SHORT REPORTS

Precocious puberty and non-accidental injury

True precocious puberty in boys is often associated with organic brain disease. Although trauma is sometimes listed as a cause of precocious puberty, in a review of recent reports no mention of such an association was found. A case is reported, therefore, of a boy who developed isosexual precocity after non-accidental head injury.

Case report

The boy was born in Britain to Pakistani parents. At the age of 6 weeks he was admitted to hospital because of convulsions. Bilateral clavicular fractures were noted and the cerebrospinal fluid was blood-stained and xanthochromic. Non-accidental injury was considered likely. The infant recovered and was discharged to the care of his parents. Ten months later he was readmitted, as bruising around his eye and many bite marks on his body had been noted. The skull x-ray film showed multiple fissure fractures and sutural diastasis. The infant was taken into the care of the local authority for a time. Sexual precocity was first noted during a routine clinic visit at the age of 4 years. Development of the penis and scrotum and of the pubic hair were consistent with advanced puberty (Tanner¹ stage four and three, respectively). He was hyperactive and exhibited considerable sexual drive. There were no neurological abnormalities. The appearances of the skull x-ray film and computerised axial tomography brain scan were normal, excluding many cerebral causes of sexual precocity. There was a pubertal-type response of the gonadotrophins—both follicle stimulating (FSH) and luteinising (LH) hormones—to luteinising hormone-releasing hormone (LHRH), indicating an intracranial cause (see table).

The results of thyrotrophin stimulation and thyroid function tests were normal and there was no evidence of adrenal insufficiency or diabetes insipidus.

Results of LHRH test

Time (min)	Serum FSH (IU/l) concentration	Serum LH (IU/l) concentration
0	5	4
20	9	18
60	12	18

Comment

As precocious puberty and severe head injury are rare, it is reasonable to speculate that their association in this boy is not coincidental. The other cerebral causes of sexual precocity have probably been excluded by the results of the investigations but it is well known that a small hypothalamic hamartoma may produce precocious puberty in early life and remain otherwise silent for many years.

Postmortem studies² have shown that ischaemic or haemorrhagic lesions of the anterior hypothalamus, or both, are common after closed head injury, especially in young people. Endocrine sequelae after severe head injury might be expected. Transient or mild disturbances of anterior and posterior pituitary function after head injury are fairly common, but permanent upsets are rare, although hypopituitarism³ and impaired secretion of antidiuretic hormone⁴ have been described. Premature pubertal development might also be expected after severe head injury, yet reports of such an association were not found in a review of recent publications. Furthermore, a review⁵ of 96 cases of precocious puberty did not implicate head injury as an aetiological factor.

In this case there appears to be a clear association between severe non-accidental head injury and precocious sexual development, further extending the range of the effects of child abuse. Furthermore, as the cause of true precocious puberty is unknown in most cases, head injury (accidental or non-accidental) may possibly be an important aetiological factor.

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¹ Tanner, J M, *Growth at Adolescence*. Oxford, Blackwell, 1962.

² Crompton, M R, *Brain*, 1971, **94**, 165.

³ Klacko, D M, et al, *Journal of Clinical Endocrinology and Metabolism*, 1968, **28**, 1798.

⁴ Knockel, J P, Osborn, J R, and Cooper, E B, *Metabolism*, 1965, **14**, 715.

⁵ Sigurjonsdottir, T J, and Hayles, A B, *American Journal of Diseases of Childhood*, 1968, **115**, 309.

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Department of Child Health, University Hospital and Medical School, Nottingham

J MCKIERNAN, MB, MRCP, lecturer in child health

Shoulder-hand syndrome after laparoscopic sterilisation

The shoulder-hand syndrome is characterised by painful restriction of shoulder movements indistinguishable from capsulitis and pain, swelling, and autonomic disturbances of the hand. Many precipitants have been described¹ but the condition has become steadily less common.² We have seen this syndrome after laparoscopic sterilisation. We report the case because this operation is widely performed and because it is difficult yet important to diagnose the syndrome early.^{2,3}

Case report

A woman aged 27 had a laparoscopic sterilisation in November 1977 because of psychosexual problems. Postoperatively she had pain in the right shoulder aggravated by respiration. The pain persisted but the pleuritic quality disappeared within a few days leaving a dull ache. The operative and postoperative periods were otherwise uneventful. Five weeks later she noticed radiation of the pain down the medial aspect of her right arm, and after a further week swelling of the right arm and hand to the extent that she could not remove her ring or put her glove on. There was pronounced non-pitting oedema of the right hand and 1½ inches (3.75 cm) difference in circumference between the upper arms. The right hand was warm and sweaty and the superficial veins were more prominent. Pain restricted movements of the right shoulder and the joints of the right wrist and fingers. Physical examination was otherwise normal. Axillary vein thrombosis was excluded by venography. Full blood count, erythrocyte sedimentation rate; radiographs of the shoulder, hand, cervical spine, and chest; protein electrophoresis; and rheumatoid and antinuclear factors were normal. The shoulder-hand syndrome was diagnosed on the clinical features and negative investigations.

Treatment with analgesics, physiotherapy, and short-wave diathermy resulted in a partial early response, but symptoms then persisted and did not respond to treatment with non-steroidal anti-inflammatory drugs or to a 12 weeks' course of low-dose prednisolone. Eighteen months after her initial presentation there was a sudden exacerbation of her symptoms with pronounced painful restriction of movements of the shoulder and hand joints. The symptoms responded promptly to large doses of prednisolone (60 mg/day) and remission was maintained when the dose was tapered rapidly. When last seen in June 1978 she had residual limitation of abduction at the right shoulder and hyperhydrosis and swelling of the right hand. X-ray examination of the right shoulder showed minimal degenerative changes and periarthral osteoporosis. Serial densitometry studies have shown no significant bone loss in the hand compared to the unaffected limb, and a ^{99m}Tc-methyl-diphosphonate scan of the shoulders was normal.

Comment

Short-lived shoulder-tip pain resulting from diaphragmatic irritation is common after laparoscopy and is generally of no consequence.

In this patient it merged into what, in retrospect, was the first symptom of the shoulder-hand syndrome. Whether the pain itself or the resulting immobility with impairment of the venous and lymphatic pumping mechanism⁴ triggers the development of the syndrome is unknown, but in any event it seems that laparoscopic sterilisation can be added to the long list of potential precipitating factors.¹ The history of psychiatric illness in this patient may also be relevant.⁵ As this case shows, the illness can be lengthy, disabling, and resistant to treatment, particularly when diagnosis is delayed.^{2,3} The syndrome is uncommon, particularly in young people,² and early diagnosis will depend on being alert to the possibility.

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¹ Steinbrocher, O, and Argyros, T S, *Medical Clinics of North America*, 1958, **42**, 1533.

² *Lancet*, 1974, **1**, 850.

³ Woolf, D, *Practitioner*, 1974, **213**, 176.

⁴ Moberg, B, *Surgical Clinics of North America*, 1960, **40**, 367.

⁵ Fleming, A, et al, *Annals of the Rheumatic Diseases*, 1976, **35**, 456.

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Department of Medicine, Gardiner Institute, Western Infirmary, Glasgow G11 6NT

L C K LOW, BSC, MRCP, medical registrar

D C McCRUDEN, BSC, MRCP, medical registrar

L E RAMSAY, MB, MRCP, lecturer in medicine

Intestinal permeability assessed by excretion ratios of two molecules: results in coeliac disease

The small intestinal mucosa in coeliac disease is abnormally permeable to large molecules—for example, intact proteins,¹ and disaccharides²—but relatively impermeable to small molecules, such as xylose. We have studied the simultaneous absorption of two molecules one of which should be absorbed in increased and the other in decreased amounts by patients with coeliac disease.

Method and results

The molecules were cellobiose, a disaccharide of molecular radius 5 Å, and mannitol, a polyhydric alcohol of radius 4 Å. The test solution comprised 5 g cellobiose and 2 g mannitol in 100 ml, to which was added 20 g sucrose and 20 g lactose to make it hypertonic (1500 mmol (mosmol)), a compromise dictated by problems of palatability and solubility. This was drunk after fasting overnight and emptying the bladder on rising. All urine passed was collected over the subsequent five hours. Mannitol was assayed by a modification of the method of Corcoran and Page.³ Cellobiose was assayed by quantitative paper chromatography.⁴ Three groups of subjects carried out the test, both inpatients and outpatients: 10 untreated adults with villous atrophy, 11 treated patients with coeliac disease, and 16 patients with normal jejunal histological appearances.

Control patients excreted about 20% (range 10.0–51.1) of ingested mannitol in five hours, and 0.5% (range 0.02–0.62) of cellobiose. Patients with villous atrophy excreted significantly less mannitol (range 1.2–9.7%, $P < 0.01$ Mann-Whitney test) and more cellobiose (range 0.34–2.76%, $P < 0.01$) than controls. Patients with treated coeliac disease had intermediate values. The ratios of cellobiose to mannitol excretion (see figure) clearly separate untreated patients with coeliac disease from the other groups.

Comment

Menzies² showed that after an oral load patients with coeliac disease excreted more lactulose than controls. This effect was enhanced when the test solution was hypertonic. We used cellobiose in preference to lactulose because it is cheaper in pure form. Although there is some cellobiose activity in human intestinal mucosa, we have shown no significant difference from lactulose in its excretion in normal subjects or in patients with coeliac disease ($P > 0.2$), under the

Ratio of cellobiose to mannitol in five-hour urinary collections. Values in all three groups differed significantly from each other ($P < 0.01$ Mann-Whitney test).

conditions of this test. We preferred mannitol to xylose, as the latter is partly actively absorbed.

The reason for the contrasting behaviour of the two molecules is speculative. The intestinal barrier has been regarded as a lipid membrane perforated by water-filled pores of a finite radius, which some workers⁵ have estimated to be about 4 Å. This may account for the relative ease with which mannitol passes compared with cellobiose, both molecules being highly water soluble.

In coeliac disease loss of intestinal surface area may result in there being fewer pores through which the mannitol can diffuse. The increased permeability to cellobiose probably reflects mucosal damage. Alternatively, the increased cell turnover which occurs in the disease implies that there may be more extrusion zones, through which large molecules might pass.

Measuring simultaneous absorption of these water-soluble molecules shows two aspects of intestinal permeability which are abnormal in coeliac disease. When expressed as a ratio it results in excellent discrimination of untreated patients from treated ones or normal subjects. It should also minimise errors due to non-mucosal factors (such as renal function). Preliminary data confirm this and we would expect fewer false-positive results than with the xylose test. We have found it useful both for screening and for following the response to treatment.

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¹ Kivel, R M, Kearns, D H, and Liebowitz, D, *New England Journal of Medicine*, 1964, **271**, 769.

² Menzies, I S, *Gut*, 1972, **13**, 847.

³ Corcoran, A C, and Page, I H, *Journal of Biological Chemistry*, 1947, **170**, 165.

⁴ Menzies, I S, *Journal of Chromatography*, 1973, **81**, 109.

⁵ Lindemann, B, and Solomons, A K, *Journal of General Physiology*, 1962, **45**, 801.

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Gastroenterology Unit, The General Infirmary, Leeds LS1 3EX

I COBDEN, MB, MRCP, research registrar

R J DICKINSON, BSC, MRCP, registrar

J ROTHWELL, technician

A T R AXON, MD, MRCP, consultant physician