Electrocardiographic changes and importance of repolarization changes in cases with acute pancreatitis

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Background/aims: Acute pancreatitis is a systemic disease with high mortality. The most common electrocardiography finding in acute pancreatitis cases is reported to be nonspecific repolarization changes in the literature. Recently, it is reported that repolarization changes carry high mortality risk. In this study, we aimed to investigate the association between repolarization changes and prognosis in acute pancreatitis cases. Methods: Patients with acute pancreatitis referred to gastroenterohepatology clinic between 2009 and 2010 were included into the study. Echocardiography, electrocardiography, chest graph, abdominal sonography and/or computerized tomography, Ranson’s and Glasgow’s parameters and routine biochemistry tests of all patients were evaluated. Results: A total of 55 cases (F/M: 22 (40%) / 33 (60%)) were included into the study. Thirty-nine of acute pancreatitis cases (70%) had electrocardiography changes. Electrocardiography changes were seen most frequently in cases with biliary (73%) and alcohol dependent pancreatitis cases (21%). The most frequently seen electrocardiographic finding was lateral early repolarization. There was a significant correlation between lateral early repolarization and Ranson score (p = 0.005). Conclusion: Early repolarization is the most common electrocardiographic findings and consistent with severity of acute pancreatitis cases.

Key words: Acute pancreatitis, repolarization changes, prognosis

INTRODUCTION

Acute pancreatitis (AP) is a common inflammatory disorder of the pancreas with a rising incidence in the western world (1-3). High morbidity and mortality can be seen in AP patients due to systemic complications and multi-organ failure. Cardiac involvement has an important place during...
systemic involvement. Impaired cardiac function in AP patients was confirmed by many authors (4-6). Cardiovascular changes occur in the early period of the disease and strongly affect the clinical outcome in AP cases. Cardiac involvement findings in AP cases were demonstrated in autopsy studies (7), hemodynamic studies (8) and by clinical findings (8-12).

In the literature, electrocardiographic (ECG) findings were evaluated, and “nonspecific” repolarization was described to be the most common ECG finding detected among ST-T changes, and it was reported to be an unimportant finding (13,14). However, the clinical significance of this finding and influence on the prognosis was not evaluated sufficiently. According to the recent literature data, early repolarization is an important prognostic parameter. While lateral early repolarization was considered to be a benign condition in the beginning, it has been shown that it increased the risk of malignant arrhythmia like ventricular fibrillation and was a cause of sudden death in individuals with no structural heart pathology. While early repolarization is seen at a rate of 1-5% in the normal population, this rate can increase to 60% in individuals who have experienced ventricular fibrillation (15-17).

B-type natriuretic peptide (BNP) is a hormone synthesized predominantly in cardiac ventricular myocytes (18). It is now generally accepted that its release into the blood is increased by factors that raise intracardiac pressure and volume overload (19-22).

The aim of this study was to investigate the association of repolarization changes in AP cases with BNP, echocardiographic data and prognostic scorings.

MATERIALS AND METHODS

The patients admitted to Şişli Etfal Training and Research Hospital Gastroenterohepatology Department between 2009 and April 2010 and diagnosed as AP were included into the study. AP diagnosis was made by characteristic findings and symptoms (upper abdominal pain and/or guarding and/or rebound tenderness), elevated serum enzymes (≥3-fold amylase and/or lipase increase) and abdominal ultrasonography (first 24 hours (h) and >twice after 24 h) and/or contrast-enhanced computed tomography (CT) performed after 48-72 h.

Acute pancreatitis (AP) was considered to be biliary in origin if stones or sludge were detected in the gallbladder and/or common bile duct and alcoholic in origin if the patient or his/her relatives reported consumption of >60 g pure alcohol/day. Serum triglyceride level >750 mg/dl and exclusion of other etiologies were accepted as hyperlipidemic etiology. Patients were classified as having an idiopathic etiology if the history and laboratory findings ruled out known etiologic factors and ultrasonography revealed a normal biliary tract.

B-type natriuretic peptide (BNP) was measured on admission using Elecsys ProBNP (Roche), a quantitative electrochemiluminescence immunoassay. Plasma BNP levels of all patients included into the study were measured twice, within the first 2 days of appearance of the clinical findings. Glucose, hemogram panel, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), albumin, amylase and/or lipase, arterial blood gases (PO2 and base excess [BE]), calcium, blood urea nitrogen (BUN), gamma-glutamyl transpeptidase (GGT), thyroid-stimulating hormone (TSH), triglyceride, total bilirubin, and direct bilirubin were measured in all patients included in the study. Serum calcium (mg/dl) was calculated by correcting with 0.8 x [4-albumin (g/dl)]. Age-matched cases with normal ranges of echocardiographic data and ECG and laboratory findings were included in the study as a control group.

Exclusion criteria were determined as follows: known congestive heart failure, ejection fraction <50% in the echocardiography, pulmonary embolism, systemic and pulmonary hypertension, arrhythmias (such as atrial fibrillation, paroxysmal supraventricular arrhythmia), chronic renal failure, cirrhosis, chronic obstructive pulmonary disease, valvular heart diseases, congenital heart diseases, beta blocker and other drug use leading to other potential cardiac repolarization changes, catecholaminergic arrhythmias described as arrhythmias occurring during catecholamine infusion or exercise test, and hyperthyroidism.

Prognostic evaluation was obtained from Ranson score, Glasgow (Imrie) score and data within the first 48 h. All CT scans were reviewed by radiologists dedicated to abdominal imaging, who were blinded to the laboratory data and clinical course.

The presence of a pleural effusion(s) was determined by a CT scan, chest radiograph or abdominal ultrasound obtained within 24 h of presentation. Imagining obtained within 24 h of presentation at
the hospital of origin for transferred patients was also collected and reviewed.

**Electrocardiography (ECG) and Echocardiography**

ECG recordings were evaluated by the same cardiologist. Standard 12-lead ECGs were performed with the subject in supine position during quiet respiration and recorded at 25 mm/s. ECG patterns were evaluated according to the commonly adopted clinical criteria (23). We evaluated baseline electrocardiograms for the presence of early repolarization, which was defined as an elevation of the QRS-ST junction (J-point) in at least two leads at the time of admission. The amplitude of J-point elevation had to be at least 1 mm (0.1 mV) above the baseline level, either as QRS slurring (a smooth transition from the QRS segment to the ST segment) or notching (a positive J deflection inscribed on the S wave) in the inferior leads (II, III; aVF), lateral leads (I, aVL and V4, V5), apical leads (V6 and V4a), or both. The anterior precordial leads (V1-V3) were excluded from analysis to avoid the inclusion of patients with right ventricular dysplasia or the Brugada syndrome (15).

Echocardiography was applied by the same cardiologist within the first two days of acute attack. Transthoracic echocardiography imagings were obtained from parasternal long-axis window and four apical windows with 2.5-3.5 MHz transducer by using GE Vivid 3 ultrasound machine. The individuals with poor echogenicity were not included in the study. Left ventricular ejection fraction (EF%) was obtained by subtracting left ventricular end-systolic volume from left ventricular end-diastolic volume and dividing this by left ventricular end-diastolic volume with Global Area Length technique.

**Statistical Analysis**

Scale variables are presented as mean ± standard deviation (mean ± SD). Categorical data were evaluated using chi-square analysis or with Pearson’s correlation as appropriate. Student’s t test was use for comparison of parametric quantitative data. A p-value <0.05 was considered significant. SPSS software (Statistical Package for Social Sciences, for Windows, release 12.0.0 standard version) was used for statistical evaluations.

The study protocol was approved by the local ethics committee, and informed consent was obtained from all patients before inclusion into the study.

**RESULTS**

A total of 55 AP cases [33 males (60%), 22 females (40%)] and 47 healthy case controls [F/M: 20 (42%)/27 (58%)] were included into the study. Among patients included in the study, 32 (58.2%) were biliary, 10 (18.8%) were alcohol-dependent, 8 (14.5%) were idiopathic, 4 (7.2%) were hyperlipidemic, and 1 (1.8%) was endoscopic retrograde cholangiopancreatography (ERCP)-dependent AP. Demographic, laboratory and prognostic scores of the patients included into the study are given in Table 1.

Thirty-nine of the AP cases (70%) had ECG changes. ECG changes were seen most frequently in the biliary (73%) and alcohol-dependent pancreatitis cases (21%). The most frequently seen ECG findings were repolarization changes, left anterior hemi-block and sinus tachycardia (Table 2).

Serum BNP level of AP patients and age-matched healthy controls (n=47) were 425 ± 299 pg/ml and 85.75 ± 22.87 pg/ml, respectively (p<0.001) (normal range of BNP: 0-120 pg/ml). Correlation of BNP with electrocardiographic intervals was evaluated. No significant relation was found between BNP and PR interval (p=0.895), QRS interval (p=0.839) and QT interval (p=0.329).

No significant relation was seen between lateral early repolarization and echocardiography findings: left atrial diameter (p=0.596), septum wall thickness (p=0.981), left ventricular posterior wall thickness (p=0.873), left ventricular end-systolic diameter (p=0.347) and ejection fraction (p=0.692).

There was a significant correlation between lateral early repolarization and BNP (r=0.353, p=0.008), Ranson score (r=0.265, p=0.005) and Glasgow score (r=0.361, p=0.007). No significant correlation was determined between lateral early repolarization and age (r=-0.252, p=0.065), gender (r=0.107, p=0.473), pleural effusion (r=0.328, p=0.095), AST (r=0.149, p=0.279), GGT (r=0.081, p=0.351), PO2 (r=0.157, p=0.737), LDH (r=0.052, p=0.736), C-reactive protein (CRP) (r=0.240, p=0.872), amylase (r=0.031, p=0.824), and body mass index (BMI) (r=0.147, p=0.709).

No significant correlation was found between apical early repolarization and BNP (p=0.436), Ranson score (p=0.475), Glasgow (p=0.764), age (p=0.252, p=0.358), gender (p=0.107, p=0.119),
pleural effusion ($r=0.328$, $p=0.654$), white blood cells (WBC) ($r=0.134$, $p=0.596$), AST ($r=0.149$, $p=0.254$), GGT ($r=0.031$, $p=0.291$), amylase ($r=0.031$, $p=0.291$), LDH ($r=0.103$, $p=0.452$), CRP ($r=0.055$, $p=0.705$), albumin ($r=0.023$, $p=0.876$), $pO_2$ ($r=0.023$, $p=0.168$), and calcium ($r=0.156$, $p=0.259$).

While there was a significant correlation between sinus tachycardia and Ranson score ($r= -0.296$, $p=0.028$), hematocrit ($r= -0.334$, $p=0.001$) and CRP ($r= -0.263$, $p=0.049$), there was no significant correlation between sinus tachycardia and Glasgow score ($r= -0.244$, $p=0.072$).

In this study, death occurred in two cases following hospitalization, and lateral early repolarization was determined in both of them.

Pleural effusion was present in 27.7% of AP cases in this study. There was a significant correlation
between both Ranson scores \((r = -0.544, p=0.003)\) and Glasgow scores \((r = -0.425, p=0.027)\) among AP cases with and without pleural effusion.

While the relation between E/A ratio and Ranson score \((r=0.547, p<0.01)\) was significant, no significant correlation was observed between echocardiographic findings such as left atrial diameter and left ventricular wall thickness and ECG and other parameters of this study.

**DISCUSSION**

In this study, we evaluated cardiac involvement and its relation with echocardiography, ECG and BNP level and their correlations with prognostic scorings and the parameters used in these scorings.

The most commonly encountered ECG findings in the studies performed in AP cases are changes in the ST-T interval \((13,14,24,25)\). Repolarization changes in these studies were described to be “nonspecific”. The most common ECG finding observed in this study was lateral early repolarization among ST-T segment changes. In the study performed by Mautner et al. \((24)\), it was reported that ST-T changes occurred most frequently, and this was most commonly associated with left ventricular hypertrophy and then with “nonspecific” ST-T changes. They did not provide detailed data regarding “nonspecific” ST-T changes. One of the most striking points is that ECG tracing described to be a normal ECG sample by Mautner et al. \((24)\) is associated with lateral early repolarization (Figure 1). Mautner et al. did not apply exclusion criteria for known ischemic heart disease and hypertension. Therefore, it is suspicious that left ventricular hypertrophy, the most common finding in the study performed by Mautner et al., is a finding secondary to AP. In this case, it would not be wrong to say that the most common ECG finding due to AP in Mautner et al.’s study is “nonspecific ST-T change”.

The most common ECG finding seen in this study is consistent with repolarization changes detected by Rubio Tapia et al. \((14)\). However, early repolarization localization was not indicated in that study, and the authors stated it to be “nonspecific repolarization” as an unimportant finding. However, according to the literature data in recent years, early repolarization (and especially lateral early repolarization) is an important prognostic parameter. While lateral early repolarization was considered to be a benign condition earlier, it was demonstrated that lateral early repolarization increased the malignant arrhythmia risk like ventricular fibrillation in individuals with no structural heart pathology and could be a cause of sudden death. While early repolarization is seen at a rate of 1-5% in the normal population, this rate can increase to 60% in individuals experiencing ventricular fibrillation \((15-17)\). Early repolarization, which is found to be associated with malignant arrhythmia and sudden death in individuals without cardiac pathology, is reported to be most frequent cause of death in cases with cardiac ischemic event \((15-17,26)\). It is not known clearly why lateral early repolarization occurs. However, according to the current experimental data, J-point elevation is associated with increased transmural heterogeneity of ventricular repolarization. It is suggested that this transmural heterogeneity increases the susceptibility to ventricular tachyarrhythmias \((27-29)\). As one of the important results of this study, the mild relation between early repolarization and BNP increase can be associated with the increase in the sensitivity in the ventricular wall due to cardiac depressant cytokines (like kinin, bradykinin, myocardial depressant factor) due to AP. This weak relation between BNP and early repolarization is a clue for another factor(s) as the cause of elevated ST interval and the exhibited repolarization changes.

A significant correlation was determined between sinus tachycardia and serum hematocrit level in this study. In contrast, in the study performed by Rubio Tapia et al. \((14)\), it was stated that sinus tachycardia was correlated with hypocalcemia, hypophosphatemia and hypomagnesemia, but its correlation with hematocrit was not evaluated. With respect to our finding a correlation between sinus tachycardia and a lower hematocrit level, the reflex tachycardia for volume depletion is a
very well-known subject. In addition, sinus tachycardia can develop due to sympathetic discharge (30), fever and hypovolemia.

In conclusion, lateral early repolarization is the most common ECG finding in cases with AP. Current opinion is focused on the importance of repolarization changes in cases exhibiting cardiovascular mortality. Our findings support this opinion.

REFERENCES