

# Primary Vasculitis at High Altitude

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**ABSTRACT.** We describe a 34-year-old mountaineer who presented with gut infarction from necrotizing vasculitis, probably due to Churg-Strauss syndrome. Subsequently, relapses occurred whenever he climbed to 4000 meters. We hypothesize that the effects of vasculitis were compounded by the physiological changes at high altitude. We suggest that patients with systemic vasculitis should be cautious about climbing and trekking at high altitude. (J Rheumatol 2004;31:1450–1)

*Key Indexing Terms:*

POLYARTERITIS NODOSA  
HIGH ALTITUDE

CHURG-STRAUSS SYNDROME  
GASTROINTESTINAL SYMPTOMS

VASCULITIS

Gastrointestinal (GI) involvement is frequent in primary necrotizing vasculitis and carries a high morbidity and mortality<sup>1</sup>. Presenting features include gut infarction, bleeding, peritonitis, and infarction of the gall bladder as well as nonspecific abdominal pain. We describe a case of GI vasculitis apparently precipitated by high altitude.

## CASE REPORT

A Caucasian man aged 21 years, an experienced mountaineer, was in good health until 1990 when he climbed Mont Blanc. At about 4000 meters, he developed vomiting, diarrhea, and profound malaise followed by severe colicky abdominal pain. He was admitted on return to the UK. Laboratory tests showed peripheral eosinophilia. His clinical condition remained unchanged despite symptomatic treatment, intravenous fluids, and broad spectrum antibiotics. Emergency laparotomy revealed extensive infarction affecting about 8 feet of the small bowel. Histopathology of the resected bowel segment revealed a full thickness infarct with mucosal ulceration and an acute inflammatory cell infiltrate rich in eosinophils in association with florid necrotizing arteritis in the serosa and mesentery. The diagnosis of polyarteritis nodosa (PAN) was made. His hospital course was difficult and complicated by upper GI bleeding and perforation of a gastric ulcer. Histology from the stomach showed several small and medium size vessels in submucosa that were infiltrated by polymorphs and eosinophils. His history was unremarkable except for mild asthma predating the onset of vasculitis by 2 years.

Treatment with cyclophosphamide and prednisolone was commenced. Following a good clinical and laboratory response, he remained in remission for almost 3 years taking low dose prednisolone and azathioprine until he embarked on a further climbing expedition.

This time, in May 1993, having again climbed to about 4000 meters, malaise, nausea, and abdominal pain recurred. He returned immediately to the UK and subsequent investigations showed acute acalculous cholecystitis in association with elevated C-reactive protein (CRP) of 116 mg/l. This

flare responded to a temporary increase in the dose of prednisolone with resultant uneventful recovery.

He remained in remission for 4 years. However, in 1997, he had 2 flares of vasculitis in succession, with predominant GI manifestations, each requiring admission to our institution. Since these failed to respond to an increase in steroids alone, treatment with intravenous immunoglobulin (IVIG) was instituted at a dose of 0.4 g/kg for 5 days and repeated annually. This resulted in good disease control with no relapse occurring for a further 2 years. In 1999, following further relapses, azathioprine was increased to 200 mg/day and IVIG was administered every 6 months. Clinical remission was reestablished.

In August 2002, he went climbing again. At about 3500 meters he developed malaise, vomiting, and diarrhea. He was admitted locally, where dehydration was corrected. The CRP was 192 mg/l. On return to the UK, all but the diarrhea and fatigue had settled. There was mild deep abdominal tenderness without guarding or rigidity. The bowel sounds were normal. The prednisolone dose was increased, followed by IVIG, again resulting in complete clinical and laboratory recovery. Since then he has remained in clinical remission.

On different occasions the eosinophil count ranged from 299.2 to 2062.8 per mm<sup>3</sup> (3.2–10.8%). Throughout, serology for antineutrophil cytoplasmic antibody was negative. Full blood counts, erythrocyte sedimentation rate, CRP, urea, electrolytes, creatinine, liver function tests, and routine urine examination obtained during clinical remissions were consistently normal (data not shown).

## DISCUSSION

This case suggests a relationship between high altitude and exacerbation of vasculitis. Of the total 12 clinical flares, 3 including the initial presentation occurred each time the patient climbed to a certain height. Importantly, each of the flares precipitated by altitude was preceded by prolonged clinical and laboratory remission.

Although initially diagnosed as PAN, features in this patient such as preceding asthma and the prominent peripheral blood and tissue eosinophilia suggest that he had Churg-Strauss syndrome (CSS)<sup>2</sup>. GI symptoms, including abdominal pain and diarrhea, occur in up to two-thirds of patients with CCS, and mesenteric intestinal ischemia and small bowel necrosis can resemble the GI features of PAN, as it did here<sup>3</sup>. Severe GI tract involvement is indeed a marker for poor prognosis<sup>4</sup>.

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A number of physiologic changes take place at high altitude. These include decreased oxygen saturation through hypobaric hypoxia, which, in order to maintain the normal blood oxygen saturation, leads to adaptive changes such as hyperventilation, polycythemia, increased cardiac output, and increased relative perfusion of various organs including small intestine. Intolerance to hypoxia at high altitude, leading to "acute mountain sickness," high altitude cerebral edema (HACE) or pulmonary edema, is due to failure of adaptive mechanisms<sup>5</sup>. These are usually relieved by descent to a low altitude, and slow ascent is the most effective prevention.

Although initially attributed to mountain sickness by the patient, the GI manifestations in this case both persisted and progressed despite descent and reflected the underlying vasculitis. We hypothesize that this became clinically manifest at altitude because of a "double-hit" phenomenon whereby the inflamed/compromised GI vasculature was unable to maintain homeostasis when faced with increased demand. Patients with previously stable coronary artery disease, for example, can develop angina after ascending to even moderate altitudes<sup>5</sup>.

Some cellular mechanisms previously proposed for HACE<sup>6</sup> may also be applicable to the small intestine. HACE has been tentatively attributed to either cellular ion pump failure from ATP depletion or high cerebral blood flow

inducing high capillary pressure and transcapillary protein leakage. Besides these, other hypothetical mechanisms include focal ischemia leading to activation and attraction of macrophages that damage the capillary basement membrane and extracellular matrix.

To our knowledge, this is the first case of systemic vasculitis being exacerbated at high altitude. Possibly, this complication could have been avoided if he had acclimatized and his ascent was more gradual.

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