Case Report

Autoimmune cholangitis presenting as pancreatic malignancy in a man with hand morphea

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SUMMARY

We report a 63 years old man with hand morhea who was admitted because of 6 weeks history of weight loss, weakness, low grade fever and jaundice. Physical examination revealed jaundice, hand morphea and a thin patient. Laboratory tests revealed aneamia, increased serum transaminase levels and an every day increasing of alkaline phosphatase, gamma-glutamyl transpeptidase and direct bilirubin, with a 3-fold increasing of Ca 19.9. The U/S, C.T and MRI of the abdomen were in favor of malignacy in the head of pancreas althought ERCP was within normal limits. Serologic tests for microbial infections were negative but immunoserologic tests, revealed ANA +1/160 (type fine speckled), AMA (-), SMA (-),centromere antibody (-), cryoglobulins (-), RF=1/320, C3=34 ui/ml, C4<6 ui/ml.

Liver biopsy revealed autoimmune cholangitis and the patient was started on 0,5 mg/kg methylprednisolone. He recovered totally within 2 months and he is still alive in exellent health with normal clinical and laboratory profile. It is known that scleroderma can co-exist with other autoimmune phenomena. We add to this that also a localized scleroderma (morphea) can co-exist with autoimmune cholangitis presenting as pangreatic malignancy.

Althought in this case the clinical, serological and radiological findings, exept ERCP, were in favor of neoplasia, immunoserologic tests and liver biopsy offered the true diagnosis before unnessescary laparotomy was performed.

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INTRODUCTION

Autoimmune cholangitis (AIC) has been described since 1987 and it represents an overlap syndrome between autoimmune hepatitis (AIH) and primary biliary cir-rhosis (PBC). Its major distinguishing feature from PBC is the absence of antimitochondrial antibodies (AMA) and the antibodies against the E2 subunits of the pyruvate deydrogenase complex.[1] Patients with AIC have also been reported to have serum antibodies to carbonic anhydrase II (CA-II) and AIC is suggested to be induced by CA-II immunization in susceptible strains of mice.[2]

It is therefore logically suggested that AIC is a subgroup of PBC, AMA-negative type[3] with respect to the four possible combinations of AMA and antinuclear antibo-dies (ANA) in autoimmune liver diseases.[4] It is also suggested that in both AIC and PBC there is an elevated activity of gamma delta T lymphocytes in blood and livers of patients as well as in other liver autoimmune diseases.[5] They include generally the same messangers for inflammation such as cytokines IL-1, IL-6, IL-8, TNF. The expression takes place in HLA II and a receptor for IgA from blood to bile is detected.[6] A case report also described a patient diagnosed initially with PBC and finally proved another case of AIH.[7]

The biochemical profile of AIC typically has a cholestatic component with elevations of serum alkaline phosphatase (ALP) and gamma - glutamyltranspeptidase (g-GT). Hepatocellular inflamation, however, as reflected in serum aminotransferase elavations, can still predominate.

Seropositivity for ANA and SMA (smoth muscle an-

tibodies) is commonly present in AIC and clinical, biochemical and histologic abnormalities usually improve during corticosteroid therapy with a rapidity more suggestive of AIH and PBC. Also ursodeoxycholic acid (UDCA) and azathioprine are suggested therapeutically.

Histological findings in AIC are similar to those of PBC at an early stage.

We can distinguish AIC from PBC due to the significantly higher incidence of asthenia, higher and earlier incidence of liver failure and higher ANA titers and serum IgG of the first.[8] Also a differential diagnosis of AIC from systemic mastocytosis is said to be included as rare cause of non cirrhotic portal hypertension.[9]

CASE REPORT

A 63 years old man diagnosed with hand morphea (localized scleroderma) for the last 10 years was admitted to our hospital because of 6 weeks history of weight loss (10 Kgr), weakness, low grade fever up to 38ºC and jaundice.

Physical examination revealed hand morphea, jaundice and a thin person with neoplastic appereance.

Laboratory exams revealed: Ht:36.4%, WBC:6700, ESR:78 mm/h, INR:1.3, ALT:478, AST:385, g-GT:129, ALP:707, TBL:3,5, DBL:2,8, AMS:65 UI/ml, (urine amylase had a three fold increase above the normal value), LDH:225 UI/ml, CRP (-) and thyroid function within normal limits. Antibodies for CMV, EBV, toxoplasma, HSV1, HSV2, leptospira interr, HAV IgMAb, HBsAg, antiHBc IgM and IgG, anti HBS, anti HCV, HIV1 Ab, HIV2 Ab all proved negative.Tumor markers CEA, aFP, PSA were within normal limits but Ca 19.9 was 250 UI/ml (normal value up to 37 UI/ml).

Serum electrophoresis revealed hypergammaglobulinaemia with no special characteristics, serum IgG was 1360mg/dl (normal values: 700-1500), direct coombs was anti lgG+2, anti IgA-, anti IgM, anti C3C-, anti C3d- and indirect coombs (-). Immunoserologic tests revealed RF=1/320, C3=34UI/ml, C4<6UI/ml, cryoglobulins (-), ANA+1/160 (type fine speckled), AMA (-), SMA (-), centromere antibody (-).

In the 7th day of admission Ca 19.9, gamma - glutamyl transpeptidase, ALP and DBL had a 3-fold increase.

Abdominal ultrasound showed only eliminated echo in pancreas (Figure 1), C.T revealed small kidney kysts and anomogeneity in the head of pancreas (Figure 2) and MRI suggested enlargement of the head of pancreas and lymph nodes of 1,8 cm near kidneys. In contrast ERCP proved within normal limits. A liver biopsy was decided before performing laparotomy and the histologic findings were compatible with autoimmune cholangitis with no signs for cirrhosis (piecemeal and spotty necrosis). In fact, there was evidence of portal infiltration (more lymphocytic and less polymorphonuclear) but with no damage of the liver architecture and the pericholangial tissue.

The patient was started on 0,5 mg/Kg methylprednisolone and ursodeoxycholic acid (UDCA) and recovered totally within 2 months period. He is still living in excellent health status with normal clinical and laboratory profile, including Ca 19-9 which turned to normal values in the first month of treatment.

DISCUSSION

We reported a case of autoimmune cholangitis (AIC)

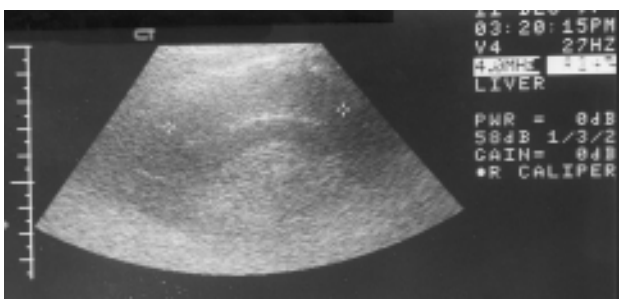

Figure 1. Ultrasonography showing hypo-echogeneity of the pancreas compatible with inflammation or oedema.

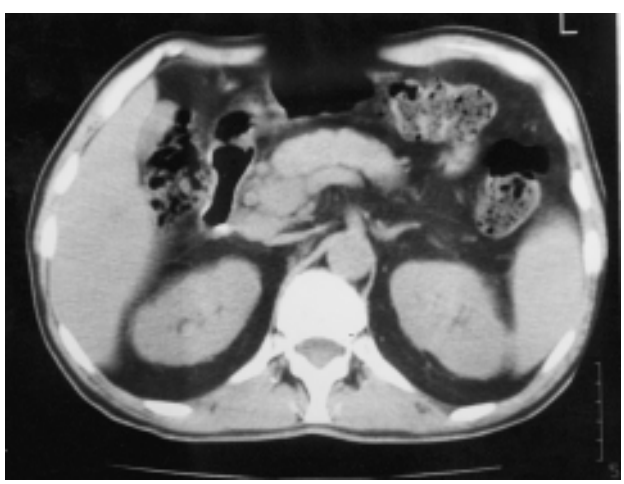

Figure 2. CT scan revealing enlargement and anomogeneity of the head of the pancreas.

as another autoimmune manifestation following localized scleroderma (hand morphea or sclerodactyly) and presenting as pancreatic malignancy. It is well known that in PBC, minor forms of scleroderma are observed in about 10% of cases. However, anticentromere antibodies are found in 10-20% of cases. Liver damage in patients with scleroderma is rare as well as in Sjogren's Syndrome.[11]

It is essential that liver biopsy must be performed in every patient with autoimmune phenomena involving liver disfunction or suspicion of pancreatic malignancy from the laboratory and the radiologic exams before deciding laparotomy. Moreover the differential diagnosis between AIC and PSC of the small bile ducts should always be in consideration and it is usually a very difficult clinical problem to solve. There is also under consideration the theory that AIC is a PBC subgroup or cases diagnosed as AIC are often hepatic types of PBC.

We must notice that Ca 19.9 can be elevated in AIC. It is well known that the elevation of Ca 19.9 over 200 ui/ml is 95% sensitive for pancreatic or bile duct malignancy.[12] Also statistically significant positive correlations were observed between Ca 19.9 and AST, ALT, ALP, TBL, and negative correlations with albumin and g-GT. The increased production of Ca 19.9 from the biliary epithelial cells and the decreased clearance due to cholestasis may be contibuting to the elevation of Ca 19.9 in the bloodstream.[13]

The proposed treatment of AIC is ursodeoxycholic acid (UCDA) and prednisolone even though is some cases beneficial results have not been impressive (inflammation reduced but γ-GT and bile duct lesions persist).[1,14-16] It is also refered that treatment with UDCA or orthotopic liver transplatation (OLT) resulted in similar outcomes in AMA negative and AMA positive patients (AIC and PBC).[17]

Finally in this rare case of autoimmune cholongitis coexisting with hand morphea we are not permitted to exclude the diagnosis of co-existing autoimmune pancreatitis strongly supported by the radiologic and serologic exams although we never performed pancreatic biopsy for evident reasons. This diagnosis could possibly be an acceptable explanation for this 3-fold increase of urine amylase, the 8-fold increase of Ca 19-9 and of the radiologic imaging consisting in enlargement, anomogeneity and oedema of the pancreas. By radiologic methods, there were more implications for a neoplastic procedure of the head of the pancreas than for pancreatitis. It is difficult to locate this suggested autoimmune pancreatitis only in the head rather the whole pancreas. A possible explanation could be the anatomical relation of the biliary system with the head of the pancreas as well as the fact of sharing common routs in the heliac net of lymph nodes and the regional blood stream.

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