A Case of Hemosuccus Pancreaticus Associated with Hereditary Pancreatitis

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MIZUTAMARI, H., MASAMUNE, A., ASAKURA, T., NAGASAKI, Y., SATOH, A., SAKAI, Y., YAMAGIWA, T. and SHIMOSEGAWA, T. A Case of Hemosuccus Pancreaticus Associated with Hereditary Pancreatitis. Tohoku J. Exp. Med., 2001, 195(3), 191–195 —— We report a 25-year-old male with hemosuccus pancreaticus associated with hereditary pancreatitis. He was originally diagnosed as having familial chronic pancreatitis at the age of 12, because his brother was also diagnosed as having pancreatitis. No history of pancreatitis was found in their parents. The patient was admitted because of a growing pancreatic pseudocyst. While he had undergone conservative treatment for the pseudocyst, computed tomography incidentally revealed a pancreatic pseudoaneurysm. Endoscopic examination revealed spontaneous bleeding from the major papilla. Interventional embolization was successfully performed. An R122H mutation in the cationic trypsinogen gene was identified in this patient, his brother, and his mother, indicating that they have hereditary pancreatitis. To our knowledge, this is the first report of hemosuccus pancreaticus associated with hereditary pancreatitis. Mutational screening is useful for the diagnosis of hereditary pancreatitis, especially in patients whose diagnosis is inconclusive based on the traditional clinical criteria. Hereditary pancreatitis; cationic trypsinogen gene; hemosuccus pancreaticus; interventional embolization

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Hereditary pancreatitis is clinically characterized by recurrent attacks of pancreatitis typically beginning in childhood or adolescence, a family history of at least two other affected members, and the absence of other known precipitating factors (Gross et al. 1962). It frequently progresses to chronic pancreatitis (CP) with calcification in the pancreas.
Recently, mutations in the cationic trypsinogen gene have been reported to be associated with this disease (Whitcomb et al. 1996; Gorry 1997; Ferc et al. 1999; Witt et al. 1999). Hemosuccus pancreaticus is an uncommon but life-threatening complication of CP. Most cases are caused by the erosion of peripancreatic arteries into a pseudocyst or a pseudoaneurysm that has ruptured into the pancreatic duct (Camishion et al. 1992; Dinu et al. 1998). Here we report a case of hemosuccus pancreaticus in hereditary pancreatitis associated with a mutation in the cationic trypsinogen gene.

**CASE REPORT**

A 12-year-old male was originally admitted to our hospital complaining of recurrent abdominal pain in 1987. A diagnosis of familial CP was made because his brother had been diagnosed as CP, although his parents had not developed pancreatitis (Fig. 1). He developed a pancreatic pseudocyst and underwent surgical drainage of the pseudocyst. Afterwards, he had suffered from recurrent attacks of abdominal pain. In 1999, the pancreatic pseudocyst appeared again and gradually increased in size. He was admitted to our hospital for the treatment of the pseudocyst in September 2000, at the age of 25. On admission, laboratory data including serum amylase, lipase, hemoglobin concentration, and fasting blood glucose levels were all normal. Computed tomography (CT) of the abdomen showed diffuse calcification in the pancreas, a pseudocyst approximately 5 cm in diameter in the pancreas body, and the development of collateral circulation around the pancreas due to occlusion of the splenic vein. While he was treated conservatively by fasting and pancreatic enzyme inhibitors, the abdominal pain occasionally recurred in spite of the unchanged size of the pseudocyst. In November 2000, CT incidentally revealed an aneurysm in the wall of the pseudocyst and a high-density lesion suggesting blood clots within the pseudocyst (Fig. 2). Endoscopic examination revealed spontaneous bleeding from the major papilla. Until then he had no signs of melena, hematemesis, or aggravation of anemia, and had been hemodynamically stable. Emergency arteriography did not reveal the aneurysm, but demonstrated micro-vessels around the pseudocyst (Fig. 3). He underwent interventional embolization of the splenic and dorsal pancreatic arteries, the feeders of the micro-vessels. A few days after the embolization, CT showed no sign of the pseudoaneurysm nor blood clots in the pseudocyst. Endoscopic retrograde cholangio-pancreatography revealed communication between the main pancreatic duct and the pseudocyst. The post treatment course was uneventful and he was discharged in February 2001. Recent reports of cationic trypsinogen gene mutations in hereditary pancreatitis prompted us to investigate the presence of the mutations in this family. We performed direct sequencing of all five exons of the
Fig. 2. CT of the abdomen incidentally revealed a contrast-enhancing lesion, suggesting a pseudoaneurysm, in the wall of the pseudocyst (arrow), and a high-density area suggesting blood clots (arrowhead) within the pseudocyst. After embolization, signs of the pseudoaneurysm and blood clots disappeared.

Fig. 3. Arteriography did not show the aneurysm, but revealed micro-vessels branching from the splenic and dorsal pancreatic arteries (arrows).

cationic trypsinogen gene as described previously (Nishimori et al. 1999) in the family members who had given informed consent. This study was approved by the Ethical Committee of Tohoku University School of Medicine. The result was that a mutation, 122Arg (CGC) to His (CAC), in exon 3 was found in two affected members (the patient and his brother) and in
the unaffected mother.

**DISCUSSION**

Hereditary pancreatitis is an autosomal dominant disorder with an estimated penetrance of 80% (Gross 1986). Since the first description in 1952 (Comfort and Steinberg 1952), more than one hundred families with this disease have been reported worldwide. In 1996, the R122H mutation in cationic trypsinogen gene was reported as a cause of hereditary pancreatitis (Whitcomb et al. 1996). This mutation is a single guanine (G) to adenine (A) transition resulting in an arginine (CGC) to histidine (CAC) substitution at amino acid residue 122 of the cationic trypsinogen. It has been hypothesized that this mutation alters a trypsin recognition site associated with the inactivation of trypsin within the pancreas, prolongs the activity of the mutated trypsin, and leads to pancreatitis (Whitcomb et al. 1996). In Japan, this mutation has been identified in at least six families including this case. Recent investigations have revealed other mutations in this gene (Gorry et al. 1997; Ferec et al. 1999; Witt et al. 1999), but the other mutations including N29I are less common than R122H. Mutations in this gene have been identified in less than 1% of Japanese patients with CP and so are rare causes of CP. Hereditary pancreatitis was traditionally defined as pancreatitis with at least three affected family members (Gross et al. 1962). However, it should be noted that there are cases such as the present one in which these criteria are not fulfilled but cationic trypsinogen gene mutations are identified.

Hemosuccus pancreaticus, frequently associated with pancreatic pseudoaneurysm, is a rare cause of gastrointestinal bleeding and a comparatively uncommon complication of CP (Risti et al. 1995). To our knowledge, this is the first report of hemosuccus pancreaticus in a patient with hereditary pancreatitis. Reportedly, CP causes an aneurysm of adjacent arteries in 10% of cases (White et al. 1976). The symptoms usually consist of episodes of gastrointestinal bleeding such as melena, hematemesis, and anemia, but it may be asymptomatic as in the present case. In patients with hemosuccus pancreaticus, immediate arteriography usually reveals the source of bleeding such as an aneurysm, enabling therapeutic interventional procedures (Baker et al. 1987; Mandel et al. 1987). However, arteriography did not show the aneurysm in the present one. One explanation may be that the pseudoaneurysm did not arise in major arteries (such as the splenic or gastroduodenal arteries) but in micro-arteries around the pseudocyst. Since the exocrine and endocrine functions of the pancreas are gradually abolished in hereditary pancreatitis, nonsurgical therapies such as interventional embolization should be the first choice for this rare complication.

**References**


