Session 4. Pancreatic Cancer-Mimicking Autoimmune Pancreatitis

Clinical approach according to the differential diagnosis and the therapeutic results of AIP

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Curriculum Vitae

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Autoimmune pancreatitis (AIP) is recognized as a distinct clinical entity, and it is also identified as a chronic inflam¬matory process of the pancreas in which the autoimmune mechanism is involved. The diagnosis of AIP is clinically challenging because it is a rare disease, which closely mimics more common pancreaticobiliary malignancies in its presentation such as obstructive jaundice and pancreatic mass. The price of misdiagnosis is high because AIP diagnosed as pancreatic cancer can lead to unnecessary surgery for the benign disease, and cancer diagnosed as AIP can delay potentially curative surgery. There is no single ideal diagnostic test for AIP; hence one has to use a set of diagnostic criteria to distinguish it from other diseases. International consensus diagnostic criteria (ICDC) and algorithm for AIP have been proposed by a consensus of expert opinion in 2011.

Two validation studies comparing the diagnostic sensitivity and specificity of the 5 major criteria using a cohort of patients with AIP and control groups with pancreatic cancer showed that the ICDC guidelines have the greatest sensitivity (90.9-95.1%) compared with Korean (90.2%), Japanese-2011 (86.9%), Asian (83.6%), and HISORt (83.6%), as well as the greatest specificity (up to 97%). However, the ICDC are very complex to remember and definition of level 1 and 2 are not evidence based in some criteria. A recent prospective study compared 32 patients with AIP with a control population of patients with pancreatic adenocarcinoma based on CT imaging features. Independently, 3 radiologists read the images and reported common features seen in each disease. The most common findings seen on CT in patients with AIP were common bile duct (CBD) stricture (63%), bile duct wall hyperenhancement (47%), and diffuse parenchymal enlargement (41%). In contrast, in the control population the most common CT imaging features were focal mass (78%) and pancreatic ductal dilatation (69%). In 10 patients with pathologically confirmed AIP, the misdiagnosis of pancreatic adenocarcinoma was made based on radiology primarily because of the presence of a focal mass, which was seen in 9 patients (90%). The primary differential diagnoses to consider in patients with suspected AIP include pancreatic cancer, idiopathic pancreatitis, primary sclerosing cholangitis, and cholangiocarcinoma. Therefore, considering the risks of an incorrect diagnosis, the initial objective for the clinician is to rule out malignancy. Apart from histology, no solitary feature is pathognomonic for AIP. A diagnosis of AIP requires a high index of clinical suspicion and is established by combining diagnostic evidence from radiographic imaging of the pancreatic parenchyma and pancreatic duct, serum IgG4 levels, other organ involvement, histology, and response to corticosteroid therapy. If the clinical and radiologic findings are not typical for pancreatic cancer, tissue acquisition is recommended by endoscopic ultrasound (EUS). EUS guided fine needle aspiration (FNA) is always technically possible and can exclude pancreatic cancer. If pancreatic cancer can be ruled out in atypical cases, a short term steroid trial is a useful method for the diagnosis of AIP.

Steroids are a standard therapy for AIP and the indications for steroid therapy in AIP include symp-

toms such as obstructive jaundice and the presence of symptomatic extra-pancreatic lesions. The initial recommended dose of oral prednisolone for induction of remission is 0.6 mg/kg/day, administered for 4 weeks. Rapid response to steroids is reassuring and confirms the diagnosis of AIP. The dose is gradually tapered to a maintenance dose of 5 mg/day over a period of 3-4 months (5mg in 2 weeks). Multi-center study showed that the relapse rate of AIP was 19% in Korea and recent single Korean center study reported 32.4% relapse rate among 37 patients with histologically proven type 1 AIP. For relapsed AIP, readministration or dose-up of steroid are effective. Immunomodulatory drugs such as azathioprine were used in addition to readministered steroid for relapsed patients, and remission was again achieved and maintained on long-term azathioprine. Although the long-term prognosis is unknown, most AIP patients treated with steroid therapy have good short-term clinical, morphological and functional outcomes. Pancreatic endocrine and exocrine functions improve in half of cases after steroid therapy. Since AIP might transform into ordinary chronic pancreatitis after several relapses, relapses of AIP should be avoided as much as possible.

References

1. Shimosegawa T, Chari ST, Frulloni L, et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology. Pancreas 2011;40:352-8.
2. Maruyama M, Watanabe T, Kanai K, et al. International consensus diagnostic criteria for autoimmune pancreatitis and its Japanese amendment have improved diagnostic ability over existing criteria. Gastroenterol Res Pract 2013;2013:456965.
3. Sumimoto K, Uchida K, Mitsuyama T, et al. A proposal of a diagnostic algorithm with validation of International Consensus Diagnostic Criteria for autoimmune pancreatitis in a Japanese cohort. Pancreatology 2013;13:230-7.
4. Zaheer A, Singh VK, Akshintala VS, et al. Differentiating autoimmune pancreatitis from pancreatic adenocarcinoma using dual-phase computed tomography. J Comput Assist Tomogr 2014;38:146-52.
5. Song TJ, Kim JH, Kim MH, et al. Comparison of clinical findings between histologically confirmed type 1 and type 2 autoimmune pancreatitis. J Gastroenterol Hepatol. 2012;27:700-8.