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Original article

Obstructive jaundice in autoimmune pancreatitis can be safely treated with corticosteroids alone without biliary stenting

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ABSTRACT

Objective: Autoimmune pancreatitis (AIP) responds dramatically to corticosteroids treatment. We reviewed our experience to determine the safety and effectiveness of treating obstructive jaundice in definitive AIP with corticosteroids alone without biliary stenting.
Methods: From our AIP database, we retrospectively identified type 1 AIP subjects whose jaundice was treated with corticosteroids alone without biliary stenting. Their medical records were reviewed and clinical data were evaluated to determine the outcomes.
Results: Fifteen AIP subjects (87% male, mean age 68.4 years) were treated with corticosteroids at initial presentation (n = 8), first (n = 5) or subsequent (n = 2) relapse. Mean values (upper limit of normal, ULN) of liver tests prior to corticosteroids were aspartate aminotransferase (AST) 203.5u/l (4 × ULN), alanine aminotransferase (ALT) 325.8u/l (6 × ULN), alkaline phosphatase (ALP) 567.4u/l (5 × ULN), and total bilirubin (TB) 5.9 mg/dl (5.9 × ULN). At first follow-up (mean 4 days) the decrease was 54.9% for AST, 51.6% for ALT, 33% for ALP and 47.2% for TB (all $p < 0.05$). After 15–45 days, all patients had normal AST, 3/15 had ALT > 1.5 × ULN, 1/15 had ALP > 1.5 × ULN, 1/15 had TB > 1.5 × ULN. No patient required biliary stent placement, or developed cholangitis or other infectious complications during steroid treatment.
Conclusion: Under the supervision of an experience pancreatologist and with close monitoring of patients, obstructive jaundice secondary to definitive AIP can be safely and effectively managed with corticosteroids alone, without the need for biliary stenting.

Introduction

Reports of steroid-responsive obstructive jaundice were described in the early 1950s, and the possibility of a pancreatic disease of autoimmune etiology was first postulated by Sarles et al., in 1961 [1], [2]. However, the term autoimmune pancreatitis (AIP) was not introduced until decades later in a review of the etiology and classification of chronic pancreatitis [3]. Shortly thereafter, Yoshida et al. described the first clinical cohort, including serological abnormalities and steroid responsiveness, of what we currently refer to as type 1 autoimmune pancreatitis [4].

AIP is a distinctive chronic condition of pancreas presumably caused by an autoimmune process. It is a fibro-inflammatory disease with lympho-plasmacytic infiltration and peculiar storiform fibrosis that can cause multi-organ dysfunction. Type 1 AIP is considered to be the pancreatic manifestation of IgG4-related

Abbreviations: AIP, autoimmune pancreatitis; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ERCP, Endoscopic retrograde cholangiopancreatography; TB, total bilirubin.

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disease with elevated serum IgG4, and abundant IgG4-positive cell infiltration in the pancreas and other organs. It is the most common form worldwide, accounting for almost all cases in Japan and Korea and more than 80% of cases in Europe and the United States [5,6]. Type 2 AIP is a pancreas-specific disorder without any association with IgG4. Both types respond rapidly to steroid treatment [6]. Approximately 75% of patients with type 1 AIP patients present with obstructive jaundice, for which the vast majority (71%) undergo ERCP with biliary stenting [6]. As steroid treatment may potentially trigger or worsen cholangitis, obstructive jaundice in AIP has historically been managed by endoscopic or percutaneous transhepatic biliary drainage before steroid administration. However, since AIP responds promptly to corticosteroids, we have recently been treating obstructive jaundice in those with definitively diagnosed AIP and in which close clinical follow-up can be ensured with corticosteroids alone (i.e., without biliary stenting). Herein, we report on the safety and effectiveness of treatment of obstructive jaundice with corticosteroids alone in definitive AIP.

Methods

This study was approved by the Institutional Review Board at Mayo Clinic Rochester. We reviewed a prospectively maintained AIP database through December 2014 to identify subjects with jaundice secondary to type 1 AIP [7]. A total of 15 subjects were identified whose jaundice was managed exclusively with corticosteroids without biliary stenting and whose laboratory data were available within 2 weeks of start of steroid therapy. The diagnosis of AIP was made according to the International Consensus Diagnostic Criteria for AIP [8]. Among these subjects, 8 were treated at initial presentation, 5 at 1st, 1 at 2nd and 1 at 3rd relapse.

Medical records were reviewed to record liver tests aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin (TB) before and after corticosteroids. Changes on cross-sectional imaging studies and treatment-related adverse events (e.g., cholangitis, infectious complications and worsening hyperglycemia) were also recorded. The initial oral prednisone dose was 40 mg/day (n = 12, 80%), 30 mg/day (n = 2, 13.3%), and 20 mg/day (n = 1, 6.7%). The initial dose was administered for 4 weeks in all cases, and then gradually tapered by 5 mg every 1–2 weeks. Data were analyzed using Prism statistical software (GraphPad Software, Inc., La Jolla, CA) and variables were compared using Fisher's t test. A p-value of less than 0.05 was considered statistically significant.

Table 2
Mean liver test abnormalities prior to and following a short course of corticosteroids (median 4 days, range 1–14 days) in 15 patients with type 1 AIP and jaundice.

	Pre-steroids	Post-steroids	%decrease	Reference	p-value
AST (U/L)	203.5 ± 157.4	56.4 ± 28.7	54.9 ± 36.3	8–43	0.001
ALT (U/L)	325.8 ± 160.1	148.4 ± 61.8	51.6 ± 24.9	7–45	<0.001
ALK (U/L)	567.4 ± 435.9	313.3 ± 168.2	33.02 ± 25.2	46–118	0.044
TB (mg/dl)	5.9 ± 2.4	3.4 ± 2.7	47.25 ± 45.0	≤1.2	0.012
DB (mg/dl)	4.2 ± 2.4	2.7 ± 1.5	46.36 ± 19.1	0.0–0.3	0.050

Results

Patient characteristics

As is typical of type 1 AIP, the majority of treated patients were male (13/15) and the mean age at time of diagnosis was 68.4 ± 14.8 (range 44–93 years). All patients presented with jaundice, eight with abdominal pain, seven with fatigue, six with pancreas mass, 1 with renal involvement and 1 with parotid gland enlargement. Eight patients were treated at initial presentation and seven were treated at their relapse. Among those treated with steroids for their relapse, five had previously had biliary stenting and one underwent Whipple procedure during their initial presentation. Patient demographics of initial presenters are summarized in Table 1. In these eight patients, CT scan was performed in all and 6/8 had diffuse pancreas enlargement; 2/8 had localized pancreas mass; 3/8 had a capsule –like rim, 6/8 had distal-bile duct stricture with associated intra- and extra-hepatic duct dilation. Four patients (4/8) had EUS and 3 showed typical AIP features and pathology either suggestive or consistent with AIP. One patient had abnormal CT scan of kidney cortex and biopsies of the kidney suggested IgG4 associated tubulointerstitial nephritis. 6/8 had elevated IgG4; 5/8 had elevated IgG4 and typical CT images of AIP (Table 2). Q2

Liver tests rapidly improve after corticosteroid treatment in AIP patients

CT scan of the abdomen showed all patients had distal common bile duct stricture and one patient had intrahepatic biliary stricture

Table 1
Clinical details of 8 newly diagnosed AIP patients.

Patient	Age	Sex	Initial presentation	IgG4 (mg/dl)	CT scan	EUS	Pathology	Prednisone dose (mg/day)
1	76	M	Painless jaundice; weight loss	341	Pancreas head fullness; Distal bile duct stricture, intra- and extra-hepatic ductal dilation.	consistent with AIP	Suggestive of AIP	40
2	59	M	New DM, weight loss	228	Diffuse pancreas enlargement with a capsule-like rim; Distal bile duct stricture, moderate intra- and extra-hepatic bile duct dilation.			20
3	44	M	Painless jaundice	109	Enlarged pancreas, distal bile duct stricture, mild intra- and extra-hepatic bile duct dilation.	Consistent with AIP	Suggestive of AIP	40
4	79	M	Obstructive jaundice	121	Diffuse pancreas enlargement; distal bile duct stricture, mild intra- and extra-hepatic biliary ductal dilation.	Pancreas head irregular hypoechoic mass; Not typical for AIP	Atypical; No increase in plasma cells	40
5	59	F	Obstructive jaundice	244	Pancreatic mass and distal common bile duct stricture; capsule rim			40
6	85	M	Obstructive jaundice, weight loss	1290	Diffuse pancreas enlargement; mild distal bile duct stricture, dilatation of the intra- and extra- hepatic bile ducts.			30
7	57	M	Obstructive jaundice	1820	diffuse pancreas enlargement with a thin rim	typical for AIP	consistent with AIP	40
8	43	M	Left flank and epigastric pain	456	diffusely pancreas enlargement; mild distal bile duct stricture; moderate bile duct dilatation; multiple small perfusion defects in the cortex of the kidneys		IgG4-related tubulointerstitial nephritis	40

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