Letters to the Editor

Serum tissue polypeptide antigen in pancreatic cancer and other gastrointestinal diseases

Tissue polypeptide antigen (TPA) is a glycoprotein produced by several tissues with keratin-like sites.¹ It possesses an excellent sensitivity for diagnosing pancreatic cancer²; in this neoplasm, as in other malignancies, it reflects tumour growth and extent.^{3,4} It is not specific, however, and raised TPA values have often been found in chronic pancreatitis and other inflammatory states.⁴

The liver probably has a key role in influencing circulating TPA by two different mechanisms; (i) by releasing it from hepatic or metastatic cells into the bloodstream; and (ii) by decreasing its metabolism.

We attempted to evaluate the influence of different types of liver damage on serum TPA in patients suspected of having a pancreatic malignancy. We studied 135 subjects: 32 controls (20 men, 12 women, aged 19-60); 23 affected by histologically confirmed pancreatic cancer of duct cell origin (18 men, five women, aged 43-73) (16 had hepatic metastases); and 13 with chronic pancreatitis (12 men, one woman, aged 26-65) in whom the diagnosis was based on previously reported criteria.⁴ Sixty seven patients (43 men, 24 women, aged 23-81) had extra-pancreatic diseases including primary liver cell cancer (26 cases), gastric cancer (n = 3), carcinoma of the colon (n = 2), carcinoma of the hepatic hilus (n = 2), retroperitoneal sarcoma (n = 1), liver cirrhosis (n = 11), gallstones (n = 5), primary biliary cirrhosis (n = 3), irritable colon (n = 3), benign stenosis of the papilla of Vater (n = 2), duodenal ulcer (n = 2), erosive gastritis (n = 2), liver steatofibrosis (n = 1), chronic cholecystitis (n = 1), hiatus hernia (n = 1), ulcerative colitis (n = 1) and retroperitoneal haematoma (n = 1).

The patients were divided into two groups: group A (n = 60) included those with anatomical liver damage (primary or metastatic cancers, cirrhosis, steatofibrosis) of whom 16 had pancreatic cancer, one had chronic pancreatitis, and 43 had extra-pancreatic diseases. Group B (n = 43) comprised all the remaining patients of whom five had pancreatic cancer, two had chronic pancreatitis, and three had extra-pancreatic diseases with a raised serum bilirubin value (> 15 µg/l).

Serum TPA was assayed by an RIA technique using a commercial kit (Prolifigen, AB Sangtec Medical, Bromma, Sweden). Due to

Table Logarithmic transformed values of serum tissue polypeptide antigen (TPA) (means, standard errors and statistical evaluation)

	TPA (U/l)	
	Mean	SE
Control subjects (n = 32)	4.20	0.05
Pancreatic cancer (n = 23)	5.76*	0.17
Chronic pancreatitis (n = 13)	4.31†	0.15
Extra-pancreatic diseases (n = 67)	5.00†	0.10
Analysis of variance	F = 24.29, p < 0.001	

Bonferroni's test for pairwise comparisons:

*p < 0.001 compared with control subjects, chronic pancreatitis, extra-pancreatic diseases.

†p < 0.001 compared with control subjects.

‡p < 0.05 compared with extra-pancreatic diseases.

the scattered distribution of TPA values a logarithmic transformation of the data was used for statistical analysis.

The table reports mean values, standard errors, and statistical evaluation of the data.

Group A patients had higher values than group B ($t = 42.3$, $p < 0.001$). Patients with raised values of total bilirubin, alanine transaminase, and alkaline phosphatase had higher TPA values compared with those with normal values (Student's t test: $t = 15.05$, $p < 0.001$; $t = 13.71$, $p < 0.001$; $t = 61.53$, $p < 0.001$, respectively).

We found grossly increased concentrations of serum TPA in patients with pancreatic cancer as previously described^{2,4}; we also found that concentrations were raised in other malignant or benign diseases, especially of the liver and biliary tract.⁵

The presence of anatomical hepatic damage is a factor of great importance in influencing serum TPA; our group A patients had higher concentrations than group B.

Patients with abnormal liver function tests had higher mean TPA concentrations, which suggests that liver dysfunction can increase circulating TPA. In addition to the presence of liver damage, cholestasis alone is associated with an increase in circulating TPA.

It may therefore be concluded that different types of liver pathologies may influence circulating TPA in patients with pancreatic cancer and other gastrointestinal diseases.

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Trisomy 11 in acute lymphoblastic leukaemia

The study of non-random, clonal chromosomal abnormalities in leukaemia has led to well established associations between a specific abnormality and a particular subtype of leukaemia. Trisomy 11 is emerging as a rare finding in clonal haemopoietic disease and thus far seems to have been associated with non-lymphoid disorders.¹⁻⁴ We present details of a child with acute lymphoblastic leukaemia (ALL) in whom trisomy 11 was found in the bone marrow cells.

A 12 year old white boy presented with oral herpes and pallor. Liver and spleen were not enlarged. Chest x-ray picture showed hilar and paratracheal lymphadenopathy. The thymus was not enlarged. A full blood count showed a haemoglobin concentration of 5.8 g/dl, white cell count of $1.7 \times 10^9/l$ (10% blasts) and a platelet count of $50 \times 10^9/l$. Many poikilocytes were present on the blood film and the mean red cell volume was 101 fl. Plasma folate and B_{12} and red cell folate concentrations were normal.

Figure G-banded karyotype obtained after relapse. Arrows point to abnormal chromosomes 1 and 3 involved in the translocation $t(1;3) (p3;q2)$ and to the extra chromosome 11.

Less than 1% of total haemoglobin was fetal. A bone marrow aspirate showed 90% blast cells. Dysplastic erythropoiesis with irregular or lobulated nuclei and an open chromatin pattern was found. The blasts were Sudan black B negative and did not contain granules or Auer rods. They were classified as L1. Immunophenotyping showed the following: Tdt, 2% of blasts; CD10, <1%; CD20, 2%; CD2, 15%; CD7, 71%; CD13, 14, 33, <1%. No reactivity was found with monoclonal antibodies AN51 or Plt 1 which detect megakaryocyte-associated antigens. ALL with early T cell features was diagnosed. He was treated with the Medical Research Council UKALL X protocol. Four weeks after diagnosis he had entered remission. He remained well in first remission till 16 months after diagnosis when relapse occurred. Immunophenotyping of the blasts remained unchanged, except that 45% were CD 2 positive. At diagnosis 14 of 18 metaphases contained trisomy 11; the remainder were normal. At relapse, of 30 metaphases, 15 had trisomy 11 as the only abnormality and five had, in addition, a translocation between chromosomes 1 and 3. A karyotype from a representative metaphase is shown in the figure.

This case represents the rare association of ALL with trisomy 11, but there are some unusual features. Severe dyserythropoiesis, manifest by poikilocytosis, macrocytosis, and dysplastic erythroblasts is unusual in childhood ALL. A diagnosis of early T cell

leukaemia was based on the CD7 positivity of the blasts and further supported by the CD2 positivity at relapse. Because of the dyserythropoiesis, evidence of non-lymphoid origin was sought but not found. The response to treatment suggested a lymphoid origin. At both diagnosis and relapse trisomy 11 was the sole cytogenetic abnormality in one cell line.

This case illustrates the point that although a specific cytogenetic abnormality might seem to be a consistent abnormality in one group of leukaemias, further experience may show that it is not restricted to that group. Whether trisomy 11 can occur in typical childhood ALL remains as yet unknown.

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Non-secretory lambda multiple myeloma

Non-secretory myeloma refers to otherwise typical multiple myeloma with no paraprotein detectable in blood or urine; this accounts for about 0.38-5% of patients with myeloma.¹⁻² Recently we studied a patient with a rare lambda chain non-secretory myeloma.

A 72 year old woman was admitted to our hospital because of abdominal and lumbar pain. On physical examination pressure of lumbar spine was tender. Hepatosplenomegaly or lymphadenopathy were not observed. Her haemoglobin concentration was 7 g/dl and white cell count $5.5 \times 10^9/l$ with 18% granulocytes, 32% lymphocytes, 7% plasma cells and 43% lymphoplasmatic cells, nearly all atypical. The platelet count was $118 \times 10^9/l$ and erythrocyte sedimentation rate/first hour 8 mm. Protein electrophoresis showed the albumin concentration to be 38.6 g/l; alpha 1, 1.84 g/l; alpha 2, 5.29 g/l; beta 5.85 g/l; and gamma 3.62 g/l. There was no proteinuria. Calcium and urate concentrations and liver and renal function tests were normal, except that GGT was 138 U/l. Skeletal x-ray studies showed diffuse osteoporosis with lytic bone images and multiple vertebral crushing. Immunoelectrophoresis showed decreased concentrations of IgG, IgM, and IgA with absence of IgD and paraprotein. Test for Bence-Jones protein and immunoelectrophoresis of urine were negative. Bone marrow aspirate contained 80% atypical plasma cells. The patient did not respond to treatment with melphalan and prednisone and died 10 months later because of infection. Periodic blood and urine immunoelectrophoresis failed to show paraprotein.

Intracytoplasmatic immunoglobulins studied with fluorescein-conjugated rabbit F(ab)₂ anti-human immunoglobulins showed only the presence of lambda light chains in the cytoplasm of bone marrow plasma cells: μ , α , τ , δ and κ chains were negative.

For molecular analysis DNA was prepared from bone marrow using standard procedures. DNA was digested with Eco RI, electrophoresed on 0.8% agarose gels, trans-