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Original article

Comparison of endoscopic retrograde cholangiopancreatography with papillary biopsy and endoscopic ultrasound-guided pancreatic biopsy in the diagnosis of autoimmune pancreatitis

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ABSTRACT

Background: International consensus diagnostic criteria (ICDC) have been proposed for the diagnostic criteria and algorithm of autoimmune pancreatitis (AIP). Although endoscopy is important in the diagnosis of AIP, practical patterns of its usage vary considerably worldwide. This study aimed to compare endoscopic retrograde cholangiopancreatography (ERCP) with papillary biopsy and endoscopic ultrasound (EUS)-guided pancreatic biopsy for diagnosing AIP using ICDC.

Methods: We retrospectively reviewed and classified 165 Korean patients diagnosed by Korean criteria from June 2007 to October 2013. Among them, 61 patients underwent ERCP with duodenal papillary biopsy (group A) and 62 patients underwent EUS-guided pancreatic biopsy (group B). We analyzed the diagnostic criteria and levels of each criterion, and type of AIP before and after endoscopic procedures.

Results: ERCP with papillary biopsy increased the diagnostic sensitivity from 65.6% (40/61) to 95.1% (58/61) ($P < 0.01$). EUS-guided pancreatic biopsy increased the diagnostic sensitivity from 50.0% (27/62) to 88.7% (55/62) ($P < 0.01$). The increases of diagnostic sensitivity in two endoscopic methods were not different statistically. In diagnosing definite AIP, EUS-guided pancreatic biopsy was more useful than ERCP with papilla biopsy (sensitivity; 79.0% vs. 65.6%, $P < 0.01$). EUS-guided pancreatic biopsy was helpful to classify type 1 and type 2 AIP in some patients. Procedure-related complication (mild pancreatitis) developed in one patient (1.6%) in group A and two patients (3.2%) in group B. ERCP with papillary biopsy was less expensive than EUS-guided pancreatic biopsy.

Conclusions: Both ERCP with papillary biopsy and EUS-guided pancreatic biopsy are safe and play important roles in diagnosing AIP according to the ICDC.

Background

Autoimmune pancreatitis (AIP) is a distinct form of pancreatitis characterized clinically by frequent presentation with obstructive jaundice with or without a pancreatic mass, histologically by a lymphoplasmacytic infiltrate and fibrosis and therapeutically by a marked response to steroids.

The diagnosis of AIP is challenging because several cases of AIP may closely mimic the pancreatic cancer [1]. Since AIP responds dramatically to steroid treatment, diagnostic criteria with a high

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accuracy are essential to avoid an unnecessary surgery. Up to now, several diagnostic criteria for AIP have been proposed [2–5]. In 2011, International Consensus Diagnostic Criteria (ICDC) for AIP were proposed [6]. These criteria comprise five cardinal features, such as imaging of the pancreatic parenchyma and ducts, serology, other organ involvement (OOI), pancreatic histology, and an optional criterion of response to steroid therapy, categorized as level 1 or 2 findings depending on the diagnostic reliability. Different from other criteria, the ICDC can diagnose type 1 and type 2 AIP independently. In addition, the ICDC defined the criteria for AIP not otherwise specified (AIP-NOS) for cases not diagnosed as type 1 and type 2 AIP.

There were various endoscopic tools for diagnosing AIP, such as endoscopic retrograde cholangiopancreatography (ERCP), duodenal papillary biopsy and endoscopic ultrasound (EUS)-guided pancreatic biopsy. For evaluating pancreas images of AIP, the diagnostic modalities to be selected, especially ERCP, have been debated among Western and Eastern countries [7,8]. IgG4-immunostaining of biopsy specimens obtained from the major duodenal papilla is useful for supporting a diagnosis of AIP with pancreatic head involvement [9]. It is easily able to be performed at the same time as ERCP. Different from typical diffuse AIP, focal or mass forming AIP is more difficult to distinguish from pancreatic cancer [10]. In these AIP cases, EUS-guided pancreatic biopsy is useful to exclude the possibility of pancreatic cancer.

Although endoscopic role is important in the diagnosis of AIP, practical patterns of its usage vary considerably worldwide. This study aimed to compare two endoscopic strategies, ERCP with papillary biopsy and EUS-guided pancreatic biopsy, for diagnosing AIP using ICDC.

Materials and methods

Patients and methods

After approval from the institutional review board, we retrospectively reviewed and classified a total of 165 patients diagnosed by Korean criteria [3] at two tertiary referral centers in Korea from June 2007 to October 2013. They were consecutively collected at our AIP registry. For the purpose of this study, these patients were reassessed radiologically and histologically and classified according to the ICDC. Thirty one patients were excluded because they did not undergo endoscopic evaluations (Fig. 1). Eighty eight patients (65.7%) had typical findings for AIP and 46 patients (34.3%) had indeterminate findings for AIP on abdominal computed tomography (CT). Among them, 61 patients underwent ERCP with duodenal papillary biopsy (group A) and 62 patients underwent EUS-guided pancreatic biopsy (group B). The group B patients underwent EUS-fine needle aspiration biopsy (FNAB) using various needles [Trucut needle 19-guage (G), 28 patients (45.2%); conventional needle 19-G, three patients (4.8%); conventional needle 22-G, 10 patients (16.1%); conventional needle 25-G, one patient (1.6%); Procore needle 22-G, 20 patients (32.3%)]. The mean number of needle punctures was 3.10. Group A and group B patients were evaluated by the evidence of serology/OOI for AIP and received steroid trials. We analyzed the diagnostic criteria and levels of each criterion, and type of AIP before and after endoscopic procedures according to the ICDC. Complications and cost were also compared between the two endoscopic methods.

Diagnostic ability of each criterion (imaging, serology, histology, and OOI) with special reference to level 1 and 2 of ICDC

We estimated the diagnostic ability of imaging, serology, and OOI using the ICDC with special reference to level 1 and 2. In pancreas imaging, level 1 parenchymal finding on CT is typical diffuse enlargement of the pancreas, and level 2 is indeterminate (segmental/focal) or atypical findings of the pancreas. Level 1 ductal finding on ERP is long (>1/3 length of the main pancreatic duct) or multiple strictures without marked upstream dilatation, and level 2 is segmental/focal narrowing without marked upstream dilatation (duct size, <5 mm). Concerning serology, elevation of serum IgG4 higher than 2 and 1 × the upper limit of normal (cut-off value of 135 mg/dl) is suggestive of AIP as level 1 and 2, respectively. Histologically, the following four lymphoplasmacytic sclerosing pancreatitis (LPSP) findings by core biopsy or resection were used: periductal lymphoplasmacytic infiltrate without granulocytic infiltration, obliterative phlebitis, storiform fibrosis, and abundant (>10 cells/high power field) IgG4-positive cells, with levels 1 and 2 having at least 3 and 2 features, respectively. OOI in AIP was defined by radiologic evidence (hilar/intrahepatic biliary stricture, retroperitoneal fibrosis, and renal involvement), physical evidence (bilaterally enlarged salivary glands), and compatible histology of extrapancreatic organs including endoscopic biopsy of duodenal papilla. Compatible histology of duodenal papilla is suggestive of AIP as level 2. ICDC criteria included responses to steroid therapy as a diagnostic component. A steroid trial was attempted by means of oral prednisolone (0.5 mg/kg/day). Steroid responsiveness was assessed 2 weeks after the initiation of the steroid therapy by means of laboratory tests and pancreas CT. Positive steroid responsiveness was defined as complete resolution or marked improvement of the main pancreatic ductal narrowing after steroid therapy and, if present, resolution or measurable reduction of the pancreatic mass as well [11]. We enrolled patients that did not show disease progression after 6 months from initiation of steroid therapy.

Statistical analyses

Descriptive statistics are reported as either frequency (percentage) or mean ± standard deviation as appropriate. Categorical variables were compared using a χ^2 test. Continuous variables are expressed by mean and range, and compared by the Mann–Whitney U test, or, if they had a normal distribution, using a 2-sample Student t test. The change of diagnostic sensitivity after each endoscopic procedure was evaluated by a generalized linear model. P values <0.05 were considered statistically significant. SPSS 19 software for Windows (SPSS, Chicago, IL) was used for all analyses.

Results

Fifty-five (62.5%) of 88 patients with diffuse type of AIP and 14 (30.4%) of 46 patients with focal type of AIP were diagnosed as definite type 1 AIP according to the ICDC, when they were not undergo endoscopic procedures. Twenty two patients (25.0%) with diffuse type of AIP and 28 patients (60.9%) with focal type of AIP were not diagnosed as AIP before they underwent additional endoscopic procedures (Table 1). The patients with diffuse type were more diagnosed as definite type 1 AIP than those with focal type without endoscopic procedures ($P < 0.01$). The more patients with focal type were not diagnosed as AIP than those with diffuse type without endoscopic procedures ($P < 0.01$).

ERCP was performed in 93 patients; 65 patients displayed diffuse type on CT and 28 patients were focal type on CT (Table 2). Level 1 ductal imaging was observed more frequently in patients with diffuse type (n = 50; 76.9%) than in those with focal type (n = 14; 50.0%) ($P = 0.01$). Duodenal papillary biopsy was performed in 71 patients; 52 patients were diffuse type on CT and 19 patients were focal type on CT. Among these patients, OOI level 2