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Short Communication

Tissue polypeptide antigen (TPA) in pancreatic cancer diagnosis

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Tissue polypeptide antigen (TPA) is a protein produced by rapidly growing tissues, such as placenta and neoplasms (Björklund *et al.*, 1976; Björklund, 1978). Increased serum levels of this antigen have been observed in a variety of malignant diseases of different origin: i.e. lung, breast, stomach and colorectal cancer (Menendez-Botet *et al.*, 1978; Schlegel *et al.*, 1981). They have also been detected in several acute and chronic inflammatory conditions, especially liver cirrhosis and acute hepatitis (Björklund, 1980). Only the occasional report appears in the literature on TPA measurements in pancreatic cancer (Andriulli *et al.*, 1983). Moreover few data are available on the utility of serum TPA assay in the differential diagnosis between pancreatic cancer and chronic pancreatitis (Panucci *et al.*, 1984).

The aim of the present investigation was to evaluate the role of TPA in detecting pancreatic malignancy and its value in distinguishing pancreatic cancer from other pancreatic and benign extra-pancreatic gastrointestinal conditions.

A total of 106 subjects were studied: 29 control subjects (19 male, 10 female, age range, 37–66 years) who were healthy members of the medical staff and blood donors; 28 with pancreatic cancer of duct cell origin (Cubilla & Fitzgerald, 1978) (20 male, 8 female, aged 43–71) always histologically confirmed; staging was: $T_1N_0M_0$ (3), $T_2N_1M_0$ (6), $T_2N_1M_1$ (9), $T_3N_1M_1$ (10); 24 with chronic pancreatitis (22 male, 2 female, aged 26–64) (7 with calcified chronic pancreatitis) diagnosed on the basis of the following examinations: abdominal x-ray for pancreatic calcifications, pancreatic ultrasonography, endoscopic retrograde pancreatography, CAT scanning. The diagnosis of chronic pancreatitis was always histologically confirmed on surgical biopsies. Twenty five were affected by gastrointestinal extra-pancreatic diseases of a nonmalignant nature (11 male, 14 female, aged 37–81): liver cirrhosis (6 cases), primary biliary cirrhosis (1), gallstones (4), common duct stones (3), benign stenosis of the papilla of Vater (2), chronic gastritis (4), duodenal ulcer (3), irritable colon (2). Diagnosis was made on the basis of the clinical picture and on the results of specific radiological and histological procedures.

Serum TPA determination was performed by an RIA procedure (Prolifigen RIA kit, AB Sangtec Medical, Bromma, Sweden). The intra-assay (no = 15, mean = 125.5, s.d. = 6.2 $U l^{-1}$) and inter-assay (no = 7, mean = 122.6, s.d. = 12.3 $U l^{-1}$) coefficients of variation were 4.9% and 10.0% respectively. Serum specimens were always frozen at −20°C immediately after collection, and the assay was performed within 1 month. Further determinations were done at 3 and 6 months on 12 samples; a significant decrease in immunoreactivity was observed ($F = 3.72$, $P = 0.0405$).

Statistical evaluation of the results was performed by means of the analysis of variance (one way ANOVA), Bonferroni's test for paired comparisons, analysis of variance with repeated measures (Brown *et al.*, 1981), chi-square test, Youden index (Armitage, 1971).

Figure 1 illustrates serum levels of TPA. A significantly increased frequency of pathological values was observed in pancreatic cancer patients ($\chi^2 = 68.8$, $P < 0.0005$).

Table I reports mean values, standard errors and statistical evaluation of TPA. Sensitivity, specificity and diagnostic accuracy (Youden index) in diagnosing pancreatic cancer were 96.4%, 67.3% and 63.8% respectively.

Figure 2 shows the individual values of TPA in pancreatic cancer divided according to the stage of the disease.

A significant linear correlation was observed in extrapancreatic diseases between TPA on the one hand and alanine-amino-transferase and albumin (increasing and decreasing values) on the other ($r = 0.8186$, $P < 0.001$ and $r = -0.4297$, $P < 0.05$ respectively). No significant correlation was

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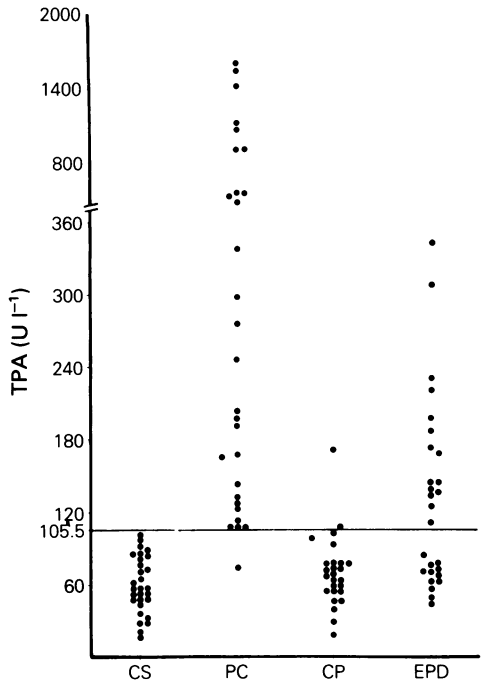

Figure 1 Individual values of serum TPA. The continuous line represents the upper normal limit ($\bar{x}$ +2s.d. of control subjects: 61.3+44.2 U l^{-1}). (CS) control subjects; (PC) pancreatic cancer; (CP) chronic pancreatitis; (EPD) extra-pancreatic diseases.

Table I Mean values, standard errors and statistical evaluation of serum TPA

	Cases No.	TPA ($U l^{-1}$) $\bar{x}$	s.e.
Control subjects	29	61.3[a]	4.1
Pancreatic cancer	28	487.3	90.5
Chronic pancreatitis	24	73.3[a]	5.6
Extra-pancreatic diseases	25	131.7[a]	15.9
	106		

$F = 17.96$
$P = 0.0000$
[a] $P < 0.001$ in respect to pancreatic cancer.

observed between these parameters in pancreatic cancer and chronic pancreatitis.

In the present study TPA increase was almost invariably observed in pancreatic cancer patients (27 out of 28); abnormal values were only occasionally encountered in chronic pancreatitis (2 out of 24). Both normal and increased serum TPA levels were found in extra-pancreatic diseases. These results show that the assay has a good sensitivity for the detection of pancreatic cancer. The sensitivity is similar to that previously reported for

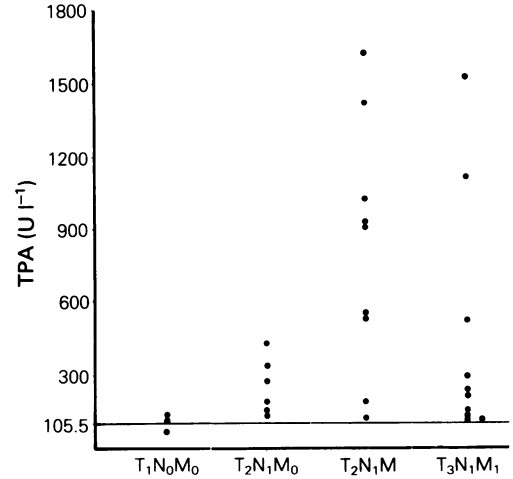

Figure 2 Individual values of TPA in pancreatic cancer patients divided according to the stage of the disease. The continuous line represents the upper normal limit.

Pancreatic oncofoetal antigen (Banwo *et al.*, 1974) and better than that found for other proposed tumour markers (Fabris *et al.*, 1981; Farini *et al.*, 1985; Kalser *et al.*, 1978; Nitti *et al.*, 1982; Reddi & Holland, 1976; Savarino *et al.*, 1984). The sensitivity of the test in our hands was better than that reported by Andriulli *et al.* (1983) possibly because our samples were always determined shortly after collection. In fact a decrease in immunoreactivity was noted after longer storage.

No clear relationship between the stage of pancreatic cancer and TPA levels was observed: a substantial number of patients in $T_2N_1M_1$ and $T_3N_1M_1$ categories had moderately increased serum TPA. However, the highest values were always observed in these groups.

TPA levels differentiated pancreatic cancer from chronic pancreatitis, and to this extent the specificity of the assay was satisfactory. However, abnormal TPA values were observed in other than neoplastic extra-pancreatic diseases. High levels were frequently found in patients with liver damage; this is supported by the correlations observed between alanine-amino-transferase and albumin on the one hand and TPA on the other. Such correlations were not found in patients with chronic pancreatic disease, suggesting that liver dysfunction does not play an important role in increasing serum TPA levels in pancreatic cancer. These data are in full agreement with our preliminary findings (Panucci *et al.*, 1984), and confirm the usefulness of TPA in detecting pancreatic malignancy.

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