

Infectious cases of acute pancreatitis

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INTRODUCTION

Acute pancreatitis is a common disease with high morbidity and mortality. Its incidence has been increased over the past decades and it is estimated in 38 per 100.000 population per year.¹ In the U.S.A. and Western Europe, most of the cases of acute pancreatitis are associated aetiologically with alcohol consumption and gallstones, while in 10% of patients miscellaneous causes such as infections by parasites, bacteria and viruses, are responsible (Table 1).² In order to evaluate the relation between each microorganism and acute pancreatitis, strict diagnostic criteria have been defined. Histological and/or imaging evidence of pancreatitis are combined with laboratory data resulting from an infectious agent, while "common" causes of acute pancreatitis are excluded (Table 2).³

PARASITES

Ascaris lumbricoides is a common cause of gastrointestinal infection in developing countries. According to various studies its prevalence in certain tropical countries is 60% in children and 30% in adults and it is a significant cause of biliary tract and pancreatic disease.⁴ In a prospective trial from India, ascariasis was the major cause of pancreatitis in 59 of 256 patients (23%) compared to 112 patients (44%) with gallstone pancreatitis.⁵ In a recent study from Syria, in 300 cases with biliary and pancreatic ascariasis, 13 of them (4,3%) developed acute pancreatitis.⁶ The most possible mechanism of acute pancreatitis is considered the obstruction of pancreatic duct, resulting from the migration of the adult *Ascaris* worms

from duodenum and jejunum via the papilla of Vater.⁷ Calcification of parasites or gallstones formed around a matrix of worms have also been accounted for recurrent episodes of pancreatitis,⁸ as well as endoscopic sphincterotomy prior to *Ascaris* infection.⁶

Ninety eight percent of patients present with abdominal pain accompanied by vomiting (25%), while laboratory investigation reveals raised serum and urinary pancreatic enzymes.^{5,6} Imaging methods such as abdominal ultrasound and computed tomography, have high diagnostic accuracy (80%). However the diagnostic method of choice is ERCP which shows not only the exact site, but the number of parasites as well. Moreover ERCP and endoscopic sphincterotomy is the treatment of choice for the extraction of parasites.⁹ Everyone agrees that endoscopic sphincterotomy has excellent results when it is performed soon after the onset of symptoms, but adjuvant antielmintic treatment is still indicated.

Other parasites such as *Clonorchis senensis* have been described as rare causes of acute pancreatitis, due to common bile duct or pancreatic duct occlusion.¹⁰ *Echinococcus granulosus* is rarely complicated by pancreatitis either due to biliary obstruction or pancreatic duct compression by an hydatid cyst, or rupture of an hydatid cyst into the biliary tree.^{11,12} Finally very few cases of pancreatitis have been complicated by *Fasciola Hepatica*,¹³ *Opistorhchis* sp and *Dicrocoelium dendriticum*.¹⁰

BACTERIA

Pancreatitis caused by bacterial pathogens has been described in several clinical settings. Haematogenous or lymphatic seeding and ascending infection of the pancreatic duct from the small intestine or biliary tree, are the major pathogenic mechanisms that have been described.³

In retrospective and prospective studies, in the mid

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seventies, *Mycoplasma pneumoniae* has been implicated as a cause of pancreatitis due to antibody detection. Leinikki et al¹⁴ detected high antibody titer to *Mycoplasma* in 18 of 56 (32%) patients with acute pancreatitis and McMahon¹⁵ in 33% of 27 cases. However diagnosis is based solely on serologic tests because evidence of pancreatic infection by *Mycoplasma* does not exist. Moreover many patients included in the above studies had a problem with alcoholism or suffered from biliary tract disease. Few other studies failed to confirm the above results,¹⁶ so many questions remained regarding the exact relationship among acute pancreatitis and *Mycoplasma* infection.

Pancreatitis has also been associated with leptospirosis which presents with hyperamylasemia (serum amylase >300 IU/L) in more than 60% of patients.¹⁷ Pancreatitis as a secondary complication of the disease is very rare and only a few cases have been described in the literature. Increased levels of serum amylase and other pancreatic enzymes are of unknown aetiology, although it is speculated that renal failure or even Reticuloendothelial system dysfunction might be the cause.¹⁸ Diagnosis of acute pancreatitis due to *Leptospira* requires apart from consistent clinical picture, elevated serum amylase fourfold normal (due to possible renal failure) and thorough investigation of the pancreas with imaging methods such as ultrasound or computed tomography. Detection of isoamylase enzymes contributes also to diagnosis. A prospective study showed that in 88 patients with leptospirosis, only 3 cases with acute pancreatitis correlated with the infection.¹⁷

Tuberculosis of the pancreas is very rare even in countries where the disease is endemic.¹⁹ Diagnosis can be made by histological examination after laparoscopy or biopsy with a fine needle. Tissue culture for *Mycobacterium* or PCR are considered to be reliable methods for detecting the causative agent.²⁰

Pathogenic bacteria of the gastrointestinal tract such as *Salmonella typhi*,²¹ *Campylobacter jejuni*,²² *Yersinia enterocolitica* and *Y. pseudotuberculosis*,²³ *Brucella*, *Legionella* and *Nocardia*³ have been described in the literature as the causes of sporadic cases of pancreatitis.

VIRUSES

The largest group of infectious agents associated with acute pancreatitis is viruses. In 1817 mumps virus was implicated for the first time as a cause of acute pancreatitis. Since then the literature contains many reports associating viral infections and pancreatitis. The clinical

picture of these patients is characterized by abdominal pain, diarrhea and the outcome of the disease is self limited.³ Diagnosis is based mainly on detecting anti-viral antibodies, the clinical picture, imaging of the pancreas and finally on the exclusion of other causes of pancreatitis.

Mumps virus is a single-stranded DNA paramyxovirus that causes infection of the salivary glands, especially parotitis which is complicated by orchitis, meningoencephalitis, arthritis and pancreatitis.

It is rather difficult to determine the incidence of mumps virus in acute pancreatitis. Symptoms consistent with acute pancreatitis have been described in 5 (15%) of 33 children, during an outbreak in an English school, in 14 patients (0,31%) of 5000 in the U.S.A. and in 12 cases (5,1%) of 250 hospitalized patients for mumps infection, also in the U.S.A.^{3,24-26}

The vast majority of reports does not contain adequate data either for the diagnosis of pancreatitis or for mumps infection. In a prospective study including 116 patients with a definite diagnosis of acute pancreatitis, 3 of them suffered from mumps infection as determined by antibody detection.²⁷ A few other sporadic cases in the literature show the possible association between acute pancreatitis and mumps-virus.³ It is very interesting to emphasize that following vaccination of the general population for measles, mumps, rubella (MMR vaccine), only one case of mumps virus associated acute pancreatitis has been described in the literature.²⁸

Coxsackievirus type B is a single-stranded RNA picornavirus with six serotypes (B1-B6) identified and it is implicated in cases of acute pancreatitis. Retrospective and prospective studies showed that patients with acute pancreatitis were affected by Coxsackievirus, based on serologic tests.^{16,30} Moreover cases have been published in which virus was isolated³¹ or identified from the pancreas by immunohistochemical methods.³² Findings from experimental models support the potential role of coxsackievirus in the etiology of acute pancreatitis. In 50% of infected by coxsackievirus, mice, pancreatic inflammation and necrosis was diagnosed. In some studies both pancreatic acinar cells and islet cells have been involved.³³ Recently it was showed that different serotypes of Coxsackievirus B4, such as CB4-P and CB4-V, may cause acute and chronic pancreatitis respectively, possibly due to different immunological mechanisms.²⁹

From the whole spectrum of hepatitis viruses, HBV is the infectious agent most implicated in acute pancreatitis. Studies of liver transplantation patients with HBV

infection recurrence, provide the best evidence of pancreatic infection by HBV.³⁴ In a series of 27 chronic HbsAg carriers, who underwent liver transplantation, 6 developed HBV recurrence early in the post-operative period and 4 suffered from acute pancreatitis. Detection of HbsAg in the acinar pancreatic cells and in the pancreatic juice, support the potential relation among HBV and pancreatitis.³⁵

Several other viruses, like CMV, Herpes simplex virus (HSV), Varicella-zoster virus are also associated with pancreatic infection.³

AIDS

In patients with AIDS the incidence of acute pancreatitis is estimated in 4-22%. Proposed aetiologies of acute pancreatitis in these patients include drugs, opportunistic infections and neoplasms associated with AIDS such as Kaposi sarcoma and lymphoma.³⁷ It is interesting that HIV patients have elevated serum pancreatic enzymes, which particularly are in linear relation with CD4 but without still any relevant clinical picture of pancreatitis.³⁸ It has not been clarified yet the exact cause and pathophysiological mechanism involved in the high incidence of acute pancreatitis in AIDS patients. Demonstration of HIV in the pancreas by in situ hybridization or PCR has not been reported yet.³

Opportunistic infections involving the pancreas in HIV patients include CMV, HSV, *Cryptococcus neoformans*, *Candida*, *Pneumocystis carini*, *Toxoplasma gondii*, *Leishmania donovani*, *Cryptosporidium*, *Mycobacterium tuberculosis* and *Mycobacterium avium*.³

CONCLUSIONS

Several infectious agents have been associated with acute pancreatitis. In many reports the diagnosis of pancreatitis is based on clinical or biochemical criteria and the diagnosis of infection only on clinical or serologic ones. Several times other common causes of pancreatitis are not excluded. How often infectious agents are involved in idiopathic pancreatitis remains unknown. Modern techniques of molecular biology (in situ hybridization, PCR) and advanced imaging of the pancreas may improve diagnostic accuracy in the future.

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