

Diagnostic pitfall; interpretation of CA 19-9 concentrations in the presence of hepatic dysfunction

S Pearce, H Thornes, D Carr, A Tanner

Abstract

A 50 year old man is described with hepatic dysfunction and chronic pancreatitis in whom greatly increased concentrations of the pancreatic tumour marker CA 19-9 combined with an abnormal appearance at endoscopic retrograde cholangiopancreatography lead to the false suspicion of pancreatic carcinoma. CA 19-9 concentrations should be interpreted with caution in patients with intrinsic liver disease or biliary obstruction.

(Gut 1994; 35: 707-708)

The non-operative diagnosis of pancreatic malignancy can be difficult and relies upon imaging techniques such as computed tomography or endoscopic retrograde cholangiopancreatography combined with histological examination from aspiration or guided biopsy of a mass.¹ Recently a monoclonal antibody against CA 19-9, a glycoprotein with structural homology to Lewis blood group antigens has been widely advocated as a specific and sensitive serum tumour marker for pancreatic malignancy.²⁻⁵ We report a patient with chronic pancreatitis and transient hepatic dysfunction in whom greatly increased concentrations of CA 19-9 lead to a false suspicion of pancreatic carcinoma.

Case report

A 50 year old man presented with a 17 kg weight loss over four months associated with anorexia and an increased frequency of pale stools. Nineteen years previously he had multiple episodes of painful acute alcoholic pancreatitis. These episodes subsided after he reduced his alcohol intake but four years later he developed diabetic ketoacidosis and has required insulin treatment to maintain normoglycaemia/euglycaemia since. He smoked 15 cigarettes daily and admitted drinking 10 units of alcohol weekly. He used 6 U of soluble human insulin before each meal and 10 U of crystalline human insulin zinc suspension at night. He had been prescribed dothiepin 75 mg at night for insomnia four weeks before presentation. He was cachectic but there were no other abnormal physical signs.

The full blood count was normal with a mean red cell volume of 99.5 fl. The Westergren erythrocyte sedimentation rate was 48 mm in the first hour. Serum creatinine, corrected calcium, phosphate, urea and electrolytes, and thyroid stimulating hormone were within the normal range. The patient had acceptable diabetic control, the highest blood glucose over a 24 hour series being 8.3 mmol/l and the fructosamine 396 µmol/l

(normal <285 µmol/l). The prothrombin time was 13 seconds (control 12 seconds). His liver function tests were abnormal (Table). Serum vitamin B-12 and red cell folate were normal. A chest radiograph was normal and an abdominal ultrasound scan showed a shrunken pancreas with areas of diffuse calcification but no abnormality of the liver, spleen or biliary tree. A double contrast barium enema examination of the colon was normal. A previously validated test of pancreatic exocrine function showed a slightly subnormal serum concentration of para-aminobenzoic acid at 90 minutes 1.91 mg/l (normal >2 mg/l)⁶ but this was not felt to explain his recent symptoms. The serum CA 19-9 estimated using a monoclonal antibody enzyme immunoassay (Abbott IMX) was greatly raised at 2690 U/ml (normal <25 U/ml). The serum carcinoembryonic antigen was 30 µg/l (normal <9 µg/l) and the α fetoprotein was 4 IU/l (normal <10 IU/l). The extremely high concentration of CA 19-9 lead us to suspect that an occult pancreatic carcinoma was the cause of the patient's deterioration. Endoscopic retrograde cholangiopancreatography showed an irregular and dilated pancreatic duct with an abrupt tapering of the main duct in the tail of the pancreas; the biliary tree was normal. These findings gave further weight to the suspicion of pancreatic malignancy and the patient was informed of the probable diagnosis. Computed tomography with intravenous contrast was performed to confirm the presence of a pancreatic mass and define operability. There was no space occupying lesion, however, within the pancreas, only heavy calcification and atrophic pancreatic tissue could be identified. The liver and spleen appeared normal. Liver biopsy was not performed.

The patient was given empirically a course of pancreatic enzyme replacements with meals and kept under observation. His dothiepin was stopped. Over the next four months the patient regained 12 kg in weight and his stools became normal. The serum CA 19-9 concentration decreased progressively, his liver function became normal (Table) and his mean red cell volume fell to 89.1 fl. Repeat computed tomography was performed nine months after initial evaluation and showed no change from the original study. The patient remains in good health and has sustained his weight gain over a one year period.

Discussion

CA 19-9 has been widely advocated as a sensitive and specific marker for pancreatic malignancy.²⁻⁵ Ritts *et al* found that a CA 19-9 concentration of

Departments of
Medicine
S Pearce
D Carr
A Tanner

and Biochemistry, North
Tees General Hospital,
Stockton on Tees,
Cleveland
H Thornes

Correspondence to:
Dr S Pearce, MRC Molecular
Medicine Group, Royal
Postgraduate Medical School,
Hammersmith Hospital,
DuCane Road, London
W12 0NN.

Accepted for publication
20 September 1993

Serial measurements of CA 19-9 and liver function

Time (months)	CA 19-9 (U/ml)	Bilirubin ($\mu\text{mol/l}$)	Alkaline phosphatase (IU/l)	AST (IU/l)	Albumin (g/l)	Mean cell volume (fl)
0	—	7	121	56	31	99.5
2	2690	28	649	213	30	101.2
3	741	22	634	126	29	102.8
4	355	9	355	71	37	98.7
5	338	6	255	50	40	95.6
7	218	7	150	35	38	92.6
9	69	10	100	35	39	89.1

Normal ranges: CA19-9 <25 U/ml, bilirubin <17 $\mu\text{mol/l}$, alkaline phosphatase 20-90 IU/l, aspartate aminotransferase (AST) <35 IU/l, albumin 40-60 g/l, mean cell volume 78-98 fl.

above 40 U/ml was present in 81% of patients with pancreatic cancer and was over 99% specific for malignancy.² Similar results have been confirmed by other investigators.^{3,4} In our own population of patients a value for CA 19-9 above 100 U/ml is 96% sensitive and 91% specific for pancreatic carcinoma.⁵

The concentration of CA 19-9 found in serum is a balance between the rate of production of the antigen by both malignant and normal tissues and the rate at which it is cleared from the blood. CA 19-9 is a glycoprotein and in common with carcinoembryonic antigen is probably cleared by hepatic metabolism and excreted in bile.^{7,8} Basso *et al*⁹ have reported CA 19-9 concentrations in excess of 100 U/ml in six of 30 patients with benign extrahepatic cholestasis all of which fell towards normal after the obstruction was relieved. This has been confirmed by ourselves and others.^{4,5} Collazos *et al*¹⁰ found that in a group of 85 patients with cirrhosis seven had CA 19-9 concentrations between 100 and 200 U/ml. Among 74 patients with non-cirrhotic liver disease only one subject with acute hepatitis B had a higher concentration (425 U/ml).¹⁰

We believe that in our patient transient hepatic dysfunction with predominant cholestasis was the cause of the raised CA 19-9 concentration

and his raised carcinoembryonic antigen concentration gives further weight to this hypothesis. The high mean cell volume at presentation together with his previous alcohol abuse point towards alcoholic hepatitis as the probable cause of his hepatic impairment, although it is feasible his recent dothiepin use was responsible for a transient hepatitis. Increase in CA 19-9 concentrations to this degree resulting from intrinsic liver disease has not been reported previously and we advise caution in interpreting serum CA 19-9 concentrations in patients with parenchymal liver disease or biliary obstruction.

We would like to thank Dr R Fifield of the Protein Reference Unit, Cardiff Royal Infirmary for providing the CA 19-9 assay results.

- 1 DelMaschio A, Vanzulli A, Sironi S, Castrucci M, Mellone R, Staudacher C, *et al*. Pancreatic cancer versus chronic pancreatitis: diagnosis with CA 19-9 assessment, US, CT and CT-guided fine-needle biopsy. *Radiology* 1991; 178: 95-9.
- 2 Ritts RE, DelVillano BC, Go VLW, Herberman RB, Klug TL, Zurawski VR. Initial clinical evaluation of an immunoradiometric assay for CA 19-9 using the NCI serum bank. *Int J Cancer* 1984; 33: 339-45.
- 3 Pleskow DK, Berger HJ, Gyves J, Allen E, McLean A, Podolsky DK. Evaluation of a serological marker, CA 19-9, in the diagnosis of pancreatic cancer. *Ann Intern Med* 1989; 110: 704-9.
- 4 Paganuzzi M, Onetto M, Marroni P, Barone D, Conio M, Aste H, *et al*. CA 19-9 and CA 50 in benign and malignant pancreatic and biliary diseases. *Cancer* 1988; 61: 2100-8.
- 5 Welfare M, Tanner A. CA 19-9 estimation in the assessment of pancreatic or biliary tract malignancy - what is the most efficient threshold value? *Eur J Gastroenterol Hepatol* 1991; 3: 539-43.
- 6 Tanner AR, Robinson DP. Pancreatic function testing: serum PABA measurement is a reliable and accurate measurement of exocrine function. *Gut* 1988; 29: 1736-40.
- 7 McFarlane IG. Hepatic clearance of serum glycoproteins. *Clin Sci* 1983; 64: 127-35.
- 8 Thomas P, Zamcheck N. Role of the liver in clearance and excretion of circulating carcinoembryonic antigen. *Dig Dis Sci* 1983; 28: 216-24.
- 9 Basso D, Meggiato T, Fabris C, Plebani M, Fogar P, Panozzo MP, *et al*. Extra-hepatic cholestasis determines a reversible increase of glycoprotein tumour markers in benign and malignant diseases. *Eur J Clin Invest* 1992; 22: 800-4.
- 10 Collazos J, Genolla J, Ruibal A. CA 19-9 in non-neoplastic liver diseases. A clinical and laboratory study. *Clin Chim Acta* 1992; 210: 145-51.