



Acute biliary pancreatitis related with pregnancy: a 5-year single center experience

Gebelikte ilişkili akut biliyer pankreatit: Tek merkezin 5 yıllık deneyimi

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BACKGROUND

Pregnancy-associated acute biliary pancreatitis is a rare but challenging clinical entity in terms of diagnosis and management. We report our institutional medical data of pregnancy-associated acute biliary pancreatitis.

METHODS

Medical records of 27 patients admitted to our clinics for pregnancy-associated acute biliary pancreatitis between January 2005 and January 2010 were reviewed.

RESULTS

Of the 27 patients, 25 (93%) were in the post-partum period, and 2 (7%) were pregnant. Seventeen patients (63%) were managed with conservative treatment, and were scheduled for interval cholecystectomy, while 10 patients (37%) had early cholecystectomy prior to discharge. The mortality rate was 3% (n=1).

CONCLUSION

Pregnancy-associated acute biliary pancreatitis usually has a mild-to-moderate clinical course with a favorable outcome, and can be managed successfully with conservative treatment. Early cholecystectomy done prior to discharge in the initial admission should be considered in mild-to-moderate pregnancy-associated acute biliary pancreatitis, except in patients within the first trimester.

Key Words: Acute pancreatitis; biliary; cholecystectomy; gallstones; pregnancy.

AMAÇ

Gebelikte ilişkili akut biliyer pankreatit (ABP) nadir bir hastalıktır, tanı ve tedavi anlamında da zorlu bir klinik tablodur. Bu yazıda, gebelikte ilişkili ABP nedeniyle takip ve tedavisi yapılan hastaların verileri sunuldu.

GEREÇ VE YÖNTEM

Ocak 2005 ile Ocak 2010 tarihleri arasında genel cerrahi kliniğinde gebelikte ilişkili ABP tanısı ile takip ve tedavisi yapılan 27 hastanın tıbbi kayıtları gözden geçirildi.

BULGULAR

Toplam 27 hastadan 25'inin (%93) puerperal dönemde ve ikisinin (%7) gebelik döneminde olduğu saptandı. On yedi hasta (%63) konservatif tedavi yapılarak ve sekiz hafta sonra kolesistektomi işlemi uygulanmak üzere taburcu edilirken, 10 hastaya (%37) ilk başvuruları sırasında taburcu edilmeden önce kolesistektomi uygulanmıştır. Ölüm oranı %3 (n=1) olarak saptanmıştır.

SONUÇ

Gebelikte ilişkili ABP genellikle hafif ile orta derecede bir klinik seyir ve yüz güldürücü sonuçlara sahip, konservatif tedavinin başarı ile uygulanabileceği bir hastalıktır. Gebelikten bağımsız ABP'lerde genel olarak kabul edildiği gibi, gebelikte ilişkili ABP'lerde de, ilk trimesterde olan gebeler hariç tutulmak üzere, ilk başvuruda taburculuk işlemi öncesi kolesistektomi uygulanması düşünülmelidir.

Anahtar Sözcükler: Akut pankreatit; biliyer; kolesistektomi; safra taşları; gebelik.

Pregnancy is a period with many alterations in physiology leading to challenges in the diagnosis and management of many diseases.^[1] Gallbladder disease is the most common non-obstetrical cause of maternal hospitalization in the first post-partum year.^[2] Acute pancreatitis during pregnancy is a rare disease, with a reported incidence of 1/1000-4000 pregnancies.^[1] Approximately 4% of pregnant women have gallbladder sludge or stones persisting to the post-partum period, and most of them remain asymptomatic; of those, 0.8% were reported to require cholecystectomy within the first year postpartum.^[2]

In this study, we reviewed medical data and management of the patients with pregnancy-associated acute biliary pancreatitis (ABP).

MATERIALS AND METHODS

The study included 27 patients who were admitted for ABP related with pregnancy between January 2005 and January 2010. Patients without a certain diagnosis of biliary etiology of acute pancreatitis and those who were not pregnant or not in the first post-partum year were excluded from the study. Pregnancy trimesters were defined as first (1-12 weeks), second (13-28) and third (29 weeks to delivery).

All of the patients had an initial abdominal sonographic scan. The patients who had Ranson score ≥ 3 , in whom the other causes of acute abdominal pain could not be ruled out, and who had progressive clinical course, underwent contrast-enhanced abdominopelvic computerized tomography (CT) scan with multidetector spiral CT scanner. Magnetic resonance cholangiopancreatography (MRCP) was utilized for the patients with abnormal common bile duct (CBD) findings in previous diagnostic procedures and/or elevated bilirubin levels. Abdominal sonographic scans were performed by the attending radiologists. CT and MRCP scans were reevaluated retrospectively by the same radiologist.

The patients with evidence of CBD stones had endoscopic retrograde cholangiopancreatography (ERCP) done by the same endoscopist.

Reviewed data included the patient's age, exact time of episode, period between onset and admission, comorbidities and other risk factors, diagnostic procedures, results of biochemical tests, management, length of stay (LOS), and maternal outcome. Severity of ABP was assessed according to Ranson criteria and Balthazar CT Severity Index.

RESULTS

The mean age was 30.2 ± 10.8 (17-44) years. The leading and constant symptom was abdominal pain that was often accompanied by nausea and vomit-

ing. The mean duration of the period between onset of symptoms and admission was 3.3 ± 2.3 (1-10) days. Two patients (7%) were pregnant; these patients were in the first and third trimester. Among 25 patients who were in the post-partum period, 33% (n=10) had normal delivery, and 60% (n=15) had cesarean section. The mean times of admission in the post-partum period for the patients who had normal delivery and cesarean section were 112.7 ± 109.4 (42-365) and 112.5 ± 102.1 (10-365) days, respectively. The results of biochemical parameters detected on admission are summarized in Table 1.

Imaging Modalities

Sonography: Twenty-five (92%) patients were demonstrated to have cholelithiasis and/or sludge in the gallbladder. The patient with a normal gallbladder was demonstrated to have gallstone(s) within the CBD. The other patient had previous cholecystectomy procedure for symptomatic gallstone disease 18 months before, and was found to have gallstone(s) within the CBD. Twelve patients (44%) were shown to have normal CBD, while 12 (44%) had either a dilated CBD (≥ 7 mm) (n=7) or an impacted gallstone(s) or sludge within the CBD (n=5). The CBD could not be evaluated in the sonographic scan in three patients (11%). The pancreas was found to be heterogeneous and swollen in 12 patients (44%), and was normal in nine patients (33%). The pancreas could not be visualized in sonographic scan in six patients (22%).

CT: Sixteen patients (59%) had contrast-enhanced abdominopelvic CT scan. CT findings were classified

Table 1. The mean values of biochemical parameters

Test	Value
Amylase	2408 \pm 1802 (277-8917)
Lipase	5511 \pm 4347 (789-13413)
C-reactive protein (IU/L)	33.4 \pm 34.2 (1.4-127)
White blood cell (per mm ³)	9721 \pm 6221 (5900-27200)
Hematocrit (%)	38 \pm 3 (32-46)
Hemoglobin (g/dl)	12.65 \pm 1.06 (11,02-15.60)
Platelet (per mm ³)	248551 \pm 112850 (178000-460000)
Glucose (mg/dl)	127 \pm 34 (83-198)
Lactate dehydrogenase (IU/L)	352 \pm 172 (138-897)
Total bilirubin (mg/dl)	2.10 \pm 1.40 (0.21-8.71)
Direct bilirubin (mg/dl)	1.44 \pm 0.96 (0.10-5.61)
ALP (IU/L)	235 \pm 373 (54-857)
GGT (IU/L)	386 \pm 297 (8-1148)
SGOT (IU/L)	265 \pm 232 (17-1113)
SGPT (IU/L)	341 \pm 259 (8-1114)
Urea (mg/dl)	23.37 \pm 16.4 (10.1-93.4)
Creatinine (mg/dl)	0.68 \pm 0.12 (0.5-1.0)

ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

Table 2. The distribution of the patients according to Balthazar CT Severity Index

Severity Score/Necrosis	n (%)
Grade A	8 (59%)
Grade B	1 (7%)
Grade C	3 (18%)
Grade D	0 (0%)
Grade E	4 (25%)
No necrosis	14 (86%)
Necrosis <30%	1 (7%)
Necrosis 30-50%	0 (0%)
Necrosis >50%	1 (7%)

according to Balthazar CT Severity Index, as demonstrated in Table 2.

MRCP: Seven patients (26%) with abnormal CBD findings in previous diagnostic procedures and/or elevated bilirubin levels underwent MRCP. Of these seven patients, two (7%) were shown to have choledocholithiasis.

Management

None of the patients was found to have additional diseases or any obstetrical risk factors except one who had diabetes and had been taking gliclazide.

Tenderness in the right upper quadrant and epigastric region was the most frequent sign on physical examination. Only one patient (3%) was found to have fever exceeding 38°C. The results of biochemical tests are shown in Table 1. The mean score of severity of ABP according to Ranson criteria was 1.1±1.0 (0-3).

Four patients (15%) with suspected biliary infection had intravenous antibiotherapy with ampicillin-sulbactam (2 g q/h). The antibiotherapy in these patients was stopped after CRP and white blood cell count had returned to normal.

Endoscopic retrograde cholangiopancreatography (ERCP) was carried out in two patients (7%) with choledocholithiasis. These patients were in the post-

partum period. Both patients had endoscopic sphincterotomy and gallstone extraction.

Laparoscopic cholecystectomy was performed prior to discharge in 10 patients (37%) who were all in the post-partum period. None of the patients had peri- or post-operative complications. Seventeen patients (63%) were scheduled for interval cholecystectomy.

Length of stay (LOS) in patients who had cholecystectomy on first admission (n=10) and in patients who had conservative treatment (n=17) was 7.0±2.4 (4-12) days and 5.8±3.6 (2-16) days, respectively. The mean interval between the first admission and cholecystectomy in patients who were scheduled for interval cholecystectomy was 137.4±96.6 (60-440) days.

Two patients (7%) were admitted to the hospital with recurrent pancreatitis episode. Both patients were treated conservatively on their first admission, and had been scheduled for interval cholecystectomy. These patients had their recurrent episode within the eight-week interval. No recurrent pancreatitis episode was observed in the remaining patients within a five-year follow-up period.

The mortality rate was 3% (n=1). The patient was in the post-partum sixth month. Grade D ABP in the initial CT scan and progression of the disease to Grade E and extensive necrotizing pancreatitis are demonstrated in Fig. 1. The patient died 32 days after admission due to systemic complications of ABP.

DISCUSSION

Previous clinical and experimental studies have reported that parity and current or previous oral contraceptive use were both associated with increased risk of biliary stasis and subsequent gallstone formation.^[3-5] This is mainly attributable to elevation in the biliary cholesterol saturation index, reduction in the nucleation time, generalized relaxation of the biliary tree, and decreased response to cholecystokinin stimulation induced by estrogen and progesterone.^[5,6] Gallbladder motility is restored after the end of the first post-par-

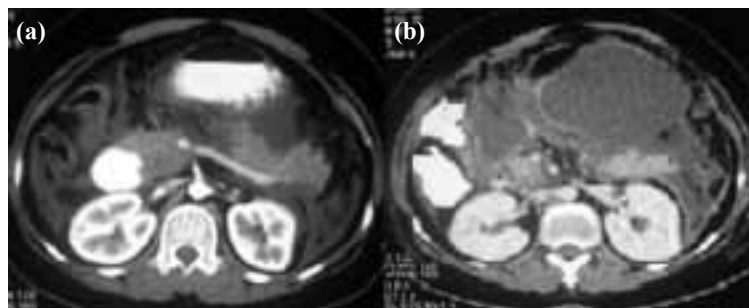


Fig. 1. Multiple peripancreatic collections, and peripancreatic inflammation (a); progression of peripancreatic collections, exudative pancreatitis, extensive necrotizing pancreatitis with the involvement of surrounding organs (b).

tum year. Both the frequency and number of pregnancies are major risk factors for cholesterol gallstones. Several studies demonstrated that the incidence of gallstone-associated biliary diseases correlates with the parity number.^[7-9]

The first step in the management of patients with pregnancy-associated acute pancreatitis should be the clarification of the etiology, since the management of ABP with natural history is quite different from that of acute pancreatitis associated with other etiologic factors.^[10,11] As the patients with ABP are at risk of a potential recurrent pancreatitis episode, it is possible to prevent the recurrence of the disease with early diagnosis and appropriate treatment.

Abdominal sonography is generally accepted as the initial diagnostic procedure in patients with clinical diagnosis of ABP supported with biochemical tests. The patients with predicted or clinically evident severe ABP and those in whom the other causes of acute abdominal pain could not be ruled out should have a contrast-enhanced abdominopelvic CT scan unless there is an absolute contraindication such as pregnancy. In addition, some authors suggested the use of endosonography for the detection of CBD stones and better evaluation of pancreatic tissue as an alternative to CT scan.^[12] MRCP is also useful for the detection of gallstones within the CBD, since sonography and CT have low sensitivities in the diagnosis of choledocholithiasis.^[13] However, the use of MRCP during the first trimester is still controversial.^[14,15] ERCP is utilized for both diagnostic and therapeutic means in ABP when other imaging modalities fail to demonstrate the biliary pathology, particularly small gallstones in the CBD, and for the treatment of CBD stones.

In this review, abdominal sonography was found to be highly sensitive in distinguishing biliary etiologies with direct or indirect findings, while it is relatively insufficient for the evaluation of the CBD and pancreatic tissue. This is most probably due to performance of sonography by the attending resident of radiology under emergency conditions. According to CT results classified by Balthazar CT Severity Index, our review revealed that more than half of the patients had mild ABP and 89% of patients did not have necrotizing pancreatitis, which was relatively inconsistent with Ranson scores. However, timing of the CT obtained for assessment of the severity of pancreatitis is important because of lack of CT findings in the early period of the disease.^[16] Therefore, the patients who had immediate CT scan on first admission could have been under-staged.

Although several scoring systems such as Apache II Scoring System, Ranson System, Imrie Scoring System, Balthazar CT Severity Index, and C-reactive

protein (CRP) are currently used for the prediction or assessment of severity of ABP, there is not yet a completely reliable diagnostic tool. Major drawbacks of the scoring systems mentioned above are complexity of performance for the Apache II System, invalidity after the 48th hour of admission for the Ranson System and Imrie Scoring System, and time-dependent findings and several contraindications of CT for Balthazar CT Severity Index.^[17,18] Of note, because one of the most important prognostic factors in ABP is persistent organ failure, some authors advocated that the Apache II System offered a better evaluation of severity of ABP.^[19,20] Neoptolemos et al.^[21] reported sensitivity and specificity values calculated 48 hours after admission for the Apache II System as 56% and 64%, for the Ranson System as 89% and 64%, and for CRP (cut-off level of 150 mg/L) as 86% and 61%. In contrast, Leung et al.^[22] suggested that Balthazar CT Severity Index had a higher sensitivity in the assessment of severity of ABP than the Apache II System and Ranson System. Nonetheless, regular measurement of CRP levels is the simplest and the most cost-effective method, and furthermore, was found to be as accurate as the other scoring systems. Regarding Ranson scores, Balthazar scores, CRP levels, and clinical courses in our review, pregnancy-associated ABP seems to have a mild-to-moderate course. Our results are compatible with recent reports in the literature.^[1,23,24]

The management of pregnancy-associated ABP is similar on a large scale. Any risks concerning fetal condition in pregnant women and the infant's condition in the case of nursing mothers should be considered. The vast majority of authors worldwide agree about the certain role of appropriate fluid resuscitation and nutrition in ABP treatment; however, the necessity of antibiotics and management of the underlying cause are still controversial. We do not use antibiotics unless there is a concomitant biliary tract infection or verified infected necrotizing pancreatitis, as many authors have suggested recently.^[25] In contrast to initial reports, laparoscopic surgery has been proven to be safe during pregnancy except during the first trimester.^[26-28] Our policy for timing of cholecystectomy in pregnancy-associated ABP is to perform cholecystectomy prior to discharge on first admission except in those in the first trimester and in those who have severe pancreatitis.

The incidence of recurrent ABP varies widely from 0% to 57% depending on the population studied, the initial treatment, and the follow-up time.^[10,29] According to our data, 7% (n=2) of patients who were managed conservatively were admitted and re-hospitalized for recurrent ABP within the eight-week interval. Unfortunately, it is impossible to predict the likelihood, timing or severity of a recurrent ABP episode; there-

fore, it is rational to consider early cholecystectomy in ABP.

In conclusion, pregnancy-associated ABP usually has a mild-to-moderate clinical course with a favorable outcome, and can be managed successfully with conservative treatment. Early cholecystectomy performed prior to discharge should be considered in patients who are in the second and third trimester, and in those who are in the post-partum period, as it is generally accepted for ABP in non-pregnant patients.

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