Short reports

Immunoreactive trypsin in Shwachman's syndrome

J F B DOSSETOR,* H C SPRATT,† C J ROLLES,‡ C P CHAN SEEM,* AND A F HEELEY§

*The Queen Elizabeth Hospital, King's Lynn; †The General Hospital, St Helier, Jersey; ‡Southampton General Hospital; and §Peterborough District General Hospital

SUMMARY We studied two infants with Shwachman's syndrome in whom the immunoreactive trypsin concentration was found to be abnormally low. Experience with several hundred assays for immunoreactive trypsin has not shown this low concentration. This finding is probably specific for pancreatic acinar deficiency at this age and strongly suggests Shwachman's syndrome.

Shwachman's syndrome consists of a failure of pancreatic development, in which the exocrine component of the gland is largely or completely replaced by fatty tissue. It is associated with other abnormalities; most commonly neutropenia and short stature.¹ Measurement of serum immunoreactive trypsin was performed in the investigation of two cases of Shwachman's syndrome and found to be undetectable.

Case reports

CASE 1

A boy, who had weighed 2600 g at birth, was referred at the age of 11 months with failure to thrive and a history of diarrhoea associated with visible greasy material in the stools. His mother dated the onset of symptoms to when he was changed to bottle feeding and solids at the age of 3½ months, but in retrospect she agreed that his stools had been foul smelling while he was breast fed. She said that he had an insatiable appetite.

Investigation showed a haemoglobin concentration of 123 g/l and white cell count of $9.33 \times 10^9/l$, with neutrophils of 13%. A sweat test was negative on two occasions (sweat chloride concentration 8 mmol/l and 13 mmol/l) and a jejunal biopsy specimen was normal. Fat globules were visible on stool microscopy and the three day faecal fat excretion was 13.0 g/day. Faecal trypsin activity was absent. Serum immunoreactive trypsin was undetectable. Duodenal juice stimulated by pancreozymin showed

very low activities for amylase and lipase and undetectable tryptic activity. Enterokinase deficiency was excluded.

The child was given pancreatic enzyme supplements at the age of 15 months, his stools became normal and he started to thrive. A computed tomogram under general anaesthetic at the age of 20 months showed the pancreas to be completely replaced by material of the density of fat. The most recent white cell count was $3.69 \times 10^9/l$ with neutrophils of 17%.

CASE 2

A boy, who weighed 3300 g at birth, had persistent feeding difficulties in the neonatal period and was first admitted to hospital at the age of 9 days. He was admitted three times in the first few weeks of life, and failed to thrive. Immunoreactive trypsin was undetectable in the peripheral blood. Initially his full blood count showed a white cell count of $13.6 \times 10^9/l$, with neutrophils of 31%. Two sweat tests were negative (sodium 8 mmol/l and 10 mmol/l).

Further investigation at a later date showed nephrocalcinosis on ultrasound, though this was not visible on the plain radiograph. Also at this time a chest radiograph showed broadened rib ends (metaphyseal dyschondroplasia), though other bones were normal. Neutropenia was by now evident (white cell count $8.2 \times 10^9/l$, neutrophils 3%) and serum immunoreactive trypsin was again undetectable. These findings led to the diagnosis of Shwachman's syndrome.

Pancreatic enzyme supplements were started and the stools became normal. Subsequently a pancreatic function test was performed, which confirmed exocrine pancreatic insufficiency. A final complication was the development of a renal stone causing obstruction to the right ureter. After removal this was found to be 90% calcium oxalate. The nephrocalcinosis and stone formation were thought to be due to excess oxalate absorption secondary to malabsorption.²

Discussion

Many of the associated abnormalities found in Shwachman's syndrome such as the neutropenia and poor growth are not necessarily present at the time of presentation so that the diagnosis may be clinically difficult.¹ A computed tomogram of the pancreas gives a characteristic appearance in Shwachman's syndrome.³ As a general anaesthetic is needed to perform this in a young infant it is not a first line investigation. Equally the practical difficulties associated with a pancreatic function test in an infant make the latter usually available only in specialised centres.

Among 711 infants aged between 1 week and 1 year whose serum immunoreactive trypsin concentrations were measured in the course of investigation for possible cystic fibrosis, immunoreactive trypsin was undetectable (that is, less than 3 µg/l) in only the two patients described. The results obtained in this large cohort of infants, of whom 165 presented predominantly with failure to thrive, lead us to conclude that when immunoreactive trypsin is undetectable in serum the cause is most likely to be the pancreatic acinar hypoplasia of Shwachman's syndrome. The immunoreactive trypsin screening test for cystic fibrosis only detects high values and will not pick up these cases, for whom the serum immunoreactive trypsin must be measured.

In patients with chronic pancreatitis⁴ and cystic fibrosis⁵ subnormal or undetectable immunoreactive trypsin may occur when pancreatic insufficiency results in steatorrhoea. In cystic fibrosis, however, undetectable serum immunoreactive trypsin concentrations are unlikely to be found before the age of 2 years irrespective of the degree of pancreatic insufficiency,⁶ and in any case cystic fibrosis would be excluded by the sweat test.

In the light of these two cases, therefore, we would suggest that measurement of immunoreactive trypsin be performed at an early stage in the investigation of suspected malabsorption. It is

remotely possible that the chronic inflammation of cystic fibrosis could destroy all the glandular tissue in infancy; but this diagnosis can be excluded by the sweat test. Hence, if serum immunoreactive trypsin is undetectably low and the sweat test is negative the inference must be that acinar production of trypsin is not occurring. This immediately makes Shwachman's syndrome very likely as the other conditions in which acinar trypsin production does not occur are very much rarer than Shwachman's syndrome. The abnormally low immunoreactive trypsin, therefore, justifies computed tomography of the pancreas as the next step, and in most cases will obviate the need for pancreatic function tests.

We thank Dr D Grant, department of surgery, St George's Medical School, London, for the measurement of duodenal juice trypsin and enterokinase activities.

References

- 1 Aggett PJ, Cavanagh NPC, Matthew DJ, Pincott JR, Sutcliffe J, Harries JT. Shwachman's syndrome. A review of 21 cases. *Arch Dis Child* 1980;**55**:331-47.
- 2 Ogilvie D, McCollum JPK, Packer S, *et al*. Urinary outputs of oxalate, calcium and magnesium in children with intestinal disorders. Potential cause of renal calculi. *Arch Dis Child* 1976;**51**:790-5.
- 3 Robberecht E, Nachtegaele P, Van Rattinthe R, Afschrift M, Kunnen M, Verharren R. Pancreatic lipomatosis in the Shwachman-Diamond syndrome. *Pediatr Radiol* 1985;**15**:348-9.
- 4 Jacobson DG, Curington C, Connery K, Toskes PP. Trypsin-like immunoreactivity as a test for pancreatic insufficiency. *N Engl J Med* 1984;**310**:1307-9.
- 5 Cleghorn G, Benjamin L, Corey M, Forstner G, Dati F, Durie P. Serum immunoreactive pancreatic lipase and cationic trypsinogen for the assessment of exocrine pancreatic function in older patients with cystic fibrosis. *Pediatrics* 1986;**77**:301-6.
- 6 Durie PR, Forstner GG, Gaskin KJ, *et al*. Age related alterations of immunoreactive pancreatic cationic trypsinogen in sera from cystic fibrosis patients with and without pancreatic insufficiency. *Pediatr Res* 1986;**20**:209-13.

Correspondence to Dr J F B Dossetor, The Queen Elizabeth Hospital, Gayton Road, Kings Lynn, Norfolk PE30 4ET.

Accepted 24 October 1988