

Late outcome after pylorus preserving pancreaticoduodenectomy for ampullary carcinoma following severe acute post-stenting pancreatitis: case report and review of the literature

Odległe wyniki leczenia po pankreatoduodenektomii z zaoszczędzeniem odźwiernika u chorych na raka brodawki Vatera po przedoperacyjnym protezowaniu dróg żółciowych powikłanym ciężkim, ostrym zapaleniem trzustki – opis przypadku i przegląd piśmiennictwa

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Słowa kluczowe: rak brodawki Vatera, protezowanie dróg żółciowych, ostre zapalenie trzustki, pankreatoduodenektomia z zaoszczędzeniem odźwiernika, powikłania.

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Abstract

Patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) should have stenting of the biliary system to prevent cholangitis. However, the most serious complication of ERCP is pancreatitis. There are only scattered data on the impact of post-ERCP pancreatitis on the surgical management of periampullary tumours. We report the case of a patient with carcinoma of the ampulla of Vater who underwent preoperative biliary stenting complicated with severe acute pancreatitis and was effectively treated by pylorus preserving pancreaticoduodenectomy (PD) 3 months later. In the postoperative course, grade A pancreatic fistula was observed, with no substantial prolongation of hospital stay. Pathological findings revealed stage II ampullary carcinoma with multiple foci of pancreatic necrosis. Three weeks after the procedure, the patient fully recovered, and started adjuvant chemotherapy. Disease free survival DFS was 27 months and OS 44 months. Pancreaticoduodenectomy can be performed after severe acute necrotizing pancreatitis caused by preoperative biliary stenting, provided adequate timing of surgery is ensured, albeit with the risk of postoperative complications. Even severe post-ERCP pancreatitis should not be regarded as a contraindication for curative PD, especially in patients with periampullary adenocarcinoma, since long-term survival can be achieved.

Streszczenie

Pacjenci poddawani endoskopowej cholangiopankreatografii wstecznej (ECPW) powinni mieć wykonywane protezowanie dróg żółciowych, aby zapobiec zapaleniu dróg żółciowych. Najpoważniejszym jednak powikłaniem po ECPW jest zapalenie trzustki. Dane z piśmiennictwa na temat wpływu zapalenia trzustki po ECPW na postępowanie chirurgiczne u chorych na raka brodawki Vatera są niepełne. Autorzy przedstawiają chorobę na raka brodawki Vatera, u której powikłaniem przedoperacyjnego protezowania dróg żółciowych było ciężkie, ostre zapalenie trzustki, które skutecznie leczono wykonaną 3 miesiące później pankreatoduodenektomią (PD) z zachowaniem odźwiernika. W przebiegu pooperacyjnym zaobserwowano wystąpienie przetoki trzustkowej (w stopniu A), bez wpływu na czas hospitalizacji. Wynik badania histopatologicznego potwierdził rozpoznanie raka brodawki Vatera w stadium II z licznymi ogniskami martwicy w obrębie trzustki. Trzy tygodnie po zabiegu pacjentka zakończyła rekonwalescencję pooperacyjną i rozpoczęła chemioterapię uzupełniającą. Przeżycie wolne od objawów choroby wyniosło 27 miesięcy, a przeżycie całkowite 44 miesiące. Pankreatoduodenektomia może być wykonana po ciężkim, ostrym zapaleniu trzustki spowodowanym endoskopowym protezowaniem dróg żółciowych, pod warunkiem podjęcia decyzji o operacji w odpowiednim czasie, z uwzględnieniem ryzyka wystąpienia powikłań pooperacyjnych. Nawet ciężkie zapalenie trzustki po ERCP nie powinno być traktowane jako przeciwwskazanie do PD z zamiarem wyleczenia, zwłaszcza u chorych na gruczolakoraka brodawki Vatera, ponieważ stwarza nadzieję na dobry wynik odległy.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a useful tool in evaluating biliary, ampullary and pancreatic ductal anatomy in patients who require either diagnosis or palliation. While the role of routine preoperative biliary stenting of patients who undergo pancreaticoduodenectomy (PD) is controversial, it is clear that patients undergoing ERCP should have stenting of the biliary system to prevent the sequelae of cholangitis.

One possible cause of an acute, even severe necrotic form of pancreatitis may be the ERCP procedure itself, so-called post-ERCP pancreatitis. The anticipated rate of post-ERCP pancreatitis ranges from 1% to 7% according to data reviewed by the Standards of Practice Committee of the American Society of Gastrointestinal Endoscopy [1]. In patients with suspected sphincter of Oddi dysfunction undergoing sphincter of Oddi manometry, the risk is up to 25% [2]. Unfortunately, despite years of research involving the search for a medication or technique that can reliably decrease the risk of post-ERCP pancreatitis, no clear solution has been found.

The first surgical resection of the ampulla of Vater was performed by Halsted in 1899. Local excision for patients with T1 carcinomas has been advocated by some; however, the question of incomplete tissue resection remains. It has also been suggested that up to 10% of patients with T1 lesions will have local lymph node involvement. For this reason, many groups prefer to perform PD, either the classic Whipple resection or the pyloric sparing procedure. Pylorus preserving pancreaticoduodenectomy (PPPD), in which the antrum and pylorus of the stomach are preserved, is routinely applied by many surgeons, as there is limited oncological value of resection of the antrum. It is believed that preservation of the antrum may lead to better overall long-term function, although this has not been demonstrated in prospective randomized trials. Morbidity associated with the procedure remains substantial, ranging from 25% to 50% [3]. Pylorus preserving pancreaticoduodenectomy is a specialized procedure best performed by those individual surgeons or groups that have sufficient experience and volume to assure satisfactory outcomes. In 2000, both the median postoperative stay declined over time to 8 days and perioperative mortality decreased to 1% [4]. Median survival after resection for carcinoma of the ampulla of Vater is 24 months with 43% 5-year survival [5].

Carcinoma of the ampulla of Vater has a higher resectability rate and a much better survival rate than pancreatic cancer. Pancreaticoduodenectomy is the treatment of choice for this tumour. However, in severe

necrotizing acute (post-ERCP) pancreatitis, immediate PD is not indicated as it is associated with high mortality rates, as well as increased risk of postoperative exocrine and endocrine insufficiency [6]. There are only scattered data on the impact of post-ERCP pancreatitis associated with preoperative biliary stenting on the surgical management of periampullary tumours, as well as late outcome.

We report the case of a patient with carcinoma of the ampulla of Vater who underwent preoperative biliary stenting complicated with severe acute pancreatitis and was subsequently treated by PD with long-term follow-up.

Case report

A 59-year-old female patient with jaundice (serum bilirubin level: 10.8 mg/dl) due to ampullary carcinoma was initially treated by preoperative biliary stenting. After the endoscopic procedure utilizing a plastic stent, she developed the severe form of acute pancreatitis (serum amylase 514 IU/l). Thereafter, the patient was hospitalized in the intensive care unit (ICU) for 3 weeks and treated medically for pancreatitis. After 3 months, both serum bilirubin and C-reactive protein (CRP) levels returned to normal values: 0.3 mg/dl and 2.2 mg/l, respectively. The patient was scheduled for elective PPPD. During the procedure, both the bile and pancreatic necrotic tissue were sampled and sent for microbiological investigation. In the postoperative period, the pancreatic fistula grade was scored according to the International Study Group on Pancreatic Fistula [7].

The course of the operation was uneventful, with no need for blood transfusion (blood loss 400 ml). Due to technical difficulties associated with the presence of pancreatic inflammation and focal necrosis, the procedure duration was 305 min. Both from the bile and pancreatic necrosis samples collected intraoperatively, *Escherichia coli* was microbiologically cultured. After the PPPD, the patient spent 5 days in the ICU, being mechanically ventilated only on the 1st postoperative day (POD 1). On POD 2, elevation of serum amylase up to 188 IU/l was observed, which returned to a normal value (31 IU/l) on POD 3. Mild superficial wound infection was noted on POD 5, and positive culture with *Enterococcus faecalis* from the wound discharge was identified. On POD 7, elevation of serum CRP level up to 159.8 mg/l, together with collection of less than 10 ml of amylase rich fluid from the abdominal drain, was observed. The postoperative grade A pancreatic fistula was recognised and treated medically, with no substantial prolongation of hospital stay. The patient was discharged from hospital on the 20th POD in good clinical condition, fully recovered, on a regular diet. Pathological

findings revealed stage II ampullary carcinoma (pT3N0M0; microscopically radical resection) with multiple foci of (infected) pancreatic necrosis. Four weeks after primary operation adjuvant chemotherapy was implemented in the regimen: gemcitabine 1000 mg/m² with cisplatin 50 mg/m², every 28 days, with good overall tolerance. Local relapse was discovered in September 2009, giving the DFS of 27 months. The patient was enrolled in a chemotherapy regimen of gemcitabine in monotherapy (intravenously in the dose 1000 mg/m² day 1, 8 and 15; repeated every 28 days). Treatment was continued without severe toxicity symptoms for 10 months, including erlotinib for the last 2 courses of chemotherapy. Because of disease progression (multiple liver metastases and ascites), the treatment schedule was changed to the LFP regimen: calcium folinate 20 mg/m², fluorouracil 300 mg/m², cisplatin 20 mg/m² intravenous infusion on days 1-5, given every 28 days, from August to October 2010. Then, due to poor tolerance of chemotherapy and further disease progression, chemical treatment was completed. The patient died 44 months after primary surgery.

Discussion

Post-stenting complications, including pancreatitis, develop in 24% of patients with ampullary cancer [8]. About two thirds of patients after placement of a plastic endobiliary stent may experience postoperative complications following PD [9]. A positive intraoperative bile culture is associated with higher morbidity and mortality rates following PD, and a positive culture in patients with preoperative biliary stenting is related to stent complications and duration of stenting [8]. Therefore, it appears prudent to delay PD for 6 weeks or more in patients who develop complications after stenting, unless serious pancreatitis develops that may considerably influence the surgical management.

Since the 1980s, severe necrotizing pancreatitis has been regarded as a relative contraindication to perform elective pancreaticoduodenectomy [6, 10]. The current report shows that pancreatic necrosis does not preclude delayed PD, especially in a patient with ampullary carcinoma.

Metal stents should be considered for patients with surgically resectable periampullary cancer, since they provide a longer patency rate, fewer ERCP sessions, and fewer episodes of cholangitis without adding any perioperative complications, especially if surgery is not immediately planned [11, 12].

Results of the recent multicentre, randomized trial constituted a milestone in assessing the merits of preoperative biliary drainage [13]. No advantage and a significantly higher rate of serious postoperative complica-

tions in patients undergoing endoscopic stenting before surgery was found in jaundiced patient periampullary malignancies [13]. Although only scattered data are available on early outcome after PD following severe post-ERCP pancreatitis [14], there are no reports on late outcome. It seems that preoperative biliary drainage and the delay in surgery do not adversely affect late outcome, with median survival time for resected periampullary adenocarcinoma of 44.7 months [15]. However, the occurrence of complications related to preoperative biliary drainage or surgery was found to be significantly associated with worse survival [15].

Conclusions

Pancreaticoduodenectomy can be performed after severe acute necrotizing pancreatitis caused by preoperative biliary stenting, provided adequate timing of surgery is ensured, albeit with the risk of postoperative complications. Even severe post-ERCP pancreatitis should not be regarded as a contraindication for curative PD, especially in patients with periampullary adenocarcinoma, since long-term survival can be achieved.

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