

SPRING CASE DISCUSSION

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A North American girl (12 years) who is menstruating is exposed irregularly to intermittent hypoxia (4,000 m.; one month at high altitude, several days at sea level in Lima, or vice versa). Her mother says that each time she has ascended to 4000m she has regression of her secondary sexual characteristics. When she goes down to sea level, menstruation, and all secondary characteristics (breast development, hair, etc) reappear. At high altitude, she loses as much as 6 kg of weight.

How can this story be explained and what investigations are warranted.

Lorna G. Moore (USA)

It would be important to verify that these symptoms truly occur and are not just in "her mother's eye". Hormone measurements would also seem justified -- LH, FSH, estradiol, progesterone, maybe cortisol? It's an odd report, given the extent of changes reported. One month at 4000 m is an awfully short time for "regression of secondary sexual characteristics" such as breast and hair development so I am somewhat skeptical of the reported observations.

Menstrual cycle disturbances are common, under a great many circumstances of changes in routine. In our 1996 Pikes Peak study, estradiol and progesterone values during the menstrual cycle were not different from values obtained in the same women during the same phase of the cycle at sea level. "Flips" from one cycle phase to the other occurred at altitude but not clearly more than at sea level.

Gustavo Zubieta-Castillo (Sr) & Gustavo Zubieta-Calleja (Jr). (Bolivia)

Delays in menstruation with altitude changes, going up or down, are quite common. This would imply a temporary hormonal alteration but fortunately with no serious side-effects. Weight loss is also frequent in a good percentage of people, going up from sea level. Aside from hypoxia, other factors are also involved: the environment, psychological, social and physiological changes. The secondary sexual characteristics follow the neuro-endocrine changes, also present in other systems. As an example, the color of the hair and skin are darker at high altitude, due to the increased melanin production, following the complex transformation of tyrosine. We suggest that she have a through check-up, and if possible at high altitude, where saturation should be normal. If it is low, then extensive pulmonary function testing should be carried out in order to determine the exact cause of hypoxemia, that would aggravate the menstrual alterations. "While scientists only try to explain the phenomena and always do so incompletely, nature wisely delays the possibility of pregnancy, until adaptation is complete".

Robert B.Schoene (USA)

Interesting case. I would find out whether this kind of pattern is common; look at the type of weight loss she is having, ie water, fat, or protein; and document her dietary habits.

At each altitude; then look at her pituitary-ovarian axis. Sounds somewhat similar to the amenorrhea of young athletes that can be intermittent. Also document her activity level.

Peter Bartsch. (Germany)

Some of the symptoms like weight loss and amenorrhea could be attributed to the effects of acute exposure to high altitude (HA). As menarche is delayed by 1-2 years in residents of HA and as travelling may interfere with the menstrual cycle, I suspect that susceptibility to such irregularities is increase shortly after onset of menarche. If the patient suffers from prolonged AMS and associated loss of appetite throughout the stay at HA - which may occasionally occur - this would contribute to weight loss. To explain a loss of 6 kg of body mass in 4 weeks, you need, however a negative energy balance of about 1500 kcal/day (7700 kcal per kg lost) which is enormous. Fluid retention often associated with AMS would counteract weight loss and digestion and resorption should function normally at this altitude. Given these tremendous changes I think one should also consider anorexia nervosa. To give advice we need further information on the family situation, purpose of the stay, symptoms of AMS, digestion, use of drugs (diuretics: Diamox!) etc.

David Murdoch, (New Zealand)

The time course of events is unclear in relation to the periods at high altitude. I presume the regression of secondary sexual characteristics occurs over many weeks to months, as the story would seem unbelievable over a shorter period.

I sought an endocrinology opinion on this case. Many stresses, (presumably including hypobaric hypoxia) and weight loss can inhibit the HPG axis. This is even more likely to occur in a 12 year old and is not unlike what happens in anorexia nervosa. My endocrinologist colleague did not see a need to investigate further and advised avoidance of these stressors in one so young and vulnerable. With the limited information provided, I would want to explore potential causes of weight loss which may not be specifically related to high altitude, e.g. does she have anorexia nervosa?

Conclusions

Katie Woods (Lecturer in Paediatric Endocrinology, Oxford, UK) and Andy Pollard (ISMM Newsletter Editor)

The practical management should involve a period of close observation including documenting weight, diet and activity in order to confirm the mother's concerns. There must be some doubt as to the reliability of these observations because of the short timescale of changes and the history needs clarification. It seems unlikely that altitude per se is the cause of the problem, oximetry might be reassuring.

If the period of observation confirms the mother's history, then the weight loss seems the most likely culprit for the regression of secondary sexual characteristics. Does her weight return to normal again at sea level? Hormonal investigation might be helpful if available. Basal LH/FSH would be relatively unhelpful due to the pulsatile release of these hormones. An LHRH stimulation test might be considered at both sea level and during the high altitude stay. Since she is menstruating, an adult

pattern would be expected but regression to an early pubertal pattern would fit with the mother's observations at altitude suggesting she is borderline for weight. Oestrogen levels would presumably be low during the regression of puberty and normal at sea level and worth measuring.

The important issue to resolve is the reason for her weight loss. Underlying chronic disease should first be excluded by history and careful examination.

Cardiorespiratory illness could decompensate at altitude leading to weight loss and hormonal changes. Does she develop intercurrent illness at altitude such as gastroenteritis, causing her to fall below her critical weight for pubertal development? Does she have anorexia nervosa? Are there other psychological or environmental factors (such as change in diet) which could make her lose weight?