

The importance of the sphincterotomy in the diagnosis of periampullary carcinoma: analysis of 664 patients who underwent ERCP

Periampuller karsinomanın tanınmasında sfinkterotominin önemi: ERKP uygulanan 664 hastanın değerlendirilmesi

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ÖZET: Amaçlar: Periampuller karsinoma anatomik yeri nedeniyle genellikle erken evrede teşhis edilebilmesine rağmen, vakaların %23-25'inde papillada ülserasyon veya kitle olmaksızın belirginleşme olması nedeniyle sadece duodenoskopi tümörü teşhis edemeyebilir. Serimizde periampuller karsinoma tanısında sfinkterotominin yararlı olduğu gösterilmiştir.

Materyal ve metod: Mart 1985 ile Eylül 1995 arasında Hacettepe Üniversitesi Hastanesinde klinik, biyokimyasal ve/veya sonografik yöntemlerle pankreatikobiliyer sistem patolojisi düşünülen toplam 664 hastaya endoskopik retrograd kolanjiopankreatikografi (ERKP) uygulandı ve tespit edilen tüm lezyonlardan biyopsi alındı.

Sonuçlar: 664 hastanın 66'sında periampuller tümör veya pankreasa ait patoloji tanısı kondu. Bunların 30'u pankreas karsinomu (14'ü baş, 15'i gövde, ve 1'i kuyruk bölgesinde), 10'u kronik pankreatit, 15'i periampuller tümör ve 11'i de diğer patolojilerdi. 15 periampuller karsinomanın hiçbir abdominal kompiütize tomografi, ultrasonografi ve pankreatik anjiyografiyle belirlenemedi. 12'sinde tümörün görülüp biyopsi alınmasıyla kondu. Geriye kalan 3 vakada ise tümör ancak papillotomi sonrasında görülebildi. Tüm vakalar pilor koruyucu pankreatikoduodenektomi ile tedavi edildiler. Ameliyat sonrası "dumping" sendromu izlenmedi. Ameliyat sonrası ortalama sağ kalım süresi 24.2 ay olarak belirlendi.

Sonuçlar: Periampuller karsinoma tanısı koymak için sfinkterotomi öncesi ve sonrasında periampuller mukozanın dikkatli şekilde incelenmesi gerekir. Pilor koruyucu pankreatikoduodenektomi uzun postoperatif sağ kalım süresi ve "dumping" sendromu saptanmaması nedeniyle oldukça başarılı bir yöntem olarak değerlendirildi.

Anahtar Kelimeler: Periampuller Karsinoma, ERKP, Sfinkterotomi, Pilor koruyucu pankreatikoduodenektomi.

ALTHOUGH pancreatic carcinoma is a disease considered by most to have a poor prognosis, those that present as periampullary tumors can have a good prognosis if they are fully resected, having been diagnosed early as a result of an evaluation for obstructive jaundice (1). ERCP with endoscopic biopsy is the preferred diagnostic technique whe-

SUMMARY: Objectives: Although periampullary carcinoma usually can be diagnosed at an early stage because of its strategic location, in a substantial number of cases (23% to 25% of cases of periampullary carcinoma), the papilla can be prominent, but without an identifiable mass or ulceration. As a result, duodenoscopy alone fail to identify the tumor. In this series, the usefulness of sphincterotomy in establishing a diagnosis of periampullary carcinoma is documented.

Materials and Methods: A total of 664 patients, who had clinical, biochemical and/or sonographic evidence of pancreaticobiliary disorders underwent endoscopic retrograde cholangiopancreatography (ERCP) at Hacettepe University Hospital between March 1985 and September 1994 were studied. All identified lesions were biopsied.

Result: In 66 of the 664 patients, a specific periampullary or pancreatic diagnosis could be made. These included 30 cases of pancreatic carcinoma (14 in the head, 15 in the corpus, and one in the tail), 10 cases of chronic pancreatitis, 15 cases of periampullary carcinoma and 11 miscellaneous. None of the 15 periampullary carcinomas was demonstrable by abdominal computed tomography, sonography or pancreatic angiography. In 12, the diagnosis was established immediately by endoscopic visualization of the tumor and biopsy. In the remaining three, the tumor was visualized as a protruding mass only after papillotomy was performed. All cases were treated surgically with a pylorus preserving pancreaticoduodenectomy. No symptoms of dumping were experienced postoperatively. The survival of these 15 patients was good with a mean survival of 24.2 months.

Conclusions: Careful endoscopic examination of the periampullary mucosa before and after sphincterotomy is required to identify periampullary carcinoma; a pylorus preserving pancreaticoduodenectomy revealed excellent post-surgical outcome with no post operative symptoms of the dumping syndrome.

Key Words: periampullary carcinoma, ERCP, sphincterotomy, pylorus preserving pancreaticoduodenectomy.

never a periampullary carcinoma is suspected. It allows for direct endoscopic inspection of the ampulla and biopsy, as well as the performance of cholangio-pancreatography to exclude a diagnosis of pancreatic head or biliary tract malignancy. Occasionally, an ampullary or very distal duct carcinoma (either common bile duct or pancreatic duct) is not visible by direct endoscopic examination.

This is particularly true if the tumor is small (<0.5 cm diameter). In such cases, a sphincterotomy may be necessary to visualize and expose these small tumors, enabling biopsy to be performed.

In 1935, Whipple et al. defined a technique for the radical excision of periampullary carcinomas (2). Since then, pancreaticoduodenal resections have undergone numerous modifications in an effort to reduce the morbidity and mortality associated with the procedure. Although some authors have suggested that the Whipple procedure should be abandoned because of its high rate of morbidity (3-6), recent reports have shown that it can be performed with acceptable morbidity and mortality rates (7-9). More recently, Traverso and Longmire (3) have described an alternative pylorus preserving procedure in an attempt to avoid the oblique post-gastrectomy symptoms of dumping, diarrhea, dyspepsia and weight loss that occur with a true Whipple procedure.

We report a series of 15 cases of periampullary carcinoma, three of which a sphincterotomy was useful in establishing a diagnosis. All were treated surgically with a pylorus preserving pancreatoduodenectomy. With this procedure, no post-operative dumping occurred and the mean survival was as good as if a true Whipple procedure had been performed.

MATERIALS AND METHODS

Patients

During a nine year period from 1985 to 1994, 783 patients with clinical evidence of pancreaticobiliary disease were seen at Hacettepe University Hospital. All 783 were evaluated using ultrasonography. 664 (85%) had an endoscopic retrograde cholangiopancreatogram (ERCP). Additional studies consisting of splenoportography, mesenteric and/or inferior vena cava graphy, abdominal tomography, laparoscopy, liver biopsy and surgical exploration were obtained as indicated in individual cases.

Informed consent

All patients gave written informed consent for each of the diagnostic procedures described.

Endoscopic Procedure

ERCP was carried out in 664 of the 783 (80%) subjects with clinical evidence of pancreaticobiliary diseases using a side-viewing duodenoscope (Olympus JT-IT 20). After cannulation of the pa-

pilla of Vater, contrast material consisting of Con-ray -60 was injected under fluoroscopic control. X-rays were obtained with the patient in the prone position and with the tip of endoscope located in the second portion of the duodenum. Subsequently the radiologic appearance of the biliary and pancreatic ducts was assessed in several different positions. The ERCP findings were compared with those obtained with each of the other diagnostic procedures. Whenever a diagnosis of periampullary carcinoma was entertained an endoscopic biopsy of the lesion was obtained for pathological confirmation.

Radiological Investigations

Ultrasonography

All patients underwent an abdominal ultrasound examination, performed while fasting and in the supine position. All scans were obtained in real time at 3.5 MHz. The common bile duct, the right and left hepatic ducts, the pancreatic duct, the portal vein, the liver and pancreas were examined in each case.

Angiography

In every case with a putative pancreaticobiliary malignancy, celiac arteriography with digital subtraction angiography (DSA) was carried out to determine whether or not there was evidence for vascular invasion or encasement.

Computed Tomography Scanning

Abdominal tomographic images were obtained at sequential five mm intervals in 27 of the patients studied, including all 15 with a periampullary carcinoma.

Biochemical and Serologic Tests

Routine blood and urine analyses were repeated every six months in each case. The biochemical evaluations consisted of the following assays: serum alanine aminotransferase (ALT), gamma glutamyl transpeptidase (GGTP), alkaline phosphatase (ALP) and direct and indirect serum bilirubin. Serum albumin and globulin levels were measured as well as. A panel of tumors markers consisting of alpha fetoprotein (AFP), carcinoembryonic antigen (CEA) and C19-9 was obtained also. Finally, markers of Hepatitis B virus infection consisting of HBsAg, HBsAb, HBcAb and anti hepatitis D determinations were obtained in each case.



Figure 1. ERCP showing common bile duct dilatation and a small mass in the distal common bile duct.

Surgical procedure

All 15 patients with periampullary carcinoma were explored with intent to resect for cure. The proximal resection margin of the duodenum was approximately two cm distal to the pylorus. Great care was taken to preserve the blood supply to the lesser curvature of the stomach and pylorus coming from the left gastric artery. The vagal innervation of the pylorus and antrum was maintained. Enteric reconstruction with an antecolic end to side duodenojejunostomy was performed. All of the surgical procedures were carried out by the same surgical team.

Statistical Analysis

Survival was determined using the method of Kaplan-Meier.

Duration of disease prior to resection was calculated from the date of clinical onset, as defined by the patient's history to the time of the operative procedure. Operative mortality was defined as any death that occurred within 30 days of the surgical procedure.

RESULTS

Of the 664 subjects undergoing an ERCP, 66 (48 men, 18 women, with a mean age of 49 ± 1.7 years ranging from 23 to 69) had some form of pancreatic or peripancreatic pathology identified. This consisted of 30 cases of pancreatic carcinoma (14 in the head, 15 in the body and only one in the tail of the pancreas), 15 cases of pancreatic carcinoma, 10 cases of chronic pancreatitis and 11 cases with miscellaneous pancreatic pathologies.

Of the 15 patients with a periampullary carcinoma, nine were diagnosed as having a carcinoma of the ampulla of Vater, two as a pancreatic carcinoma (located in the head of the pancreas), two had a duodenal carcinoma and two had a distal common bile duct tumor. Jaundice was the principal presenting complaint and was present in 12 (80%) of the 15 patients with a periampullary tumors. The other presenting signs or symptoms were abdominal pain in nine, weight loss in six and pruritis in five. An elevated serum alkaline phosphatase and total bilirubin level were the most common biochemical abnormalities present. Three patients, who initially were suspected of having pancreaticobiliary pathology on the basis of a very high serum alkaline phosphatase level, were found to



Figure 2. A resected specimen reveals a small tumoral lesion just behind papilla.

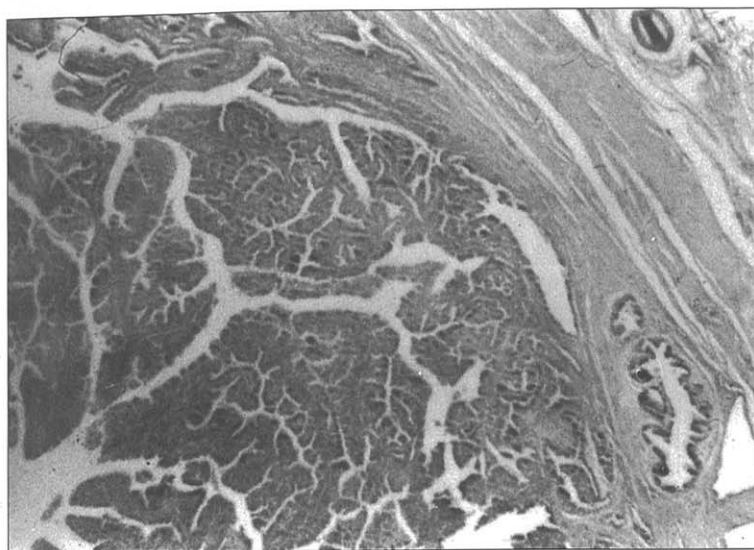


Figure 3. Microscopic examination of the resected specimen shown no tumoral infiltration into the duodenal wall.

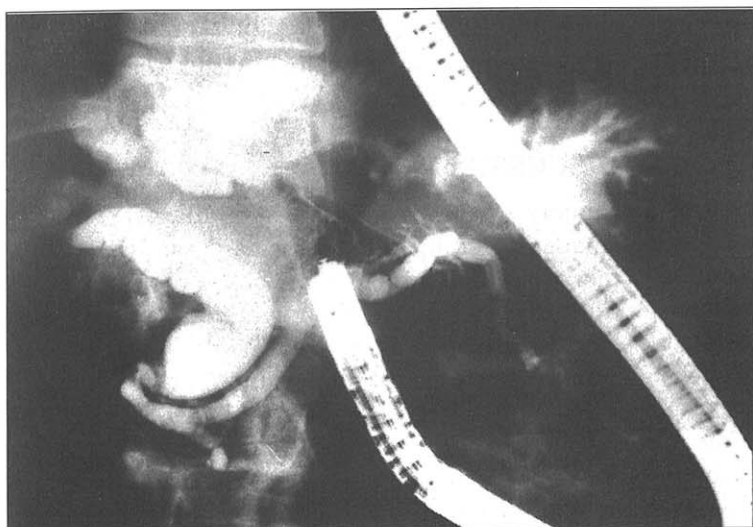


Figure 4. ERCP demonstrates the dilatation in both ducts.

have a small periampullary carcinoma recognizable only after a sphincterotomy was performed. As shown in Fig. 1, the ERCP in one of these cases revealed a dilated common bile duct obstruction, but the lesion responsible for the obstruction could not be visualized until a sphincterotomy was performed. The subsequent surgical specimen documented a tumor located in the periampullary area which was six mm in diameter (Fig 2). Microscopic examination documented the absence of cancer infiltration to the muscular layers of the duodenum (Fig 3). Currently, this patient is alive, doing well with no evidence of disease and has been symptom free for 3.5 years. As seen in Fig four, the second of these three unusual periampullary tumors was located just behind the papilla and was not visible during ERCP until a sphincterotomy was performed, exposing the tumor and enabling it to be bi-

posied. The third periampullary cancer presented with very high alkaline phosphatase like the first case. The ERCP in this case revealed only a dilated common bile duct. After a sphincterotomy was performed, a small tumor was seen protruding from the sphincterotomy site and was biopsied.

In this relatively small series, three of 15 periampullary tumors (20%) were too small to be directly visualized endoscopically and were also missed with sonographic, abdominal computed tomography and ERCP studies, until a sphincterotomy enabled the endoscopist to visualize the tumor protruding into the sphincterotomy site. As exemplified in Fig five, all 15 tumors in this series were located strategically to obstruct the ampulla enabling them to come to medical attention early. Interestingly, two of the three patients with small periampullary tumor detected after sphincterotomy,

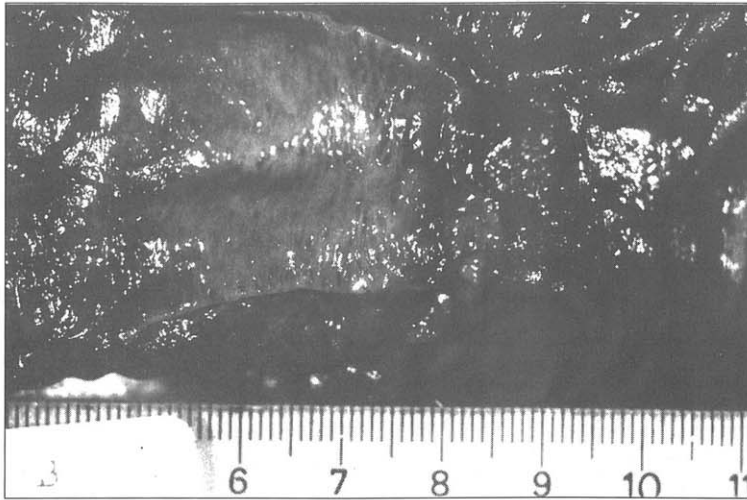


Figure 5. A small periampullary tumor located in a strategic area causing biliary obstruction, a resected specimen.

were not jaundiced despite the presence of overt common bile duct dilatation. The third had a mildly increased serum direct reacting bilirubin level as well as a dilated distal common bile duct.

All 15 underwent surgical resection consisting of a pylorus saving pancreaticoduodenectomy. The mean operative time was six hours. The mean operative blood transfusion requirement was 1.8 units. Nine patients did not require blood transfusion. In all 15 cases, pathologic examination of the tissue confirmed the endoscopic diagnosis. The judgment of the surgeon relative to the adequacy of the surgical resection was correct in 12 cases with an overall accuracy rate of 80 percent. The mean time of postoperative nasogastric intubation and prohibition of oral feeding were five and six days respectively. In the early postoperative period, six patients developed one or another postoperative complication. These included a wound infection, a pleural effusion, an intraabdominal abscess and delayed gastric emptying. The overall complication rate was 40 percent.

None of the patients experienced any postprandial tachycardia, flushing or cramping consistent with the dumping syndrome. No operative mortality or biliary, and/or pancreatic leaks occurred. Moreover, none experienced gastrointestinal hemorrhage, marginal ulceration or jejunal ulceration.

Postsurgical follow-up has ranged from 26 to 90 months. One patient with a carcinoma of the ampulla died 14th months postoperatively. One patient with carcinoma of the head of the pancreas experienced a recurrence at 27 months and died at 31 months. Two patients, one with a duodenal and one with a distal common bile duct cancer died of

disease recurrence 24 and 28 months postoperatively. The mean survival was 24.2 months. Eleven of the patients are still alive with a mean follow-up 41 ± 1.3 months.

DISCUSSION

Tumors of the papilla and ampulla of Vater are frequently grouped together as periampullary tumors (10). The principal reasons why they are grouped together is that their symptoms and the surgical approach to their treatment are essentially the same. Three of the 15 tumors in this series of periampullary tumors were only identified after a sphincterotomy was performed enabling the endoscopist to see and subsequently biopsy the lesion. The macroscopic findings of the three tumors at the time of surgical correlated well with the finding at endoscopy. All three were too small to completely obstruct the bile tree. Nonetheless, all three were associated with clinical and biochemi-

Table 1. Shows characteristics of the 15 patients with various periampullary carcinomas

Characteristics	Values
Gender (Men/women)	13/2
Mean Age, year (range)	49 (29-69)
Means of definitive diagnosis	
Endoscopic biopsy + ERCP findings	12
Sphincterotomy + ERCP + biopsy	3
Location of Tumors	
Duodenal wall @	2
Distal CBD*	2
Distal PD**	2
Ampulla	9

*common bile duct; ** pancreatic duct
@ duodenal wall surrounding the ampulla

cal evidence of incomplete biliary obstruction.

Topazian et al. (11) have reported that cancer can cause sphincter dysfunction not only of the distal esophageal sphincter but also at the level of the sphincter of Oddi. Unfortunately sphincter of Oddi monometry was not available in the present cases and no data relative to this issue are available in this series.

Periampullary carcinoma can be difficult to recognize. The classic triad of jaundice, a palpable gallbladder and anemia with occult gastrointestinal bleeding is not present in most cases. Icterus, the most dependable sign, is absent in as many as 25% of cases. Anemia, a palpable gallbladder, and cholangitis are each present in <50% of cases (12-17). In this series, three of the 15 patients with periampullary carcinoma, were not clinically jaundiced but had an increased serum alkaline phosphatase level which was directly useful in the evaluation and forced the performance of an ERCP and sphincterotomy that enabled the endoscopist to see the tumor.

The papilla in cases of periampullary tumors may appear prominent, without a distinct mass or ulceration being recognized, as was the case in all three of the patients in the current series. In the three cases in this report the small tumors were identifiable only after a sphincterotomy was carried out. In two other recent studies, a prominent papilla without either ulceration or an identifiable mass was observed in 23% and 25% of the cases reported (17,18).

Substantial improvements in the morbidity and mortality rates related to pancreaticoduodenec-

tomy have been reported in the last decade (3,19,20). Serious complications, like pancreatic, biliary and enteric fistula, determine operative mortality. In this series, no major operative morbidity or mortality occurred. Careful evaluation of each patient with particular attention being paid to the presence of volume and electrolyte disorders probably accounts for the good postoperative results in this series (19-21). The use of a pylorus preserving procedure reduced the operative time by eliminating the need for a gastric dissection, resection and vagotomy. Thus, both surgical morbidity and mortality were reduced (22,23). Moreover, post-resection dumping did not occur. Recently, there has been a tendency to be less aggressive in the treatment of ampullary tumors. Asbun et al. (24) have successfully treated patients with ampullary tumor with local resection. Others support this approach (25,26). Clearly, it is quite reasonable that with smaller tumors, less aggressive surgical procedures might be possible. In the present series all were treated with a pylorus preserving pancreaticoduodenectomy with good results.

Based on this clinical experience, it can be concluded that: 1) a combination of a careful endoscopic examination of the periampullary region before and after sphincterotomy, with biopsy of any abnormal appearing tissue is the best method for establishing a diagnosis of periampullary carcinoma; 2) Although the Whipple's procedure is an established procedure, pylorus preserving pancreaticoduodenectomy appears to be a reasonable approach for smaller tumors and is not associated with post-operative dumping.

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