Short report

Late onset post-traumatic hypothalamic hypothermia

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SUMMARY A case of post-traumatic hypothalamic hypothermia is described. An unusually selective defect in thermoregulatory function was demonstrated together with a defect in thyroid function suggestive of impaired hypothalamic control.

Hypothermia due to hypothalamic dysfunction is an uncommon clinical problem and few cases have been analysed by careful thermoregulatory testing or had the site of damage defined anatomically. We have investigated a patient with late onset post-traumatic hypothalamic hypothermia with thermoregulatory and endocrine testing. Hypothalamic damage has been identified by high resolution computed tomography (CT).

Case report

In November 1975 a 10-year-old boy was admitted to hospital after sustaining a severe head injury in a road traffic accident. On admission he was unconscious and he had fixed dilated pupils. Skull radiographs revealed a fracture of the left parietal bone and CT scan showed a large frontal extradural haematoma. This was evacuated. After operation recovery was slow and complicated by hydrocephalus which stabilised with acetazolamide therapy. He remained unconscious for two months and a repeat CT scan at this time showed an extensive area of infarction and dilated ventricles. After 5 months he was discharged; he was blind, with bilateral optic atrophy, had a severe dysarthria and a spastic tetraparesis of mild degree.

Three years later, in November 1978, he was re-admitted to hospital with a history of increasing drowsiness. One week prior to admission he suffered two generalised convulsions. On examination he was rousable with difficulty. His other neurological signs were unchanged. The CT scan was unchanged and an electroencephalogram showed diffuse slow wave activity with maximal abnormality in the right frontal area. The patient improved rapidly after admission and returned to his usual status within 48 hours. No firm diagnosis was reached. He continued to suffer

episodic drowsiness and was admitted to hospital for this on four occasions. On the fifth admission to hospital his core temperature was found to be 31.8°C. He was now peripubertal and obese. Besides drowsiness there was no change in his neurological state. His parents reported that although he had been free from this problem until 1978, since then he had often felt cold to touch but had never complained of cold and had never been seen to shiver. Retrospective analysis of hospital records revealed that after operation in 1975 his temperature had been normal, but on each admission since 1978 his temperature had been below the scale on the standard clinical thermometer. Investigations on this admission revealed a platelet count of

Fig 1 CT scans reconstituted in the sagittal and coronal planes showing extensive anterior cerebral damage and involvement of the hypothalamus.

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$45 \times 10^9/l$ which returned to normal on rewarming. A high resolution CT scan was performed and images were reconstituted in the coronal and sagittal planes (fig 1). This showed old infarction in the right fronto-parietal region and destruction in the area of the hypothalamus. Plasma cortisol on admission was 308 nmol/l and urinary free cortisol was normal. An insulin stress test showed an adequate response to cortisol and growth hormone to hypoglycaemia. Serum thyroxine varied between values of 49 nmol/l and 117 nmol/l but the free thyroxine index was 49 (normal range 58–174). The response of TSH to 200 μ g TRH was exaggerated and delayed. The basal TSH value was 5.8 mu/l and rose to 16.0 at 20 minutes and 27 mu/l at 60 minutes. Thyroid auto-antibodies were negative. Serum prolactin was at the lower limit of normal at 116 iu/l. Urinary concentrating ability was normal with a rise in urine osmolality to 840 mosm/l on water deprivation. Autonomic function tests were performed. He had normal cardiovascular responses to deep breathing, carotid sinus massage, valsalva test and tilting.

Thermoregulatory tests

The patient first lay in still air at a temperature of 20°C for a period of 17 minutes after which the air speed was increased to 0.5 m/s for 20 minutes for convective cooling. Finally the temperature of the moving air was increased to 40°C in order to rewarm the patient. Skin temperature (foot) and core temperature (aural) were measured and skin blood flow was estimated by a pulsometer. Changes in skin and core temperature are shown in fig 2; the changes in the

patient are clearly abnormal in comparison to the mean response of a control group of young people (eight males, average age 27 years). The absence of shivering in the face of such falls in temperature is also abnormal. Changes in peripheral blood flow (pulsimeter amplitude) are shown in fig 2. Resting blood flow and skin temperature of the hand were abnormally high in control conditions and cooling produced a marked and rapid vasoconstrictor response. Finally, the onset of sweating in response to radiant heat was observed. This occurred normally at a core temperature of 37.0°C.

Discussion

Studies of defective thermoregulatory function due to structural brain lesions in man are rare. Bannister¹ reported a case of syphilitic endarteritis in whom thermoregulatory responses were absent. Hockaday² analysed three patients who had persistent hypothermia. One of these had no detectable response to either central or peripheral thermal stimuli. The other two had normal responses and hypothermia was explained on the basis of an abnormal set point. In one case necropsy revealed multiple areas of infarction which included the hypothalamus. Fox³ studied a patient with hypothermia who was unable to respond to a cold stress by either vasoconstriction or shivering. Heat dissipation was normal. Necropsy demonstrated gliosis confined to the anterior and medial hypothalamus.

Our patient had a different and unusually selective impairment of thermoregulatory function. He was able to sweat normally but during cold stress he was unable to maintain core temperature. He did not complain of cold and made no behavioural adjustment. He was unable to shiver, but his peripheral vascular responses were intact and hyper-active, possibly in compensation for his defective central function. In particular, rapid vasodilation on rewarming occurred while the patient's core temperature was still falling suggesting that cutaneous blood flow was mirroring skin temperature alone with inputs from central receptors being overridden. The occurrence of profound hypothermia in this young man despite active peripheral reflexes demonstrates the importance of behavioural, metabolic and shivering thermogenesis in the defence of body temperature in man.

The late presentation, four years after the original head injury, is unusual and has not been previously described. There was a delay in diagnosis in this case and it is clearly important to be aware of the possibility of a latent defect in thermoregulatory function in such patients.

Mainly from stereotactic studies in animals Benzinger⁴ has proposed an anterior hypothalamic centre for heat dissipation and a posterior centre for

Fig 2 Responses of skin temperature, core temperature and peripheral blood flow to convective cooling and warming in the patient (SG) and control group.

heat conservation. This simplified view has been questioned by Bligh⁵ and is at odds with Fox's observations.³ In man lesions are usually extensive and correlation between anatomy and pathophysiology is difficult. Such was the case in our patient although high resolution CT scan demonstrated damage in the hypothalamus. The selectivity of the defect in this patient does suggest that pathways for control of heat conservation and dissipation are at some stage anatomically distinct in man.

The only endocrine abnormality was a borderline impairment of thyroid function. A delayed and exaggerated response to TRH is unusual in primary hypothyroidism^{6, 7} and in our patient it probably reflected hypothalamic dysfunction. In man very high concentrations of TRH are found both in the anterior hypothalamus and in the posterior nucleus.⁷ Thyroid hormones are involved in non-shivering thermogenesis and the concurrence of such an abnormality with defective shivering in this patient, might imply a common anatomical control site for both these mechanisms of heat generation.

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