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Research Article

Is There an Association Between Gallbladder Dyskinesia and Idiopathic Acute Pancreatitis?

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Abstract

Objectives: The etiology of acute pancreatitis remains unclear in a significant number of patients. This study aimed to assess gallbladder dysfunction diagnosed using hepatobiliary iminodiacetic acid (HIDA) scan in patients recovering from idiopathic acute pancreatitis. **Methods:** This retrospective observational study included 22 consecutive patients with clinical and laboratory evidence of idiopathic acute pancreatitis. A HIDA scan was performed 8-10 weeks after the episode of pancreatitis. **Results:** Of the 22 patients, 14 (63.6%) were males. Their ages ranged from 18 to 79 years (mean, 47.5 ± 19.5). The co-morbid conditions observed were hypertension in eight patients, followed by diabetes in seven, ischemic heart disease in five, and miscellaneous in five. The HIDA scan revealed a gallbladder ejection fraction of less than 35% in seven (31.8%), suggesting a gallbladder dysfunction. Non-visualization of the gallbladder was observed in two patients. Biliary to the bowel transit time (BBTT) was 25.8 ± 8.7 minutes, and visualization of the gallbladder (n=20) was seen in 13.6 ± 11.4 minutes. **Conclusions:** Some patients with idiopathic acute pancreatitis have gallbladder dysfunction as evidenced by a decreased gallbladder ejection fraction or lack of visualization on the HIDA scan. Gallbladder dyskinesia should be checked in these patients to plan further management including cholecystectomy.

Keywords: Cholescintigraphy; 99mtc HIDA; Acute pancreatitis; Gallbladder emptying; Biliary dyskinesia.

Introduction

Pancreatitis is an inflammatory process that occurs due to abnormal trypsin activation causing auto-digestion of the pancreas [1]. Several etiological factors are reported, with gallstones and alcohol being the most common. The rest includes biliary tract diseases, infection, trauma, hypercalcemia, autoimmunity, toxins, tumors, hypertriglyceridemia, pancreatic developmental disorders, some drugs, and more [2]. The etiology of acute pancreatitis remains unclear in about 12-35% of patients in different studies [3-5] and the term idiopathic acute pancreatitis is used for such cases.

Biliary dyskinesia is a condition in which the coordinated contraction of the gallbladder, bile ducts, or sphincter of Oddi is disrupted, leading to disruption of the process of emptying bile into the duodenum [6]. Cholescintigraphy, commonly known as HIDA (hepatobiliary iminodiacetic acid) scan, noninvasively assesses the anatomy and activity of the biliary system and liver via excretion of the radioactive tracer, the 99mTc-labeled iminodiacetic acid derivative disofenin [7]. It has been mainly used to diagnose acute cholecystitis, chronic hepatobiliary diseases, biliary dyskinesia, biliary obstruction, and biliary leaks [8]. Imaging shows radiotracer in the liver and biliary tract and then in the gallbladder and small bowel. After Cholecystokinin (CCK) or fatty meal provocation, the gallbladder contracts and empties, and the amount of tracer that comes out is calculated, referred to as the gallbladder ejection fraction (GBEF). A GBEF of less than 35 percent is considered an abnormal HIDA scan in most studies [9].

This study aimed to evaluate the presence of malfunctioning acalculous gallbladder with reduced ejection fraction on HIDA scan in patients recovering from idiopathic acute pancreatitis when no other precipitating etiological factor for acute pancreatitis could be identified on routine examinations.

Methods

This was a retrospective cross-sectional study that included all patients seen in one year both male and female, who had clinical and laboratory evidence of idiopathic acute pancreatitis, were older than 18 years at the time of presentation, and whose imaging studies revealed no evidence of gallstones. Acute pancreatitis was diagnosed by the presence of at least two of the following: acute epigastric pain; elevated serum lipase≥3 times the upper normal limit; characteristic CT findings [10]. Exclusion criteria were patients with abdominal pain without clinical presentation of pancreatitis, pregnant women, patients with a history of alcohol consumption, trauma or toxin ingestion, patients with known cases of autoimmune pancreatitis, cystic fibrosis, and chylomicronemia, patients with gallstones or bile duct stones or gallbladder and biliary sludge as evidenced by imaging studies (ultrasound, CT, or MRCP), patients with ascariasis and post-cholecystectomy status. Idiopathic acute pancreatitis was defined as acute pancreatitis after excluding the above etiologies.

Radionuclide hepatobiliary scintigraphy was performed during the follow-up, 8- 10 weeks after the acute episode. 5 millicuries mCi of Tc-99m DISIDA, given intravenously, and 1-hour anterior projection dynamic images were acquired. This was followed by sequential static images anteriorly after a meal for three hours. Briefly, dynamic images revealed the traveling of the bolus through cardiac chambers followed by large abdominal vessels and perfusion blush over the liver. The tracer was then taken up by the functioning hepatocytes. Activity in intrahepatic bile ducts was noticed. Sequential images revealed hepatocytic clearance of the tracer with the appearance of a gall bladder. Gallbladder visualization time (GBVT) and time for the tracer to flow into the intestinal loops (biliary bowel transit time, BBTT) were noticed. When the radioactivity was maximal in the gallbladder and minimal in the liver, a fatty meal was given. After the meal, the contraction of the gallbladder was recorded, and the gallbladder ejection fraction was calculated.

A proforma was prepared to record patient data, laboratory tests, abdominal ultrasound findings, CT scans, and gallbladder ejection fraction. The study was performed following the ethical standards laid down in the Declaration of Helsinki. All the diagnostic tests were part of the routine care provided at our hospital. The protocol of this retrospective observational study was approved by the Ethics Review Committee (ERC) of the University Hospital (Ref: 5250322HHMED). The informed consent requirement was waived by the ERC due to retrospective design.

The data was analyzed using the SPSS software package (IBM SPSS Statistics 20; Chicago, IL, USA). Descriptive statistics were calculated, presenting means and standard deviations for continuous variables, and numbers with percentages for categorical variables. Pearson's correlation coefficient was employed to examine the relationships between variables, providing insight into the strength and direction of associations.

Results

Of 22 patients, 14 (63.5%) were males, The ages ranged from 18 to 79 with a mean age of 47.5 ± 19.5 years. 13 patients were of age above 50 or above. Body mass index (BMI) ranged between 16.8 to 32.2 (mean 23.3 ± 3.7). Six patients had a BMI greater than 25 kg/m2. The most common comorbidities were hypertension in eight patients, diabetes in seven, and ischemic heart disease in five. Other comorbidities included chronic obstructive pulmonary disease, chronic kidney disease, hypothyroidism, psychiatric disorder, and G6PD deficiency in one each. The laboratory investigations have been mentioned in (Table 1).

Parameter	**Value**
Gender: male: female	14:8
Age, years: median (range)	51 (18-79)
mean ± S.D.	47.5 ± 19.5
BMI (kg/m^2)	23.3 ± 3.7
Comorbidity	
Hypertension	8 (36.3%)
Diabetes	7 (31.8%)
Ischemic heart disease	5 (22.7%)
Miscellaneous	5 (22.7%)
Laboratory investigations (mean ± S.D.)	
Bilirubin (mg/dL)	0.98 ± 1.00
Alanine aminotransferase level (IU/L)	44.5 ± 64.4
Aspartate aminotransferase (IU/L)	51.9 ± 60.4
Gamma-glutamyl transferase (IU/L)	121.5 ± 195.5
Alkaline phosphatase (IU/L)	168.8 ± 178.5
Albumin (g/dL)	3.8 ± 0.3
Amylase (IU/L)	1188.2 ± 1113.1
Lipase (IU/L)	1964.0 ± 2383.8
Cholesterol (mg/dL)	181.6 ± 78.3
Triglyceride (mg/dL)	182.3 ± 125.1
Cholescintigraphy	
Non-visualized gallbladder	2 (9.1%)
Time to visualize gallbladder (minutes) (n=20)	13.6 ± 11.4

Gallbladder ejection fraction (%) (n=20)	61.1 ± 29.7
Ejection fraction of gallbladder	
<35%	7 (31.8% of study patients)
>35%	13 (59.1% of study patients)
Biliary to the bowel transit time (minutes) (BBTT)	25.8 ± 8.7

Table 1: Characteristics of the study patients (n=22)

The HIDA scan performed at the follow-up visit revealed a gallbladder ejection fraction of less than 35% in seven (31.8%), suggesting a gallbladder dysfunction. Non-visualization of the gallbladder was seen in two patients. Visualization of the gallbladder was seen in 13.6 ± 11.4 minutes in the rest of the 20 patients. The biliary to bowel transit time (BBTT) was 25.8 ± 8.7 minutes in this study. There is a correlation of BBTT with gallbladder visualization time (GBVT) (p = 0.015 by Pearson correlation test). No correlation of ejection fraction with BBTT or GBVT could be found.

Discussion

The objective of this study was to document the presence of the malfunctioning gallbladder diagnosed by HIDA scan in patients recovering from idiopathic acute pancreatitis. Previous studies concluded that the HIDA scan could distinguish gallstone pancreatitis from pancreatitis without biliary stones, when performed in the acute phase, with non-visualization of the gallbladder in many patients with biliary stones [11-13]. Our study was conducted to search for an association between gallbladder dysfunction in idiopathic acute pancreatitis in which no gallstones could be detected on ultrasound, CT, or MRCP.

It has been shown that the changes detected by the biliary scintigraphy done during the acute phase can be transient as some of these patients show reversibility [13,14]. This may be due to cystic duct edema or disturbed motility resulting in non-visualization of the gallbladder. Moreover, inflammation and swelling of the pancreas can lead to obstruction or compression of the bile ducts, which may result in delayed or impaired flow of bile into the bowel. To minimize the effects of acute inflammation, we carried out cholescintigraphy in the follow-up period as an outpatient examination after discharge from the acute phase, to allow the disease to evolve and settle to a point where HIDA imaging can provide the most accurate information for diagnosis and treatment planning.

We also checked whether there is a correlation between intestinal and bile transit time and the time required for visualization of the gallbladder. The time it takes to visualize the gallbladder (GBVT) determines how well and how fast the gallbladder takes up the radiotracer. The biliary to the bowel transit time (BBTT) represents how well and how much the tracer passes through the tract which can help analyze for any leak or obstruction in the biliary system. There was a correlation between GBVT and BBTT (p=0.015). However, no correlation of ejection fraction with BBTT or GBVT could be found indicating isolated gallbladder dyskinesia.

The study has a clear and specific research objective. The etiology of acute pancreatitis remains unknown in a significant number of patients [3-5]. However, it has been suggested that microlithiasis not detected by the standard imaging techniques might be an etiological factor in a subset of patients with idiopathic acute pancreatitis [15,16]. Reduced ejection fraction of the gallbladder may lead to the formation of microlithia [17]. This study offers possible implications for the management of idiopathic acute pancreatitis. The usual practice is not to offer cholecystectomy in patients with gallbladder dysfunction without pancreatitis [18]. A systematic review and meta-analysis have shown that cholecystectomy after an episode of idiopathic acute pancreatitis reduces the risk of pancreatitis recurring [19]. Scanning can help identify a subset of patients who have occult biliary disease and may benefit most from cholecystectomy.

The sample size of 22 patients, while small, is appropriate for a retrospective observational study. Moreover, idiopathic acute pancreatitis is not so common in our region, seen in only 12% of the cases in a recent study [5]. Using a radioactive tracer and a HIDA scan to assess gallbladder ejection fraction is an appropriate technique for the study objective. The study was conducted in a single hospital on patients without a control group for gallstone pancreatitis. It is difficult to choose a control group because when the etiology is obvious, a HIDA scan is usually not indicated. We could not find any patients with gallstone pancreatitis who had the HIDA scan. However, our study suggests a causal relationship between gallbladder dyskinesia and idiopathic acute pancreatitis.

Conclusion

We demonstrated the presence of malfunctioning acalculous gallbladder with reduced ejection fraction on HIDA scan in one-third of patients recovering from idiopathic acute pancreatitis. Further studies are needed to examine its possible implications for clinical practice, including the decision to perform cholecystectomy to prevent further episodes of pancreatitis in a subset of patients with idiopathic acute pancreatitis who have reduced ejection fraction of gallbladder.

Ethical considerations

The protocol of this retrospective observational study was approved by the Ethics Review Committee (ERC) of the University (Ref: 5250322HHMED). The informed consent requirement was waived by the ERC due to retrospective design.

Disclosure statement

All authors declare that they have no conflict of interest.

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