Postgrad Med J 1998;74:543–544 © The Fellowship of Postgraduate Medicine, 1998

Increased serum CA 19-9 antibodies in Sjögren's syndrome

Rifaat Safadi, Moshe Ligumsky, Eran Goldin, Yaron Ilan, Yosef S Haviv, Samir Nusair

Summary

A 67-year-old woman with a history of thyroiditis presented with recent intermittent epigastric pain and nausea. Hyperamylasaemia, oedema of the pancreas, and high serum levels of lipase and CA 19-9 were found. Xerostomia and dry eyes developed later, accompanied by an abnormal Schirmer's test. The diagnosis of Sjögren's syndrome was confirmed by increased anti-Ro and anti-La antibodies and the histological findings of parotid gland biopsy. Two additional cases of Sjögren's syndrome with elevated serum CA 19-9 are also described. These observations of elevated serum lipase and serum CA 19-9 in Sjögren's syndrome without evidence of malignancy may reflect pancreatic involvement in this disorder.

Keywords: Sjögren's syndrome; pancreatitis; amylase; lipase; CA 19-9

Pancreatic involvement in patients with Sjögren's syndrome is usually subclinical or expressed as acute or chronic pancreatitis.[1–4] This report describes three cases of Sjögren's syndrome with elevated serum levels of CA 19-9 in whom malignancy has been excluded at the present time.

Case reports

Case 1

A 67-year-old woman had had thyroiditis 16 years ago accompanied by an elevated erythrocyte sedimentation rate (ESR), the presence of antithyroid antibodies, and decreased iodine uptake. She subsequently developed hypothyroidism and has been maintained on thyroxine supplement. Six years ago she experienced an episode of acute epigastric pain accompanied by hyperamylasaemia of 300 Units. Blood count, serum lipids, liver and renal biochemistry were normal. Abdominal ultrasonography was normal but abdominal computed tomography (CT) scan suggested a swelling of the lower part of the head of the pancreas, suspected to be a mass (figure 1). The endoscopic retrograde cholangiopancreatography (ERCP) was normal. CT-guided pancreatic biopsy revealed normal pancreatic tissue with few inflammatory cells. Even after becoming asymptomatic, serum amylase and lipase were sustained at levels of twice the normal values. Yearly follow-up abdominal CT scans were normal with no evidence of pancreatic pathology. Repeated tests for CA-125 and CEA were normal, but an increased CA 19-9 level of 79.1 U/ml was found (normal range 0–37). Colonoscopy and upper endoscopy were normal except for mild gastritis. Recent dryness of the mouth and eyes with a positive Schirmer's test developed. Salivary gland biopsy disclosed mild multifocal chronic inflammation compatible with sialoadenitis of Sjögren's syndrome (figure 2). Serum IgG was 24 g/l and no paraprotein was found. Complement proteins C3 and C4 were also normal. Antinuclear antibodies were detected at 1:160 dilution, antithyroglobulin antibodies were 1:6400. Anti-Ro (SSA) and anti-La (SSB) antibodies were positive.

Case 2

A 50-year-old woman presented with recurrent arthritis, oral and ocular dryness, and 5 kg weight loss. Examination revealed signs of arthritis and effusion in both knees. Blood count, biochemistry (including diastase and lipase) were normal with an ESR of 35 mm after one hour. Antinuclear antibodies and C3 were normal. Serum IgG was 20 g/l. Latex fixation test was positive at a dilution of 1:320 and Rose-Waaler at 1:8. Schirmer's test was markedly abnormal while the anti-Ro and anti-La antibodies were negative. Serum CA 19-9 was 100 U/ml and CEA levels were normal. Abdominal ultrasound and CT scan excluded liver, pancreatic or biliary pathology and barium contrast studies of the upper and lower gastrointestinal tract were normal. The patient's clinical and laboratory findings are consistent with primary Sjögren's syndrome. Following treatment with oral prednisone she gained weight and after 6 months ESR and serum levels of CA 19-9 returned to normal.

Case 3

A 34-year-old woman had suffered from xerostomia and ocular dryness, autoimmune chronic active hepatitis, recurrent pericarditis, and pancreatitis for the previous 10 years. A diagnosis of Sjögren's syndrome was supported by the presence of antinuclear and anti-Ro antibodies. She was admitted several times for severe hyponatraemia due to either inappropriate antidiuretic hormone secretion or compulsive water drinking. Later, new symptoms emerged including orthostatic hypotension and neurogenic bladder leading to urinary retention and recurrent urinary infections. This autonomic neuropathy was successfully treated with fludrocortisone. She has also experienced episodes of diarrhoea and weight loss. Serum CA 19-9 was 89 U/ml

Gastroenterology Unit, Division of Medicine, Hebrew University School of Medicine & Hadassah Medical Center, Jerusalem, 91120 Israel
R Safadi
M Ligumsky
E Goldin
Y Ilan
Y S Haviv
S Nusair

Accepted 10 March 1998

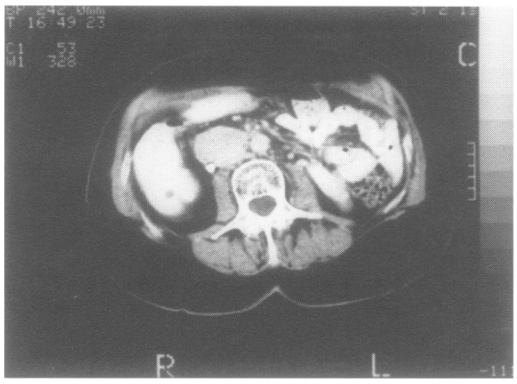

Figure 1 Abdominal CT showing oedema of the lower part of the head of the pancreas

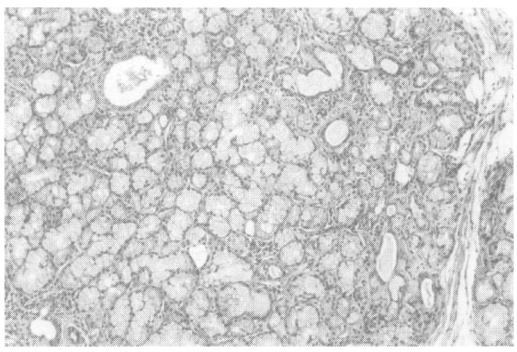

Figure 2 Parotid gland histology showing lymphocytic infiltrates, compatible with Sjögren's sialoadenitis (H & E stain).

while CEA was normal. A thorough work-up which included abdominal ultrasound, brain, chest, abdominal and pelvic CT, and endoscopic examination of upper and lower gastrointestinal tract did not reveal any pathology.

Discussion

Elevated serum pancreatic enzymes may grossly reflect the damage to the pancreatic parenchyma induced by the inflammatory process. Elevated levels of pancreatic amylase isoenzyme have been found in Sjögren's syndrome, especially in protracted disease. However, salivary amylase was found to be decreased, probably reflecting a state of hyposecretion of the salivary glands.[5 6]

CA 19-9 is a known tumour marker used for detection and follow-up of abdominal epithelial tumours, especially pancreatic adenocarcinoma. It is detected by a monoclonal antibody that recognises certain carbohydrate groups newly shed from the surface of the pancreatic cells by the action of abnormal glycosyltransferases which are activated during oncogenic transformation.[7] The specificity and sensitivity of CA 19-9 in detecting pancreatic carcinoma among a high-risk population are 87% and 70%, respectively.[8] High levels of serum CA 19-9, up to 100 U/ml, have been reported in nonmalignant conditions such as pancreatitis, cholelithiasis, cholestasis, cirrhosis and certain lung diseases. However, values of 1000 U/ml or more are highly suggestive of malignancy.[10] A survey of serum CA 19-9 levels in autoimmune diseases revealed marked elevation of CA 19-9 levels in six patients: two with Sjögren's syndrome, two with mixed connective tissue disease and two with dermatomyositis.[9] None of these six patients had any evidence of malignancy. In contrast to this study, normal serum levels of CA 19–9 were found in 27 women with collagen vascular disorders including systemic lupus erythematosus, scleroderma, dermatomyositis, and Sjögren's syndrome.[10]

Causes of serum CA19-9 elevation

- gastrointestinal malignancies
- nonmalignant causes: pancreatitis, cholelithiasis, cholestasis, cirrhosis, certain lung diseases; auto-immune diseases including SLE, mixed connective tissue disease, scleroderma, dermatomyositis and Sjögren's syndrome

Our first patient presented with relapsing or chronic pancreatitis. High lipase serum levels, which have not yet been described in Sjögren's syndrome, may reflect pancreatic involvement. All three patients exhibited moderately high increases in CA 19-9 serum levels (2–3 times 'normal' values), without any evidence of abdominal malignancy. Two of them (cases 1 & 3) had pancreatitis. Increased serum CA 19-9 in Sjögren's syndrome may reflect inflammatory pancreatic involvement with abnormal exposure of antigenic carbohydrate groups on the surface of the injured cells. The inflammatory process may lead to accumulation of the antigen due to obstruction of the pancreatic ducts. The role of the inflammatory process in increasing CA 19-9 levels is supported by the fact that the CA 19-9 level returned to normal in patient 2 following treatment with prednisone, which probably reduced inflammation within the pancreatic parenchyma. CA 19-9 has been detected on mucin of salivary glands,[11] but so far no association has been described with inflammation or a malignancy of the glands.

1 Constantopulos SH, Tsianos EV, Moutsopoulos HM. Pulmonary and gastrointestinal manifestations of Sjögren's syndrome. *Rheum Dis Clin N Am* 1992;**18**:617–35.
2 Valdez IH, Fox PC. Interactions of the salivary and gastrointestinal systems. II Effects of salivary gland dysfunction on the gastrointestinal tract. *Dig Dis* 1991;**9**:208–10.
3 Tsianon EV, Moutsopoulos HM. Sjögren's syndrome and the gut. *Bailliere Clin Rheumatol* 1989;**3**:357–70.
4 Manthorpe R, Jacobsson LT. Sjögren's syndrome. *Bailliere Clin Rheumatol* 1995;**9**:483–96.
5 Tsianos EB, Vasakos S, Drosos AA, Malmou-Mitsi VD, Moutsopoulos HM. The gastrointestinal involvement in primary Sjögren's syndrome. *Scand J Rheumatol* 1986; **61**(suppl):151–5.
6 Pal B, Griffiths ID, Katrak A, Junglee D, Dandona P. Salivary amylase and pancreatic enzymes in Sjögren's syndrome. *Clin Chem* 1987;**33**:305–7.
7 Andren-Sandberg A. CA 50 and CA 19-9 in serum as tumor markers for pancreatic cancer: a review of the literature. *Acta Chirurg Scand* 1989;**549**(suppl):75–81.
8 Pleskow DK, Berger HJ, Gyves J, Allen E, McLean A, Podolsky DK. Evaluation of a serologic marker, CA 19-9, in the diagnosis of pancreatic cancer. *Ann Intern Med* 1989;**110**:704–9.
9 Cantagrel A, Moulinier L, Beljio K, Duffaut M, Laroche M, Mazier B. Increase of CA 19-9 in dysimmune inflammatory rheumatism. Apropos of 6 cases. *Rev Rheumatol* 1994;**161**: 599–606.
10 Kimura K, Ezoe K, Yokozeki H, Katayama I, Nishioka A. Elevated serum CA-125 in progressive systemic sclerosis with pleural effusion. *J Dermatol* 1995;**22**:28–31.
11 Ho JJ, Norton K, Chung YS, Kim YS. Expression of CA 19-9, DU-PAN-2, and SPan-1 antigens on two types of normal salivary mucin. *Oncol Res* 1993;**5**:347–56.