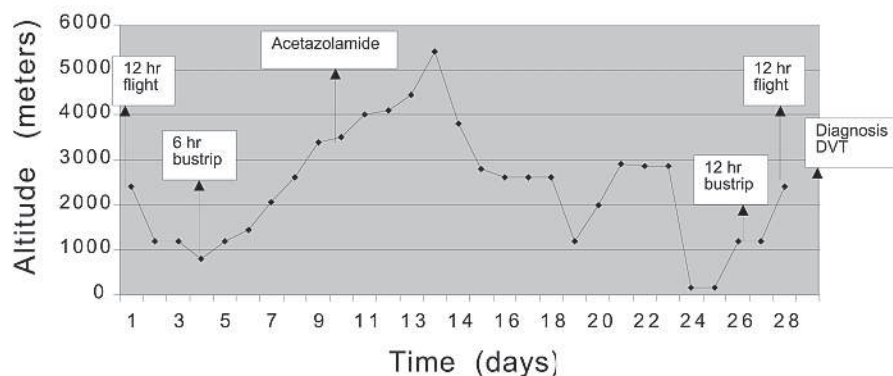


Figure 1: The patient's travel diary. The figure shows the altitude at which our patient travelled during her hiking trip and the time line of events. The two flights are also expressed in altitude, namely 2438 meters (altitude that corresponds to conditions in the cabin).

thrombogenic side effect of diuretics in the treatment of altitude sickness (11). Such a contributing effect of dehydration in the pathogenesis of deep vein thrombosis could be suggested as well for air travel related thrombosis since air travel also leads to mild dehydration (12).

Venous thrombosis is a multicausal disease and several of its risk factors are well known today (13). In this case, two known risk factors were present (immobilisation, and the FVL mutation). Whether or not the use of a progestin-only pill contributes to an increased risk is still a matter of debate, but any effect appears to be limited (14). It may well have been that hypobaric hypoxia and dehydration during her stay at high altitude – the latter worsened by the use of acetazolamide – have con-

tributed to the first event on top of the existing risk factors (13). This is in line with the concept that thrombosis occurs when a combination of certain risk factors leads to crossing the thrombosis threshold (13). That she is susceptible to such a mechanism may be inferred from the second thrombotic event she developed after the long haul flight to Sydney.

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