

Acute Cholangitis in Elderly Patients Exploring Diagnostic Clues and Clinical Signs

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ABSTRACT

AIM: Patients with acute cholangitis (AC) have poor prognoses when treatment is delayed. Diagnostic clues from clinical characteristics are evaluated with case study.

METHODS: We retrospectively investigated the case records of AC patients >65 years of age between April 2008 and June 2011. Our institutional ethical committee determined that this study was not a clinical trial as diagnostic investigations were based on daily clinical practices.

RESULTS: Seventeen patients (7 men and 10 women) were enrolled in this study. All patients were treated endoscopically and common bile duct (CBD) stones were successfully removed. Four patients (23.5%) presented with Charcot's triad. Ten patients (58.8%) presented with fever and 9 (52.9%) patients presented with abdominal pain. One patient presented with nausea without fever or jaundice. Nine and 10 patients had elevated white blood cell counts and

elevated C-reactive protein levels, respectively. Liver dysfunction was observed in most patients. Six patients showed normal CBD diameter on ultrasonography. CBD stones were discovered in 6 patients, 2 of which had normal-sized CBDs.

CONCLUSION: Fever and elevated alkaline phosphatase level are clues for a diagnosis of AC. Ultrasonography should be performed focusing on CBD stones even if CBD diameter is not dilated.

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Key words: Alkaline phosphatase; Ultrasonography; White blood cell count

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INTRODUCTION

Patients >65 years of age lose physiologic reserves, gaining concomitant systemic illness, resulting in worse outcomes compared with the younger population^[1]. Cooper *et al*^[2] reports that elderly patients present symptoms, such as fever and nausea, half as often as younger patients. This sometimes makes it difficult to diagnose infectious diseases of elderly patients.

Acute cholangitis (AC) is caused by calculous obstruction of the common bile duct (CBD). The obstruction can develop an infection mainly from gram-negative bacteria^[3]. Autopsy results reveal that the frequency of cholecystitis and AC increases with age, and 30% of people have gall bladder (GB) stones^[4]. Furthermore, AC patients are usually elderly^[5]. Classical symptoms experienced by AC patients include fever, abdominal pain, and jaundice (Charcot's triad)^[6]. In elderly patients, typical symptoms are obscured possibly due to nonspecific signs of sepsis^[7]. Cholecystitis and AC comprise 12% of all abdominal sepsis cases. Elderly patients have greater morbidity (37.8%) and mortality (10.8%) compared with younger patients (16.9% and 3.2%, respectively)^[8]; therefore, the correct diagnosis is critical for prompt endoscopic treatment to decrease mortality^[9]. Hence, in this study, we retrospectively analyzed AC

patients in search of diagnostic clues.

METHODS

The case records of patients who were diagnosed with AC between April 2008 and June 2011 were retrospectively reviewed. Only patients older than 65 years and with evident CBD stones with endoscopic retrograde cholangiopancreatography (ERCP) were enrolled in this study. AC was diagnosed using the guidelines set forth by Miura *et al.*^[10]. Briefly, the diagnosis of AC based on combination of clinical features suggestive of acute inflammation (fever, and abdominal pain) and bile duct obstruction [abnormal liver function, ultrasonography (US), and/or computed tomography (CT)]. Patients were classified as severe AC when they had Reynolds' pentad (Charcot's triad plus shock and a decreased level of consciousness). ERCP was performed for patients suspicious of biliary or pancreatic diseases using a duodenoscope (JF-260V; Olympus Optical Co. Ltd., Tokyo, Japan), and written informed consent was obtained from all patients. Our study was reviewed by our institutional ethical committee and they determined that it did not constitute a clinical trial as the tests were performed as part of routine clinical practice. White blood cell count (WBC), c-reactive protein (CRP), total bilirubin (T-Bil), alkaline phosphatase (ALP), aspartate amino transferase (AST), alanine aminotransferase (ALT), and gamma-glutamyltransferase (G-GTP) were evaluated. US findings such as CBD diameter, CBD stone, and GB stone or sludge were also analyzed. A diameter of intrahepatic or extrahepatic bile duct more than 2 mm or 7 mm was considered dilatation with US^[11]. Fisher's exact probability test was performed using JMP 8.0 (SAS Institute Japan, Tokyo, Japan). A *P*-value of <0.05 was considered statistically significant.

RESULTS

During this period, 101 ERCP were performed for seventy-one patients. thirty-six patients were diagnosed as AC with CBD stones. seventeen out of thirty-six patients were enrolled in the present study. CBD stones were detected in six patients to confirm bile duct obstruction with US. The rest of eleven patients showed CBD dilatation suggestive of bile duct obstruction. All the seventeen patients were diagnosed with AC because they had clinical symptoms of AC and US findings of bile duct obstruction. No patients underwent cholecystectomy. Bile duct stones were confirmed and successfully removed from all patients. Seven patients were male and 10 were female. Patient symptoms included fever (10/17, 58.8%) and fever with abdominal pain and jaundice (Charcot's triad) (4/17, 23.5%). A complete list of symptoms can be found in table 1. One patient presented with nausea without fever or jaundice. This patient was referred to our hospital for investigation on the basis of elevated ALP (1095 IU/L); on US, the patient's CBD was dilated (10.3 mm) and CBD stones were observed.

Table 2 illustrates laboratory data. Nine and 10 patients had above normal levels of WBC and CRP, respectively. Seven patients had hyperbilirubinemia. ALP, AST, ALT, and G-GTP were elevated above normal ranges in most patients. ALP was elevated to greater than twice the normal level in 6 patients, and 1 patient had an ALP level more than 5 times the normal limit. Finally, CBD diameter was increased in 11 patients (Table 3).

There was no relationships between the severity of AC and diagnostic clues.

One patient with normal CBD diameter had dilated intrahepatic bile ducts. CBD stones were visualized ultrasonographically in 6 (35.3%) patients. Two patients had CBD stones although their CBD

diameters were within normal range. Fifteen patients had GB stones or sludge.

Two patients had normal CBD diameter. Their clinical and laboratory features were described in table 4. Patient 1 had fever, elevated WBC, and CRP, suggesting acute inflammation. Patient 2, on the other hand, had normal WBC, and slightly elevated CRP and T-Bil. It was speculated that patient 2 had acute inflammation weaker than patient 1. Both of them showed elevated ALP twice the normal level indicating obstruction of CBD.

Table 1 Symptoms reported by AC patients over 65 years of age.

	Number	Percentage (%)
Fever	10	58.8
Abdominal pain	9	52.9
Jaundice	7	41.2
Nausea	4	23.5
Confusion	4	23.5

Table 2 Laboratory data.

	Median	Range	Number	Percentage (%)	Normal range	Unit
WBC	81	40-264	9	52.9	35-85	$\times 10^3/\mu\text{L}$
CRP	5.9	0.2-26.5	10	58.8	<0.3	mg/dL
T-Bil	1.29	0.38-9.16	7	41.2	0.3-1.2	mg/dL
ALP	500	332-2158	15	88.2	115-359	IU/L
AST	58	20-661	16	94.1	13-33	IU/L
ALT	92	21-1095	16	94.1	6-27	IU/L
G-GTP	251	12-1095	14	82.4	10-47	IU/L

Number: number of patients with data above the normal range; WBC: white blood cells; CRP: C-reactive protein; T-Bil: total bilirubin; ALP: alkaline phosphatase; AST: aspartate amino transferase; ALT: alanine aminotransferase; G-GTP: gamma-glutamyltransferase.

Table 3 Ultrasonographical findings.

	Number	Percentage (%)
CBD diameter greater than the normal range	11	64.7
CBD stone	6	35.3
GB stone or sludge	15	88.2

CBD: common bile duct; GB: gall bladder; normal range of CBD: < 7 mm.

Table 4 Characteristics of patients with normal diameter of common bile duct with ultrasonography.

	Patient 1	Patient 2	Normal range	Unit
Sex	male	female		
age	75	66		
Clinical symptoms	Fever, abdominal pain	Abdominal pain		
WBC	176	48	35-85	$\times 10^3/\mu\text{L}$
CRP	13.8	0.4	<0.3	mg/dL
T-Bil	1.29	1.14	0.3-1.2	mg/dL
ALP	1105	889	115-359	IU/L
AST	116	20	12-33	IU/L
ALT	204	21	6-27	IU/L
G-GTP	319	251	10-47	IU/L

WBC: white blood cells; CRP: C-reactive protein; T-Bil: total bilirubin; ALP: alkaline phosphatase; AST: aspartate amino transferase; ALT: alanine aminotransferase; G-GTP: gamma-glutamyltransferase.

DISCUSSION

It has been reported that 50-70% of severe AC patients present with Charcot's triad and Boey *et al* report that 7% of AC present with the complete pentad (the triad with confusion and hypotension)^[12,13]. In our series, 23.5% of patients presented with Charcot's triad and 1 patient had the complete pentad. Our patients were limited to those older than 65 years of age; thus, the lower percentage of those presenting with either the triad or the pentad might obscure AC diagnosis^[6].

The percentage of patients with fever varies by investigator: Csendes *et al* report 38.7%^[12], Thomas *et al* 100%^[7], and Boey *et al* 86%^[13]. In our series, 58.8% patients presented with fever, which is lower than most studies but is still within the reported levels for AC. This may be because our study was restricted to elderly patients.

One patient in our cohort presented with only nausea. Under normal conditions, this patient might be misdiagnosed with gastrointestinal or other disorders. Therefore, blood examination should be considered for patients that present with what seem like gastrointestinal conditions. This patient was correctly diagnosed with AC by US.

An 81-year-old male patient progressed to severe AC with the pentad within 4 h from fever onset. Elderly patients should be diagnosed precisely and promptly because advanced age is one of the risk factors for AC mortality^[14]. Liver dysfunction was observed in most of our patients. AST and ALT are not specific for AC because they are elevated in hepatitis, fatty liver, alcoholic liver disease, and other liver ailments. On the other hand, elevated ALP and G-GTP are good markers of AC as they are specific to biliary diseases^[15]. 88.2% (15/17) of our patients showed ALP elevated above normal level. 35.3% (6/17) patients had ALP levels twice the normal level. Another study reports that 55 patients (55.6%) had ALP levels elevated twice the normal range^[13]. It was suggested that elevated ALP was a good marker of AC. Elevated ALP of patient 1 and 2 supported this hypothesis in that their ALP elevated twice the normal level even their CBD diameter was normal. Elevated total bilirubin correlates with mortality and leukocytosis and indicates a need for urgent ERCP^[16]. It is intriguing that ALP was useful for AC diagnosis in our study but not for predicting prognosis by Salek *et al*^[16].

Most CBD stones originate from the gall bladder^[17]. Five percent of patients with CBD stones do not have GB stones^[17]. In our series, GB stones were not observed in 2 patients (11.8%) by US. Interestingly, CBD stones were observed in 2 patients who had normal CBD diameter. Therefore, we recommend that physicians search for CBD stones even if CBD diameter is within the normal range.

In conclusion, atypical clinical manifestations are not uncommon in elderly patients with AC in summary part. In addition, Fever and elevated alkaline phosphatase level are clues for a diagnosis of AC in elderly patients. The possibility of AC by CBD stone can be considered when there are prominent finding of liver function test with certain clinical symptoms because elderly patients do not have typical findings of AC compared to younger patients.

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