Serum trypsin levels in acute pancreatic and non-pancreatic abdominal conditions

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Summary

Serum trypsin levels have been estimated by radioimmunoassay in 26 healthy controls (248 ± 94.9 $\mu\text{g/l}$; mean $\pm$ s.d.), 12 patients with chronic renal failure (1100 ± 584 $\mu\text{g/l}$), 34 with acute pancreatitis (1399 ± 618 $\mu\text{g/l}$) and 23 with acute non-pancreatic abdominal conditions. Mean serum trypsin in acute pancreatitis and in chronic renal failure was significantly higher than in control group ($P < 0.001$). Serum trypsin levels were well above the upper limit of normality in all patients with acute pancreatitis and in all but one with chronic renal failure. Serum trypsin was markedly raised in one patient with a traumatic haemoperitoneum and in one of the 11 with peptic ulcer perforation, and moderately raised in 3 of the 6 with acute cholecystitis.

Determination of serum trypsin seems to be a specific test for acute pancreatitis, provided renal failure has been excluded. However, the authors suggest it should be prospectively measured in a larger series of acute non-pancreatic abdominal conditions.

Introduction

Although increased circulating concentrations of amylase and lipase are very useful for the diagnosis of acute pancreatitis, they are not entirely specific (Banks, 1979; Lifton *et al.*, 1974; Elias, Redshaw and Wood, 1977). In fact, it has been reported in many other acute non-pancreatic abdominal conditions such as peptic ulcer perforation, ileus or ischaemic bowel infarction (Banks, 1979; Warshaw and Lesser, 1975; Salt II and Shenker, 1976; Webster and Zieve, 1962a,b; Nardi, 1958).

Trypsin, unlike amylase and lipase, reflects only production by the pancreas (Elias *et al.*, 1977) but

until recently was not as readily measurable (Elias *et al.*, 1977; Temler and Felber, 1976). Since a specific, sensitive radioimmunoassay has been reported (Elias *et al.*, 1977; Temler and Felber, 1976), raised immunoreactive serum trypsin has been found in a small series of acute pancreatitis, common duct gall-stones and chronic renal failure (Elias *et al.*, 1977; Temler and Felber, 1976). In carcinoma of the pancreas immunoreactive serum trypsin may be normal or high (Elias *et al.*, 1977) and normal or subnormal in chronic pancreatitis (Elias *et al.*, 1977). As far as can be ascertained no other acute non-pancreatic abdominal conditions such as peptic ulcer perforation, acute cholecystitis, ileus or acute appendicitis have yet been tested by a radioimmunological method. Circulating trypsin has been estimated, however, in some isolated cases of acute non-pancreatic abdominal conditions, with variable results, by an enzymatic method.

The results of serum trypsin determination in a series of patients with chronic renal failure and acute pancreatic and non-pancreatic abdominal conditions are reported.

Material and methods

Patients

Serum trypsin was measured in 26 healthy controls and in 69 patients (See Table 1). Healthy controls were voluntary blood donors (Group I). Creatinine clearance was below 30 ml/min in all 12 patients with stable chronic renal failure (Group II). Group III was composed of 34 consecutive patients admitted with the diagnosis of acute pancreatitis. Serum amylase and lipase were above 1000 and 3 Coleman units/l respectively in all of them. Laparotomies were performed in 8 of them and a post-mortem in 4. In all 23 patients (Group IV) with acute non-pancreatic abdominal conditions, the pancreas was grossly normal at laparotomy, serum amylase and lipase were

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TABLE 1. Data on groups in which serum trypsin was estimated

Group	Diagnosis	Total no.	Mean age (years)	Age-range (years)	Males no.	Females no.
I	Healthy controls	26	35	20-52	14	12
II	Chronic renal failure	12	62	45-72	8	4
III	Acute pancreatitis	34	51.6	32-75	25	9
	Alcoholic (13)					
	Biliary disease (9)					
	Idiopathic (11)					
	Recent surgery (1)					
IV	Acute non-pancreatic abdominal conditions	23	55.7	20-67	16	7
	Peptic ulcer perforation (11)					
	Acute cholecystitis (6)					
	Ileus (2)					
	Acute appendicitis (2)					
	Traumatic haemoperitoneum (1)					
	Choleperitoneum (1)					
		95			63	32

normal, bile duct gall-stones were absent and renal function was normal, at least at the time of obtaining the blood sample.

Serum samples and trypsin assay

Serum trypsin estimations were performed in duplicate on one basal sample. Serum samples were obtained early after admission and before any medical or surgical treatment was started. Serum was stored at -20°C for not more than 5 months.

Serum immunoreactive trypsin was estimated by means of one classic double-antibody radioimmunoassay (Ria-Gnost® Trypsine, Behring Institut). The directions of the kit were carefully and precisely followed. In the authors' laboratory the within-assay and the between-assay variance was 6.2% and 8.2% respectively. The lower and upper limits of detection were 18.7 and 1050 $\mu\text{g/l}$. The assay was most precise between 75-550 $\mu\text{g/l}$. Expected normal values ranged between 140-400 $\mu\text{g/l}$.

Statistical methods

Groups were compared using the Student-*t* test. A statistical significant difference was admitted if *P* was less than 0.05.

Results

The distribution of serum trypsin concentrations in healthy controls and in various conditions is shown in Fig. 1. Mean serum trypsin ($\pm$ s.d.) in healthy controls was 248 ± 94.9 $\mu\text{g/l}$ (range 58.2-437.8 $\mu\text{g/l}$; mean ± 2 s.d.). Mean serum trypsin in acute pancreatitis (1399 ± 618 $\mu\text{g/l}$; mean $\pm$ s.d.) and

in chronic renal failure (1100 ± 584 $\mu\text{g/l}$; mean $\pm$ s.d.) was significantly higher than in the control group ($P < 0.001$). Serum trypsin levels were above the upper limit of the normality in all patients with acute pancreatitis and in all but one with chronic renal failure. Serum trypsin was markedly raised in one patient with a traumatic haemoperitoneum, and in one of the 11 with peptic ulcer perforation, and moderately raised in 3 of the 6 with acute cholecystitis (see Fig. 1).

Discussion

The radioimmunoassay of trypsin measures its immunological concentration and not its enzymatic biological activity (Elias *et al.*, 1977; Temler and Felber, 1976; Borgstrom and Ohlsson, 1978; Lake-Bakaar *et al.*, 1980a). The radioimmunoassay of trypsin seems to be specific for trypsin and its pro-enzyme trypsinogen, and not to be affected by the presence of circulating trypsin inhibitors (Elias *et al.*, 1977; Temler and Felber, 1976). These inhibitors such as α_1 -antitrypsin and α_2 -macroglobulin make the measurement of trypsin as enzymatic activity difficult (Elias *et al.*, 1977; Temler and Felber, 1976). Radioimmunoassay has been successfully applied to determine trypsin in serum, urine and duodenal fluid (Elias *et al.*, 1977; Temler and Felber, 1976; Lake-Bakaar, McKavanagh and Summerfield, 1979; Lake-Bakaar *et al.*, 1980a).

Serum trypsin has been reported to be constantly raised in acute pancreatitis (Elias *et al.*, 1977). The authors' results in a relatively large unselected series of acute pancreatitis support this. Therefore a normal

FIG. 1. Serum trypsin concentrations (mean $\pm$ s.d.). ■, Peptic ulcer perforation; □, cholecystitis; ▲, haemoperitoneum; △, others.

serum trypsin measurement might be very valuable to exclude acute pancreatitis in patients with increased serum amylase and lipase of non-pancreatic origin (Elias *et al.*, 1977). Other conditions such as carcinoma of the pancreas and common duct gallstones can also occur with increased serum trypsin levels (Elias *et al.*, 1977). Hypertrypsinaemia has been found in one and 2 patients with carcinoma and acute alcoholic hepatitis (Lake-Bakaar *et al.*, 1978a). A rapid increase in serum trypsin has also been reported after endoscopic retrograde cholangiopancreatographic examination (Borgstrom and Ohlsson, 1978) although an acute pancreatitis is an uncommon complication (Borgstrom and Ohlsson, 1978; Banks, 1979; Zimmons *et al.*, 1975).

For the diagnosis of acute pancreatitis trypsin has the advantage over α -amylase and lipase in that it reflects only production by the pancreas (Elias *et al.*, 1977). However, the way by which trypsin and other pancreatic enzymes reach the circulation, is not completely known (Elias *et al.*, 1977). The venous, lymphatic and peritoneal absorption routes have been

mentioned (Temler and Felber, 1976; Webster and Zieve, 1962a, b). An enteropancreatic circulation has been suggested for amylase and chymotrypsinogen (Liebow and Rothman, 1975), and convincingly demonstrated for trypsin (Lake-Bakaar *et al.*, 1978b; Lake-Bakaar, Smith-Laing and Summerfield, 1978c; Lake-Bakaar *et al.*, 1980b). A leakage of intraluminal contents, and peritoneal reabsorption might be the explanation of the raised serum trypsin level in the reported patient with perforated peptic ulcer. Increased serum trypsin was also found in 3 of 6 cases of acute cholecystitis and in one case of haemoperitoneum. It was found difficult to provide a reasonable explanation. However, minimal pancreatitis cannot be excluded. Although the pancreas seemed grossly normal at laparotomy, even the palpating surgeon may be frequently uncertain as to the normality of the pancreas (Levitt and Johnson, 1978).

The kidney seems to play a quantitatively important role in trypsin elimination (Elias *et al.*, 1977; Borgstrom and Ohlsson, 1978). According to the

present results and others (Elias *et al.*, 1977) serum trypsin levels in chronic renal failure can be as high as those achieved in acute pancreatitis. Immunoreactive trypsin has been estimated in urine after concentrating it up to 25 times (Lake-Bakaar *et al.*, 1979; Lake-Bakaar and Summerfield, 1978). Its urinary clearance is very low and it increases in pancreatic carcinoma and in about 67% of patients with acute pancreatitis (Lake-Bakaar *et al.*, 1979). The mechanism is still unknown. It might be an interference in the tubular reabsorption and digestion of the filtered trypsin (Lake-Bakaar *et al.*, 1979; Borgstrom, 1978).

Measurement of serum trypsin seems to be a specific test for the diagnosis of acute pancreatitis. Renal failure must always be excluded. Furthermore, it is suggested that serum trypsin should be prospectively measured in a larger series of acute non-pancreatic abdominal conditions, especially in those such as peptic ulcer perforation, which can clinically imitate acute pancreatitis (Banks, 1979), and not infrequently occurs together with high serum levels of amylase and even lipase (Banks, 1979; Salt II and Shenker, 1976).

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