The seasonal occurrence of clinical symptoms is well known in Hartnup disease. The skin rash is photosensitive and generally appears in the late summer. Our patient showed the same features; all the admissions to hospital occurred in November and neither a skin rash nor any other symptom was noted during other times of the year. Dietary tryptophan deficiency with decreased nicotinic acid production was not responsible for the clinical manifestations as the child regularly received a diet containing sufficient tryptophan.

The cause of the neurological disturbances in patients with the classical form of Hartnup disease has not been clearly established. Most doctors believe that the high content of tryptophan in the intestine gives rise to an increased quantity of degradation products by the intestinal flora which are absorbed into the blood stream and are responsible for the neurological symptoms. In our patient the mechanism seems to be different, since the absorption of the tryptophan from the jejunum was normal. It may therefore be assumed that either a production of an abnormal by-product or deficiency of a metabolic end-product in tryptophan degradation pathway (Figure) is the reason for the neurological and other clinical signs in our case. The striking response of these patients to administration of nicotinamide favours the possibility of a metabolic block in tryptophan degradation.

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References

- 1 Smith J. Amino acids, amines, and related compounds. In: Smith J, ed. *Chromatographic techniques*. London: Heinemann, 1963: 82-142.
- 2 Spackman D H, Stein W H, Moore S. Automatic recording apparatus for use in the chromatography of amino acids. *Anal Chem* 1958; **30**: 1190-206.
- 3 Mondino A, Bongiovanni G, Fumero S. A new approach for obtaining total tryptophan recovery in plasma samples deproteinised with sulfosalicylic acid. *J Chromatogr* 1975; **104**: 297-302.
- 4 Price J M, Brown R R, Yess N. Testing the functional capacity of the tryptophan-niacin pathway in man by analysis of the urinary metabolites. *Adv Metab Disord* 1965; **2**: 159-225.
- 5 Curzon G, Walsh J. A method for the determination of the urinary indoxyl sulphate (indican). *Clin Chim Acta* 1962; **7**: 657-63.
- 6 Tada K, Ito H, Arakawa T. Congenital tryptophanuria with dwarfism ('H' disease-like clinical features without indicanuria and general amino-aciduria): a probably new inborn error of tryptophan metabolism. *Tohoku J Exp Med* 1963; **80**: 118-34.
- 7 Wong P W, Forman P, Tabahoff B, Justice P. A defect in tryptophan metabolism. *Pediatr Res* 1976; **10**: 725-30.

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Rigid spine syndrome and fatal cardiomyopathy

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SUMMARY A 7½-year-old girl had the clinical features of the rigid spine syndrome of Dubowitz. Muscle biopsy showed a predominance of type 2 fibres with neither myopathic features nor an increase in connective tissue. In addition, she had a hypertrophic cardiomyopathy with which she presented in heart failure and from which she died suddenly one month later. The association of rigid spine syndrome with cardiomyopathy has not been reported previously.

We record the unusual combination of the rigid spine syndrome of Dubowitz and fatal cardiomyopathy.

Case report

A girl, aged 7½ years, presented with breathlessness on exercise and increasing tiredness over 2 months. She had had no blue attacks, chest pain, or fainting, nor had she any other complaint; she had attended school normally. She was the first child of unrelated parents. Pregnancy and birth had been normal. Her two siblings were normal. There was no family history of neuromuscular or cardiac disease. At 5 years, she had been noted to have an extended neck, restricted spinal movement, and to be thin.

She was very thin (Fig. 1). There was loss of subcutaneous fat with relative sparing of the face. Her height was average for her age and greater than her

Fig. 1 Age 7 years. Note loss of adipose tissue with facial sparing, fixed shrugging of shoulders and extension of neck, and funnel chest.

Fig. 2 Age 7½ years. Neck is maximally flexed. Shoulders are permanently shrugged.

She was not cyanosed. Her chest wall was thin and expansion restricted to 1 cm. She had a funnel chest. There were no basal crepitations. The pulse was normal and all peripheral pulses were present. The jugular venous pulse had a prominent 'a' wave. The apex beat was displaced to the 7th intercostal space in the anterior axillary line. There were left and right ventricular heaves, a triple rhythm, and a soft midsystolic murmur at the left sternal edge.

Routine haematology and biochemistry investigations gave normal results. Erythrocyte sedimentation rate was 2 mm in 1st hour. Chromosomes, thyroid function, serum, and urinary amino-acids were normal. Rheumatoid factor, antinuclear factor, and immune complexes were negative. Creatine phosphokinase 210 IU/l. Human leucocyte antigens A24, A19, B37, BW4. Metacarpal index was normal. X-ray of cervical spine showed bilateral cervical ribs, no bony fusion or ankylosis, normal intervertebral foramina, and increased diameter of cervical canal at C3 and C5. Chest x-ray showed pulmonary congestion, upper lobe diversion, septal lines at the bases, and enlarged left atrium. Electrocardiogram (ECG) showed hypertrophy of left atrium and left ventricle. The echocardiogram (Fig. 3) showed enlarged left atrium, gross hypertrophy of the interventricular septum, hypertrophy of the posterior left ventricular wall, and early closure of the aortic valve. Electromyogram of erector spinae showed normal inhibition at rest, normal motor

span: upper segment to lower segment ratio was 0.9. She held her neck in hyperextension, and there was restriction of flexion, lateral flexion, and rotation of the cervical spine. She held her shoulders permanently shrugged (Fig. 2). There was restricted thoracolumbar flexion and loss of lumbar lordosis. There was no joint hyperextensibility, no scoliosis, and no limb contractures. There was palpable 'stiffness' of erector spinae, neck muscles, intercostals, and abdominal muscles. There was no detectable weakness of proximal, distal, axial, or facial muscles. There was no muscle tenderness, fasciculation, or dimpling. All tendon jerks were absent and both plantars down-going. Sensory function, cerebellar function, and cranial nerve function were normal. There were no lens dislocations. Respiratory rate was 30/min, heart rate 120/min, and blood pressure 110/70 mmHg.

Fig. 3 Echocardiogram showing enlarged left atrium (LA), thickened inter-ventricular septum, early closure of aortic valve (AV), and normal movement of mitral valve (MV).

units, and normal interference pattern. Motor nerve conduction of lateral popliteal was 47 metres/second. Muscle biopsy from erector spinae showed no increase in connective tissue and no inflammatory reaction. There were normal peripheral nuclei and fibres of normal size, apart from a few fibres (<3%) which were atrophic. ATPase preparations showed type 2 predominance and a few atrophic type 1 fibres.

On the basis of the clinical, radiological, and echocardiographic findings a diagnosis of rigid spine syndrome was made, together with heart failure secondary to a hypertrophic cardiomyopathy. She was started on 5 mg a day of bendrofluazide but not digitalised. She died suddenly at home 2 weeks after her discharge from hospital. Permission for necropsy was refused.

Discussion

The rigid spine syndrome is a rare disorder of children and young adults characterised by restricted spinal flexion, an overextended spine, thinness and loss of adipose tissue, and reduced muscle bulk with retention of muscle power. Its natural history is generally nonprogressive except for the slow development of mild scoliosis and limb contractures. Dubowitz¹ attributed the basis of the syndrome to a myopathic process, since in his cases serum creatine phosphokinase level was moderately raised, the electromyogram showed a myopathic pattern, and muscle biopsy showed variation in fibre size. Biopsy also showed a great increase in perimysial and endomysial connective tissue. More recently² the syndrome has been associated with a muscle biopsy pattern in which there is little evidence of myopathic change or changes in the connective tissue, but in which there is type 1 fibre predominance and atrophy

of these fibres. Goebel *et al.*³ have demonstrated, in the same patient, the type 1 predominance and the connective tissue changes in biopsies from different muscles.

The syndrome should be distinguished from congenital muscular dystrophy which presents in infancy and in which muscle biopsy demonstrates striking myopathic change, out of proportion to the mild degree of weakness and the fairly good prognosis. It must also be distinguished from Marfan's syndrome which has specific skeletal, lens, and cardiac abnormalities. Bradley *et al.*⁴ reported a syndrome of myosclerosis in 3 patients, with contractures and a 'woody' feel to their muscles. However, in his 3 cases, there was little spinal involvement, but 2 of them had features characteristic of spinal muscular atrophy, and the third had a raised erythrocyte sedimentation rate and polymyositic features.

Apart from the absence of scoliosis and distal limb contractures, the child we report had features which fitted well with Dubowitz's description of the syndrome. The biopsy findings added little to the reports already discussed and leave unanswered the question of whether the muscle involvement is primary or secondary to disuse or to anterior horn cell disease.

The additional feature of special interest was the cardiomyopathy, not previously described in the syndrome. The patient had overt heart disease with gross hypertrophy of the interventricular septum and some hypertrophy of the posterior left ventricular wall. Using echocardiography, it is now realised there is a spectrum of cardiomyopathy present in adults and children. It can be overt or subclinical, it may have asymmetric septal hypertrophy, and it may have outflow obstruction, the last being appreciated by the character of the pulse, early aortic

valve closure on ultrasound, and systolic anterior movement of the anterior mitral cusp. Hypertrophic cardiomyopathy is seen in infants of diabetic mothers, Pompe's disease, and Friedreich's ataxia, and there is often a strong familial tendency. Maron *et al.*⁵ reported 46 cases in childhood of asymmetric septal hypertrophy and noted the high incidence of sudden death (30%) especially in those with overt heart disease. They could not predict those at risk on the basis of echocardiogram, ECG, left ventricular function, or outflow obstruction. Beta-blockers or surgery in selected patients did not reduce mortality.

Rigid spine syndrome is of unknown aetiology. In earlier reports it was associated with a good prognosis. The association with hypertrophic cardiomyopathy indicates that the prognosis may not always be good and may support the idea that the syndrome is a disorder of muscle rather than of bone, nerve, or connective tissue.

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References

- ¹ Dubowitz V. *Muscle disorders in childhood*. Philadelphia: Saunders, 1978: 239-43.
- ² Seay A R, Ziter F A, Petajan J H. Rigid spine syndrome. A type I fiber myopathy. *Arch Neurol* 1977; **34**: 119-22.
- ³ Goebel H H, Lenard H G, Gorke W, Kunze K. Fibre type disproportion in the rigid spine syndrome. *Neuropädiatrie* 1977; **8**: 467-77.
- ⁴ Bradley W G, Hodgson P, Gardner-Medwin D, Walton J N. The syndrome of myosclerosis. *J Neurol Neurosurg Psychiatry* 1973; **36**: 651-60.
- ⁵ Maron B J, Henry W L, Clark C E, Redwood D R, Roberts W C, Epstein S E. Asymmetric septal hypertrophy in childhood. *Circulation* 1976; **53**: 9-19.

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Screening for cystic fibrosis by a stool trypsin method

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SUMMARY Mass screening for cystic fibrosis by a trypsin assay of stool dried on filter paper was evaluated in 20 000 5-day-old babies. Sweat tests were required in only 7 babies. Three of them had cystic fibrosis. The test gave a false-negative result in at least 2 babies, but each had normal pancreatic function. This is not an ideal screening test for cystic fibrosis, as it misses cases with normal pancreatic function, but it is very cheap, highly specific, and appears to be the best currently available screening test.

A screening method for cystic fibrosis has long been sought. Of methods based on an assay of pancreatic function, those using meconium are inconvenient: a second sample cannot be obtained, the test cannot be performed at a central laboratory, and all have had reports of high false-positive and false-negative rates.¹⁻² The method of Crossley *et al.*,³ which assays stool trypsin content, seemed sufficiently promising for a large-scale evaluation, as samples

could be sent by post, and repeat samples obtained noninvasively.

We conducted a study in New South Wales, Australia to evaluate Crossley's method of screening, and this paper reports the results.

Samples and methods

Stool samples from 20 000 5-day-old babies were collected on to filter paper, dried, and posted to the laboratory. Five Sydney and 20 country hospitals took part in the project which lasted a year and so included the hot summer months.

The method of Crossley *et al.*³ was used to assay trypsin activity. Discs 6 mm in diameter were punched from faeces-impregnated filter paper, incubated overnight with benzoyl-L-arginine-p-nitroanilide hydrochloride (L-BAPNA). Trypsin present in samples cleaves a yellow p-nitroanilide molecule from the L-BAPNA. Samples deficient in trypsin remain colourless or very pale yellow. The test result can be read by eye. If the yellow colour was