CASE REPORT

Fatal Acute Pancreatitis with Cystic Formation in Reactive Systemic AA Amyloidosis Secondary to Rheumatoid Arthritis

Masayuki MATSUDA, Shunpei SAKURAI**, Akio SUZUKI***, Masumi KADOYA* and Shu-ichi IKEDA

Abstract

We report a patient with reactive systemic AA amyloidosis secondary to rheumatoid arthritis who showed fatal acute pancreatitis with a cystic formation in the pancreas head. The pancreatitis rapidly worsened despite intensive treatment and resulted in death. In this patient severe deposition of amyloid in the gastrointestinal tract was considered to play an important role in the pathogenesis of the acute pancreatitis. This is an unusual complication in patients with AA amyloidosis, but we should consider it as a possible diagnosis when patients with AA amyloidosis show recurrent or intractable pain in the upper abdomen.

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Key words: pseudocyst, serum amyloid A, gastrointestinal tract, magnetic resonance cholangiopancreatography, renal fascia, pleural effusion

Introduction

Reactive systemic AA amyloidosis occasionally develops in patients with a long history of inflammatory disorders such as rheumatoid arthritis (RA). In this type of amyloidosis, the gastrointestinal (GI) tract is commonly involved from the early phase of illness, and shows various symptoms, including diarrhea, intestinal pseudo-obstruction and the malabsorption syndrome (1, 2). Hepatobiliary and/or pancreatic symptoms are, however, relatively rare even in the advanced stage (2). Here, we report a patient with RA-related reactive systemic AA amyloidosis who suffered fatal acute pancreatitis, focusing on its pathogenetic mechanism.

Case Report

A 72-year-old man with a 13-year history of RA was admitted to our hospital with a diagnosis of intestinal pseudo-obstruction ascribed to systemic reactive AA amyloidosis in March 2002. In gastroduodenal specimens taken at biopsy, extensive deposition of AA amyloid was observed mainly around the submucosal excretory glands and partly on vascular walls (Fig. 1). Because he showed no signs of peritoneal irritation, including rebound tenderness and abdominal wall resistance, he was conservatively treated with total parenteral nutrition and intravenous administration of prednisolone at a dose of 30 mg/day to improve his general status with a decreased production of serum amyloid A (SAA). On radiological examination the intestinal pseudo-obstruction gradually improved, and he started to take enteral nutrition in addition to intravenous hyperalimentation from April despite the persistence of decreased motility of the bowel. In May he was transferred to a neighboring hospital with intravenous prednisolone at a dose of 15 mg/day.

The volume and concentration of enteral nutrition were carefully increased, but intravenous hyperalimentation could not be stopped because the patient sometimes complained of a feeling of abdominal fullness and nausea. The serum level of SAA was kept at less than 50 μg/ml (normal value less than 8 μg/ml) with intravenous prednisolone at a dose of 10 to 15 mg/day. From the beginning of August he frequently experienced upper abdominal pain and vomiting. Upper GI endoscopy showed no abnormal lesions throughout the stomach and duodenum, and the ampulla of Vater appeared normal. To relieve his abdominal symptoms enteral nutrition was completely stopped, as he was suspected of having an exacerbation of intestinal pseudo-obstruction based on computed tomography (CT) demonstrating remarkable amounts of gas mainly in the small intestine (Fig. 2). His symptoms improved for a while, but again worsened from the begin-
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Figure 1. Immunohistochemistry of the biopsied duodenal specimen, showing extensive deposition of AA amyloid (arrowheads) mainly around the submucosal excretory glands (A) and some deposition on vascular walls (B). Bar=100 µm.

Beginning of September. Laboratory data demonstrated hyperamylasemia (790 IU/l, normal 44–127 IU/l) in addition to slight anemia (hemoglobin 11.7 g/dl, normal 13.4–17.7 g/dl), hypoproteinemia (total protein 4.7 g/dl, normal 6.8–8.3 g/dl; albumin 1.7 g/dl, normal 4.2–5.1 g/dl), elevated hepatobiliary enzymes (alkaline phosphatase 2,388 U/l, normal 124–367 U/l; aspartate aminotransferase 85 U/l, normal 12–37 U/l; alanine aminotransferase 72 U/l, normal 7–45 U/l; lactate dehydrogenase 605 U/l, normal 114–222 U/l), and highly positive inflammatory reactions (CRP 15.0 mg/dl, normal value less than 0.1 mg/dl). He showed no autoantibodies, including anti-SS-A and SS-B. Abdominal CT and magnetic resonance imaging (MRI) demonstrated a slightly diffuse swelling of the pancreas with a cystic formation and no apparent mass lesions in its head (Figs. 2 and 3), left thickened renal fascia (Fig. 2), and bilateral pleural effusion predominant on the left side. In magnetic resonance cholangiopancreatography (MRCP) the cystic lesion was adjacent to the non-dilated main pancreatic duct (Fig. 4).

Despite intravenous administration of gabexate mesilate and ulinastatin his symptoms and laboratory data did not improve. From the end of September disseminated intravascular coagulation developed and rapidly induced multiple organ dysfunction, including acute renal failure. At the beginning of October he died of metabolic acidosis. Autopsy was not permitted.

Discussion

At the onset of recurrent upper abdominal pain and vomiting this patient was suspected of having an exacerbation of intestinal pseudo-obstruction due to severe amyloid deposition in the GI tract based on X-ray findings, but these symptoms gradually worsened with no signs of peritoneal irritation despite the cessation of enteral nutrition. Laboratory data showed hyperamylasemia with an increase in acute phase reactants, and abdominal CT and MRI demonstrated a cystic formation in the pancreas head with left thickened renal fascia, leading to the diagnosis of acute pancreatitis. Based on MRCP showing a non-dilated main pancreatic duct with no irregularity on the wall, the cystic formation was considered to be a pseudocyst formed by autodigestion, probably due to activation of proteolytic enzymes in the pancreas; endoscopic retrograde cholangiopancreatography could not be performed in order to exclude malignancy because of his poor general condition.

The pancreas is a visceral organ rarely involved in any type of amyloidosis (3). Malabsorption syndrome with steat-
Figure 2. Although abdominal CT demonstrated no abnormal findings other than remarkable amounts of gas mainly in the small intestine at the onset of recurrent abdominal pain and nausea (A, B), a cystic formation in the pancreatic head (C, arrow) and left thickened renal fascia (D, arrowheads) were seen around one month later.

Orrhea can develop as a result of acinar atrophy due to amyloid deposition, but associated acute pancreatitis is quite rare (3). In general, the most common causes of acute pancreatitis are excessive intake of alcohol and cholelithiasis (4). Considering that acute pancreatitis developed under parenteral nutrition with no findings suggestive of gallstones on abdominal CT and ultrasonography, these common causes are not considered relevant to the pathogenesis in this patient. He also had no history of either drugs or toxic agents causative of pancreatitis. In addition, MRCP demonstrated no dilatation of the main pancreatic duct, indicating that there was no obstruction causing an acute inflammation around the pancreatic head. The precise pathogenetic mechanism of the pancreatitis was unclear in this patient, but there are two possibilities: one is autoimmune inflammation and the other is an amyloidosis-related mechanism. Autoimmune pancreatitis is characterized by diffuse swelling of the pancreas with irregular stenosis of the main pancreatic duct, showing hyper-γ-globulinemia and auto-antibodies in laboratory data and a favorable response to corticosteroid therapy (5-8). This type of pancreatitis is sometimes associated with autoimmune disorders, particularly Sjögren’s syndrome (9-11). In this patient, however, the autoimmune mechanism is unlikely because acute pancreatitis developed during treatment with intravenous prednisolone and there were no characteristic features on radiological examinations, including abdominal CT and MRI. Despite an RA history of around 13 years, he had never shown either symptoms or autoantibodies suggesting any association with Sjögren’s syndrome.

The other possibility is an amyloidosis-related mechanism. There are several defense mechanisms against pancreatitis in the pancreatic duct, including the duodenal major papilla (12, 13). According to a recent case report, amyloidoma around the duodenal papilla disturbed pancreatic excretion and induced recurring acute pancreatitis in systemic AL amyloidosis (14). Although no amyloidoma-like lesions could be found on upper GI endoscopy in this patient, AA amyloid was probably present in the mucosal tissue around the papilla given the severity of deposition in biopsied gastroduodenal specimens. As a result of amyloid deposition...
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deposition, dysfunction of the duodenal papilla might have developed with bacterial infection and/or excretory disturbance in the pancreatic duct, leading to acute and intractable inflammation in this patient. With regard to excretory disturbance, the pseudocyst in the pancreatic head also might have played a role in the persistence and worsening of the acute pancreatitis. As another possible amyloidosis-related mechanism, a circulatory disturbance was speculated to cause acute pancreatitis in a recent case report (15), and also in this patient amyloid deposition was demonstrated partly on vascular walls in the biopsied gastroduodenal tissues. Considering that the pancreatitis gradually worsened during a relatively long clinical course of around two months, despite intensive therapy, circulatory disturbance due to involvement of microvasculatures was not acceptable as the main cause but was considered relevant at least to the resistance to therapy in this patient.

Acute pancreatitis is a rare complication of systemic amyloidosis, and there are only a few clinical reports (14, 15). This complication might, however, frequently be fatal even in cases that are relatively mild at the onset, as in this patient, because systemic amyloidosis usually involves overt or subclinical dysfunction in multiple vital organs. When patients with AA amyloidosis show intractable or recurrent pain in the upper abdomen, acute pancreatitis should always be considered as a possible diagnosis in order to start intensive treatment as early as possible.

References