

Short report

Chronic hypothermia in multiple sclerosis

F SULLIVAN, M HUTCHINSON, S BAHANDEKA, R E MOORE

From the Department of Neurology, Adelaide Hospital, Dublin, and Department of Physiology, Trinity College, Dublin, Ireland

SUMMARY Two patients with clinically definite multiple sclerosis presented with acute hypothermia and on recovery were found to be chronically hypothermic. Thermoregulatory studies indicated a central, hypothalamic defect which is presumed to be due to a plaque of demyelination.

Chronic hypothermia due to hypothalamic dysfunction is a rare clinical disorder; previous case studies have indicated a lesion in the anterior hypothalamus as responsible.^{1,2} Although demyelination in the hypothalamus is recognised by the pathologist³ there have been few clinical reports of hypothalamic disturbance and none of acute chronic hypothermia in multiple sclerosis. We report two patients with clinically definite multiple sclerosis who presented with acute on chronic hypothermia and in whom thermoregulatory function studies indicated a lesion in the hypothalamus.

Case report

Patient 1 A 41 year old woman with a seven year history of clinically definite multiple sclerosis (Kurtzke Disability Status Scale 7)⁴ was admitted to her local hospital in November 1984 with a one week history of confusion and generalised weakness. She was found to be stuporose with marked limb spasticity. She was treated for bronchopneumonia, gradually improved and was discharged home after six weeks, feeling well. During the first week in hospital an unexplained fall in haemoglobin from 12.0 g/dl to 9.8 g/dl was noted.

The patient was admitted to the neurology ward in January 1985 with a three week history of progressive confusion and apathy. She was found to be drowsy, unresponsive to commands and mute with marked rigidity of all limbs. The rectal temperature was 32.6°C. With passive rewarming her temperature returned to 36.0°C and after six days there was full clinical recovery. On admission the haemoglobin was

13.0 g/dl and platelet count was $181 \times 10^9/l$. Serum electrolytes and thyroid function tests were normal. One week later the haemoglobin had fallen to 7.9 g/dl and platelet count to $61 \times 10^9/l$. The peripheral blood counts returned to normal over the next two weeks. CT scan of the brain showed no abnormality.

Over the following two weeks the rectal temperature remained mainly in the range of 34–35°C. The patient noted that any attempt to increase body temperature above 35°C resulted in an increased weakness in her legs. At 8.00 am with a rectal temperature of 36.5°C (in a heated room) she had severe weakness in the legs (MRC grade 2 at best) and was unable to stand. Later in the same day, with rectal temperature of 35.0°C, an improvement in leg strength was noted (grade 3 in flexors). At this stage she could walk five metres with a Zimmer frame. Over the next nine months at home the rectal temperature remained in the 33.0 to 35.2°C range.

Patient 2 A 52 year old woman with a 24 year history of multiple sclerosis (Kurtzke Disability Status Scale grade 8) was admitted to the neurology ward in January 1984, with a three week history of confusion and lethargy. She was comatose with a rectal temperature of 31°C. Investigations revealed a serum sodium of 107 mmol/l and platelet count of $50 \times 10^9/l$. She was treated with steroids, hypertonic saline, frusemide and passive rewarming. The hyponatraemia was shown to be due to inappropriate secretion of ADH (renal, thyroid and adrenal function normal) and over the next five days the patient improved to her premorbid state. At this stage the haemoglobin had fallen to 7.4 g/dl and platelet count to $28 \times 10^9/l$. These abnormalities had cleared after a further two weeks. CT scan of the brain was normal. Over the following year daily rectal temperatures were persistently low, averaging 35°C, without clinical problems.

Thermoregulatory function studies

The two patients were studied in a climatic chamber by exposure to environmental air temperature of 27°C (thermo-neutral), 15°C (cold) and 35°C for succeeding periods of

Address for reprint requests: Dr M Hutchinson, Adelaide Hospital, Peter Street, Dublin 8, Ireland.

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30–50 minutes. A patient with paraplegia due to a spinal arteriovenous malformation was similarly examined as a volunteer control. Skin temperature was measured from five sites and core temperature from the external auditory meatus. Oxygen consumption and carbon dioxide output were recorded continually as a measure of metabolic rate. A surface EMG electrode over trapezius monitored shivering.

During exposure to cold the finger-tip temperature in both multiple sclerosis subjects fell much less than expected, remaining several degrees above ambient temperature. The core temperature in the multiple sclerosis patients fell (from 35.52°C to 35.23°C for patient 1) in response to cold exposure whereas the core temperature in the control paraplegic patient rose during cold exposure from 36.42°C to 36.67°C. The finger-tip temperature in the control patient fell rapidly in cold and rose rapidly on rewarming.

Both the multiple sclerosis patients had a modest increase in metabolism of about 15% with little or no EMG response from shoulder girdle muscles. The control patient had an approximately 18% increase in metabolism with marked shivering in the cold in the shoulder girdle muscles. Throughout the study all patients were well aware of the cold and exposure was as short as possible to avoid distress.

After the period of cooling, air temperature was increased to 35°C for 30 minutes. In both multiple sclerosis patients the fall in core temperature stopped and core temperature remained mildly reduced compared with the initial (thermoneutral) measurement. Finger-tip temperature returned to the same levels as in the thermoneutral environment.

Discussion

Two patients presented to the neurology department with life threatening episodes of acute hypothermia during winter months and following recovery they had persistently low rectal temperatures without clinical complications. Both patients had been known to the neurology unit from the onset of their multiple sclerosis and in the two years prior to this presentation had normal body temperature recordings.

The laboratory evidence of a fall in core temperature and a restricted skin vasoconstrictor response in a cold environment indicated a lesion in a thermoregulatory centre which was most probably the preoptic hypothalamus. The thermoregulatory studies were of relatively short duration because of the discomfort felt by both patients when exposed to the cold. This awareness of the ambient temperature indicated that the thalamo-cortical pathway was at least partially intact. Both patients had a limited vasoconstrictor response from the five cutaneous sites studied. The finger-tip temperature, normally a sensitive indicator of the response to cold fell much less than expected and remained several degrees above the ambient temperature. This lack of vasoconstrictor response was associated with a modest fall in core temperature. Both patients showed a modest increase in metabolism of about 15% with little or no evidence of

shivering from the shoulder girdle muscles. The control paraplegic patient with a normal resting core temperature exhibited a small increase in core temperature and rapidly reacting skin temperatures in response to cold exposure. The evidence from the laboratory studies was that the two multiple sclerosis patients had a central defect of thermoregulation probably in the preoptic hypothalamus. Vasoconstriction (that is, heat loss control) was clearly defective, and thermogenesis was not adequate to prevent a fall in core temperature. The small increase in metabolism was possibly generated humorally as there was no evidence of shivering. It is probable that the lesions in the anterior hypothalamus in both the multiple sclerosis patients were plaques of demyelination. CT scans were normal but magnetic resonance imaging was not performed.

Despite the occurrence of demyelination around the third ventricle,³ hypothalamic disturbance has been infrequently reported in multiple sclerosis⁵ and hypothermia had not been observed in this disease. The syndrome of inappropriate secretion of anti-diuretic hormone seen in our second patient has been described previously in a patient with presumed multiple sclerosis and hypothalamic demyelination was suggested as the cause.⁶ It is not clear whether the profound hyponatraemia in the second patient was due to the hypothermia per se or an effect of an hypothalamic lesion. The severity of the coma was consistent with the degree of hypothermia and it is probable that this was the main cause of the neurological deterioration.

The thrombocytopaenia and fall in haemoglobin observed in both patients during the recovery period has been previously reported in experimental hypothermia⁷ and in neonatal cold injury⁸ and is thought to be due to sequestration of peripheral blood cells in extravascular sites especially the liver and spleen.

The development of chronic hypothermia in the first patient was of incidental therapeutic effect. The patient was able to walk short distances with a body temperature of 35°C but became chair-bound at a higher body temperature. This is in keeping with the beneficial effect of reduced temperature on conduction along demyelinated axons.⁹ Artificially induced hypothermia has been shown to improve muscle strength and reduce ataxia and spasticity in patients with multiple sclerosis as long as the hypothermia was maintained.¹⁰

Thus mild reduction in body temperature by a few degrees may improve function in disabled multiple sclerosis patients but more marked hypothermia may cause stupor and coma. Although uncommon, hypothermia may be the cause of unexplained deterioration in multiple sclerosis patients.

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