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An initial appraisal of the value of serum carbohydrate antigenic determinant (CA 19–9) levels in patients with pancreatic cancer

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Abstract—*Serum CA 19–9 levels have been determined in 20 patients with pancreatic cancer, 18 patients with primary hepatocellular cancer, 15 patients with metastatic liver disease and 10 patients with colorectal cancer. Market elevations 3 times the upper limit of normal were found in all 20 patients with pancreatic cancer, 10 out of 15 with metastatic liver disease and 7 out of 18 with hepatoma. As serum AFP and CEA levels are normal in those with pancreatic cancer, the serum CA 19–9 level provides a sensitive and specific test for this malignancy.*

INTRODUCTION

THERE is a need for biochemical markers for pancreatic cancer as one main dilemma in the diagnosis of pancreatic cancer is said to be the lack of symptoms in the early stages of the disease. Several markers which have been tested and found too insensitive and too unspecific are isoenzymes, especially isoamylase [1], pancreatic ribonuclease [2] and peptide hormones [3]. Further search for biochemical markers for screening and diagnosis of risk groups is necessary and of special interest in this respect is the potential of monoclonal antibodies. Such an antibody has been described by Koprowski *et al.* [4] who immunised mice with a human cell line derived from a colorectal carcinoma. The antibody reacts with a carbohydrate antigenic determinant (CA 19–9) which has been identified as a sialylated lacto-*N*-fucopentaose II, an oligosaccharide related to Lewis blood group substance [5].

Del Villano *et al.* [6] have developed an immunoradiometric assay for CA 19–9 which is now available commercially in kit form from CIS (UK) Ltd. We report our preliminary findings using this kit to measure serum CA 19–9 levels in healthy individuals, patients with acute and chronic pancreatitis and patients with pancreatic, liver and colorectal cancers.

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PATIENTS AND METHOD

Serum CA 19–9 levels were determined in 19 healthy individuals, 9 patients with acute pancreatitis, 6 patients with chronic pancreatitis and 63 patients with histologically-proven malignant disease. These included 20 patients with pancreatic cancer, 18 patients with primary hepatocellular carcinoma, 15 patients with metastatic liver disease and 10 patients with colorectal cancer.

Serum samples were obtained from the patients prior to surgery or treatment and were stored at −20° C until analysed. All analyses were performed in duplicate using the immunoradiometric assay kit obtained from CIS (UK) Ltd. and employing an overnight second incubation. Del Villano *et al.* [6] described in their paper that the second incubation should be 3 hr with no greater than a ± 5% variation. We found a longer second incubation gave higher bindings and a more sensitive standard curve as suggested in the instructions of our kit. The assay has a dynamic range of 5–120 U/ml. Using the immunohistochemical staining kit from CIS (UK) Ltd., the carbohydrate antigenic determinant (CA 19–9) was localised in the ductal linings of the pancreas (Fig 1).

RESULTS AND DISCUSSION

CA 19–9 is a tumour marker, the concentration of which is expressed in U/ml where one unit corresponds to approx. 0.8 ng of a highly purified mucin-like glycoprotein expressing the CA 19–9 determinant.

The CA 19–9 level of 19 healthy adult controls ranged up to 28 U/ml with a median value of 5 U/ml. The coefficient of variation for within and between batch precision was better than 10%. The serum CA 19–9 levels of patients with acute pancreatitis, chronic pancreatitis and cancer involving the pancreas, liver, colon and rectum are summarised in Table 1, and the summary of the clinical details of the patients with pancreatic cancer is shown in Table 2.

Ritts *et al.* [7] in their initial clinical evaluation of serum CA 19–9 levels in 171 cancer patients arbitrarily chose a cut-off limit of 40 U/ml. Using this value they found elevated serum CA 19–9 levels in 70% of patients with pancreatic carcinoma, 67% of patients with hepatobiliary carcinoma, 62% of patients with gastric carcinoma and 18% of patients with colorectal carcinoma. Employing the same cut-off limit, we have found abnormal CA 19–9 levels in all 20 patients with pancreatic carcinoma, 13 out of 18 patients with primary hepatocellular carcinoma, 11 out of 15 patients with metastatic liver disease and 5 out of 10 patients with colorectal carcinoma. Seven out of 15 patients with benign pancreatic disease also had elevated levels.

The serum levels of CA 19–9 found in pancreatic carcinoma were all greater than three times the cut-off limit of 40 U/ml and there was no variation in the CA 19–9 level according to the site of the tumour (i.e. head, body or tail). Using the 120 U/ml cut-off limit, elevated levels were

Table 1. *Serum carbohydrate antigenic determinant (CA* 19–9) *levels in patients with acute and chronic pancreatitis, cancer of the pancreas, liver, colon and rectum*

	No. cases	Range	No. of cases >40 U/ml	No. of cases >120 U/ml
Normal	19	<5–28	0	0
Acute pancreatitis	9	19–103	6	0
Chronic pancreatitis	6	<5–57	1	0
Ca pancreas	20	130–>12000	20	20
Colorectal Ca	10	<5–91	5	0
Hepatoma	18	<5–4700	13	7
Metastatic liver disease	15	<5–>12000	11	10

Table 2. *Summary of the patients' characteristics*

Case No.	Age/Sex	Tumour site	Stage of disease	Presenting symptoms
1	83 F	Head	Causing obstructive jaundice	Jaundice, pale stools and dark urine
2	49 F	Head	Liver metastasis	Abdominal pain
3	57 F	Body and tail	Liver metastasis	Epigastric pain, vomiting and weight loss
4	55 M	Head	Causing obstructive jaundice	Jaundice, abdominal distention
5	61 F	Head	Causing enlarged tender liver	Jaundice, malaise
6	57 F	Body and tail	Local disease	Epigastric tenderness, loss of appetite
7	63 M	Neck and proximal body	Liver and spleen metastases	Weight loss
8	45 F	Body	Carcinomatosis	Weight loss, anorexia, malaise and ascites
9	56 F	Head	Causing obstructive jaundice dilated common bile duct	Jaundice, pale stools and dark urine
10	75 M	Head	Liver metastases	Jaundice, pale stools and dark urine
11	80 F	Head	Liver metastases	Abdominal pain
12	64 F	Tail	Local disease	Recurrent abdominal pain
13	52 F	Head	Causing obstructive jaundice	Jaundice, abdominal pain
14	60 M	Head	Unresectable	Epigastric pain, jaundice
15	76 M	Head	Causing obstructive jaundice with dilated ducts	Jaundice, abdominal pain
16	49 M	Head	Unresectable (local invasion)	Abdominal pain, weight loss, diarrhoea, pale stool, jaundice
17	68 M	Tail	Local disease	Abdominal pain
18	59 F	Head	Unresectable	Jaundice, abdominal pain
19	73 F	Body	Liver metastases	Weight loss, epigastric pain
20	48 M	Head	Causing obstructive jaundice	Jaundice, abdominal pain

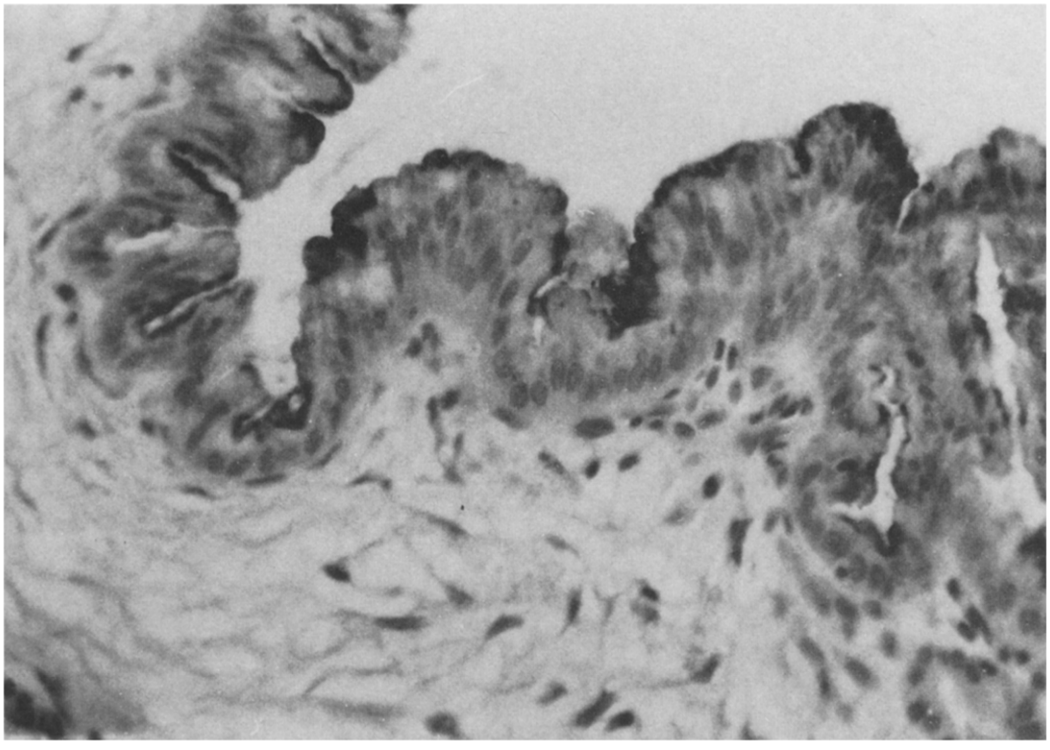

Fig. 1. *The ductal linings of the pancreas staining positive for CA* 19–9 *antigen (darkly-staining cells). Immunohistochemical stain* × 512.

again found in all 20 patients with pancreatic carcinoma but in none of those with acute or chronic pancreatitis (Table 1). Elevated serum CA 19–9 levels were also found in some patients with primary hepatocellular carcinoma and metastatic liver disease (Table 1). Estimation of the serum alpha-fetoprotein (AFP) level together with its concanavalin A reactivity and the carcinoembryonic antigen (CEA) levels could however be used to differentiate these latter conditions from pancreatic cancer. It has already been demonstrated [8] that primary hepatocellular carcinoma and metastatic liver disease can be delineated by their serum AFP–concanavalin A reactivity. In addition, patients with metastatic liver disease tend to have higher serum CEA levels than those with primary hepatocellular carcinoma (PK Buamah, unpublished observation). All twenty cases of pancreatic carcinoma we have so far studied have yielded serum AFP levels within the normal reference range and 3 out of 20 patients gave CEA values between 6.4 and 8.2 ng/ml (reference range < 5.0 ng/ml).

The preliminary findings are extremely encouraging and we have started an extensive study of serum CA 19–9 levels in various malignant conditions to determine more precisely its role in clinical oncology. Should this test confirm itself as a reliable indicator of pancreatic cancer, it will provide a more economical diagnostic tool than computed tomography and abnormal ultrasound.

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