Pancreatitisis-associated unique duodenal fistula: an autopsy case

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Abstract
Duodenal fistula may be caused by severe pancreatitis, although viral pancreatitis is usually mild. We present a unique duodenal fistula that occurred upon repeated (fatal) myocardial infarctions during viral pancreatitis. Autopsy revealed a duodenal fistula with a unique appearance: it had two orifices, the proximal of which involved the minor papilla, and two intrapancreatic extensions (one along the course of the Santorinii duct and one along a so-called fusion line of pancreatic anlages). Three conditions superimposed upon cytomegalic viral pancreatitis (1) Santorinii duct obstruction, 2) athero-embolism, and 3) a a so-called fusion line] may have contributed to this unique fistula formation.

Introduction
Gastrointestinal fistula is a well-known complication of acute necrotizing pancreatitis, and common sites for such pancreatis- associated fistulas are the colon, jejunum, and duodenum. Duodenal fistula has been observed in 0-24% of severe pancreatitis, with most being located in its descending portion [1,2]. Cytomegalovirus (CMV) frequently produces only mild pancreatitis, which is not usually clinically apparent [3]. Fat necrosis or duct necrosis seems not to accompany this type of pancreatitis [4]. We present here an autopsy case manifesting a unique duodenal necrotic fistula that occurred during CMV pancreatitis and discuss the mechanisms that may have led to its formation.

Report of a case
A 76-year-old, diabetic, Japanese man was admitted to the National Defense Medical College Hospital (Tokorozawa, Japan) because of a recent myocardial infarction and renal failure. He had past histories of diabetic retinopathy, cholelithiasis, and brain and myocardial infarctions. On admission this time, he was given supportive care for cardiovascular collapse. He was also given continuous hemodialysis for intractable oliguria. His vital signs became stable during his hospitalization, but his condition deteriorated again on April 23, 2018; and a computed tomogram (Figure 1A) each showed enlargement of the pancreas head. These findings were consistent with acute pancreatitis. A pancreatic pseudocyst may communicate with the duodenal lumen in severe necrotizing pancreatitis [5]. It is well-known that CMV pancreatitis is usually not accompanied by tissue necrosis. In the present case, however, three unfavorable conditions seemed to be superimposed upon it: 1) necrosis of the Santorinii duct (and its orifice; i.e., the minor duodenal papilla) due to obstructive changes, 2) local hypoperfusion due to obstruction, and 3) a so-called fusion line of pancreatic anlages. The fistula was situated away from the Wirsung pancreatic duct, choledochus, and a concomitant juxta-papillary duodenal diverticulum. The background pancreatic parenchyma displayed edema, lymphocytic infiltration, and viral inclusion bodies, findings consistent with CMV pancreatitis (Figure 1E, F). In addition, organizing cholesterol emboli were revealed within small branching blood vessels (Figure 1G). The duodenal wall exhibited submucosal fibrosis and hemosiderin deposition in a widely distributed fashion, findings considered to reflect a chronic ischemic condition.

Comment
The pathogenesis of pancreatitis-associated gastrointestinal fistulas is considered to be multifactorial, and to include activation of intrinsic pancreatic enzymes and local ischemia [1]. A pancreatic pseudocyst may communicate with the duodenal lumen in severe necrotizing pancreatitis [5]. It is well-known that CMV pancreatitis is usually not accompanied by tissue necrosis. In the present case, however, three unfavorable conditions seemed to be superimposed upon it: 1) necrosis of the Santorinii duct (and its orifice; i.e., the minor duodenal papilla) due to obstructive changes, 2) local hypoperfusion due to...
Concerning the first unfavorable condition, obstruction of the pancreatic duct is considered one of the main mechanisms associated with acute pancreatitis [6]. In the present case, the Santorinii duct itself caused necroinflammation (forming both the proximal orifice and the proximal extension of the fistula), and this inflammation may have propagated directly to the duodenal wall (forming the wide cavity seen in the duodenal wall). Local ischemia caused by athero-embolism, the second unfavorable condition, may have caused secondary structural fragility and exacerbated the degree of inflammation [7]. This factor may have contributed to the formation of the cavity in the duodenal wall and the distal orifice. The last unfavorable condition is a native structural fragility in the pancreas. A so-called fusion-line of pancreatic anlages tends to be subject to involvement in inflammation [8]. In our case, the distal intrapancreatic extension probably have resulted from inflammation propagated along this anatomically fragile site. In this situation, the role of the viral pancreatitis itself in the formation of the unique fistula is not clear, although it may have exacerbated the necroinflammation, such as that secondary to the local ischemia resulting from athero-embolism.

In conclusion, we present a unique duodenal fistula that accompanied CMV pancreatitis. We considered necrosis of the Santorinii pancreatic duct to be the best candidate for the main mechanism, and the inflammation to have been exacerbated by two conditions that lead to structural fragility: hypoperfusion due to athero-embolism and the presence of a so-called fusion line of pancreatic anlages. Viral pancreatitis may have contributed by its exacerbating those conditions.
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