CASE REPORT

Management strategy for an advanced head of pancreas carcinoma patient with obstructive jaundice

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ABSTRACT

Background: Pancreatic cancer (PC) is still considered incurable, with overall survival 3–5 months and 5-year survival 3% in advanced stage. Obstructive jaundice often complicates head of pancreas carcinoma. Strategy for bile diversion and chemotherapy regimen choices is needed to prolong survival and good quality of live. **Case:** Male, 64 years old, with abdominal discomfort and jaundice. Abdominal CT scan showed caput pancreas mass 43 mm ×39 mm attached to common mesenteric artery. The FNAB showed adenocarcinoma pancreas well differentiated. The diagnosis of PC adenocarcinoma well-differentiated T3N1M0 Stage III was made. Metal stent placement by ERCP to diverse bile. Chemotherapy with gemcitabine and carboplatin for six cycles, results in stable disease. The patient still has good performance status (PS 0-1), so second line chemotherapy regimen with 5- fluorouracyl, folinic acid, and oxaliplatin were given for 6 cycles. In month 15, the patient wished for oral chemotherapy, and capecitabine was given. His condition deteriorated with peritoneal metastase. The patient passed away in month 26 due to pneumonia and sepsis. **Discussion:** In locally advanced PC, resectability assessment is important. With mesenteric artery contact, resection is impossible. Endoscopic placement of a metallic biliary stent is strongly recommended for diversion. First-line chemotherapy of gemcitabine carboplatin can be given for fit patients. In refractory stage, second-line 5-fluorouracyl, folinic acid, and oxaliplatin significantly extend overall survival. **Conclusion:** Management strategy in advanced pancreatic carcinoma is important due to the poor prognosis nature. Bile diversion and prompt chemotherapy regimen choice can prolong survival and improve patient's quality of live.

KEY WORDS: Bile diversion, Chemotherapy, Pancreatic cancer

INTRODUCTION

Pancreatic cancer (PC) is still considered incurable with short overall survival, 3–5 months and 5-years survival 3% in advanced stage. The unspecific symptoms at the early stages causing most new patients (80%) come in advanced stage. Malignant bile obstruction is a common complication of head of pancreas cancer. Its development contributes to poor outcomes including cholangitis, delay in treatment (including chemotherapy or surgery), decreased quality of life, and shortened overall survival.[1,2] Strategy for bile diversion and chemotherapy regimen choices is needed to prolong survival and good quality of live. Resectability status of the tumor, bile diversion methods options and how long to wait bilirubin decreases before starting chemotherapy will be discussed in this case report. In this report, we present the case of an Asian male with locally advanced PC complicated by obstructive jaundice with survival more than 2 years.

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CASE REPORT

A 64 years old male came with nausea, weight loss, upper abdomen discomfort, and jaundice since a month before. Laboratory result showed increase bilirubin total 6.5 mg/dl and direct bilirubin 5.8 mg/dl. Others laboratory result such as transaminase and renal function was within normal limit. Tumor marker Ca 19–9 increases to 8035 unit/mL. Abdominal CT scan with contrast showed malignant caput pancreas mass 43 mm ×39 mm attached to gastric anthral, duodenal bulb, common mesenteric artery, portal vein, and common hepatic artery. Ten lymph node in abdominal aorta is suspected involved. There is no distant metastase in liver and lung by CT scan. Fine-needle aspiration biopsy is performed with the result

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is adenocarcinoma pancreas well differentiated. The diagnosis of PC adenocarcinoma well-differentiated T3N1M0 Stage III (AJCC) was made.

Jaundice was treated surgically with biliary bypass. Endoscopic retrograde cholangiopancreatography with metal stent placement was done to diverse bile [Figure 1]. The jaundice subsides and in 5 weeks the total bilirubin decrease to 2 mg/dl and direct bilirubin 1.6 mg/dl. Chemotherapy with gemcitabine and carboplatin was performed six cycles, in evaluation there was stable disease. The patient's abdominal discomfort decrease and performance status was good PS 0–1 ECOG. Second-line chemotherapy started with 5-fluorouracil, folinic acid, and oxaliplatin for six cycles. The evaluation showed stable disease with acceptable side effect leukopenia Grade 1. The patient still able to work and witnessed his first grandson birth. However, in month 15, the patient wished for oral chemotherapy only, and capecitabine was given. The clinical condition continues to deteriorate with peritoneal metastase and best supportive care was given. The patient passed away in month 26 due to pneumonia and sepsis.

DISCUSSION

PC was the fourth most fatal cancer in men after lung, colorectal, and prostate cancers in Europe 2014. Pancreatic cancer also the fourth leading cause of cancer death in women after breast, colorectal and lung cancers. The life expectancy is still low about 5% at 5 years and the prognosis has not improved over the past 20 years, The death rate in Europe was 75,439 in 2009 to a projected 82,300 deaths in 2014.[3] PC was diagnosed in 46,420 persons in the United States (US) in 2014 and will cause 39,590 annual deaths according to the American Cancer Society. PC accounts for 2.7% of all new cancer cases in the US and about 4% of cancer deaths worldwide.[4] In our country, Indonesia, there were 4.940 new cases in 2018 and 4.812 death in the same year.[5]

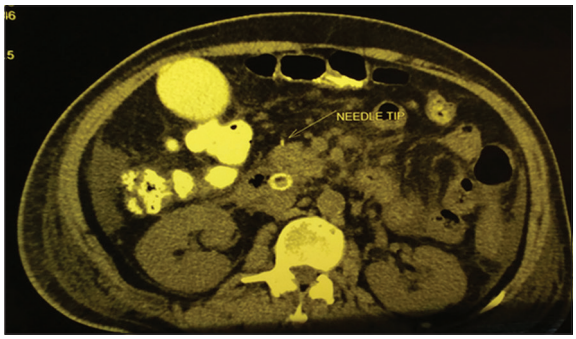

Figure 1: Malignant caput pancreas mass attached to gastric anthral, duodenal bulb, common mesenteric artery, portal vein, and common hepatic artery. Ten lymph node in abdominal aorta is suspected involved. Metal tip in common bile duct

The vast majority (>80%) of PC patients come in locally advanced or metastatic stage due to vague symptoms. Symptoms of PC result from a mass effect, approximately 60–70% of PC arises in the head of the pancreas, 20–25% in the body and the tail, and the remaining 10–20% diffusely involve the pancreas. Presenting symptoms of PC jaundice (head of pancreas tumor), and other none specific symptoms such as abdominal pain, weight loss, and steatorrhea.[6]

Pathology assessment and staging should be made before starting treatment. In patients with locally advanced disease resectability assessment is also important, and this can be performed by multidisciplinary team.[7] American Hepato-Pancreato-Biliary Association consensus report classify pancreatic ductal adenocarcinoma as resectable, borderline resectable, or unresectable.[8] Evaluation of arterial vessels, three situations can exist: Vessel tumor contact <180° without deformation, more than 180° without deformation, or with deformation. Venous vessels evaluation is soft-tissue contact and tears drop deformation at the tumor contact. Abdominal CT scan or MRI are able to determine the non-resectability of the tumor with a high positive predictive value (>90%).[9] In this patient, there is solid tumor contact with superior mesenteric artery, making resection is not possible.

Obstructive jaundice is a frequent complication of PC. In PC before starting systemic chemotherapy, patients with biliary obstruction should be considered for diversion. Many chemotherapy drugs require intact mechanisms of bilirubin excretion and bile drainage to prevent toxicity. Typically, a bilirubin level <2 mg/dL is required before the initiation of therapy. There are two options for biliary drainage, percutaneous drainage or biliary stent in centers with ERCP availability.[2] Endoscopic biliary stent insertion is a well-established method for providing biliary drainage. In addition to symptom relief, biliary stenting may provide the opportunity for further treatment in the form of systemic chemotherapy. A trial by Weston *et al*., 2008, in 156 patients underwent endoscopic retrograde cholangiopancreatography with stent placement.[10] The time to achieve a bilirubin level 2 mg/dL was the primary endpoint because this is the level required by most chemotherapy protocols. Some variables that are considered to have role in the time needed to achieve bilirubin level <2 mg/dL are cancer type, liver metastasis, and previous chemotherapy. Stent variables included type, dimension, stricture location, and sphincterotomy. The 10-year study by Weston *et al*. in 2008 showed that despite comparable survivals, costs to time of death for the endoscopic group are approximately one-half of those expended in surgically treated patients. Hence, in these situations, the adverse nature of biliary obstruction can be

improved with decompression.[10] For palliation, decompression can improve patient comfort by relieving jaundice and pruritus.[11] It can also facilitate treatment by allowing total bilirubin levels to drop to <1.5 times the upper limit of normal, which is necessary to prevent toxicity in some chemotherapy regimen. Waiting time to normalize bilirubin status could be from 3 to 6 weeks, depends on the previous bilirubin level, 6 weeks if previous bilirubin level was >10 mg/dL and 3 weeks if their present bilirubin level was <10 mg/dL.[10]

Depending on performance status, mono or combination chemotherapy can be considered for initial treatment in patients with locally advanced PC. Stereotactic body radiation therapy after initial chemo should be avoided if there is direct contact or invasion of the bowel and stomach.[12] In PS 0-1 patient, first-line chemotherapy of gemcitabine carboplatin can be given. Other options are FOLFIRINOX or gemcitabine –albumin bound paclitaxel. These chemotherapy options are extrapolations from RCT in metastatic disease. Gemcitabine in advanced PC has low toxicity and good compliance because the nausea vomiting side effects are low.[13]

After gemcitabine based chemotherapy evaluation showed refractory stage, second-line 5-fluorouracyl (5-FU), folinic acid, and oxaliplatin were given to extend the duration of overall survival. The FOLFIRI regimen for heavily pretreated locally advanced or metastatic PC with manageable PC showed a modest clinical activity with acceptable toxicity profile. FOLFIRI consists of irinotecan 180 mg/m^2 iv on day 1, leukovorin 200 mg/m^2 iv on days 1 and 2, 5-FU 400 mg/m^2 iv bolus on days 1 and 2, and 5-FU 600 mg/m^2 iv 22 h on days 1 and 2. One cycle repeated every 2 weeks. Other options are FOLFIRINIX, FOLFOX, oxaliplatin/capecitabine regimen, or immunotherapy pembrolizumab in MSI-H dan dMMR tumors.[12,14]

Capecitabine is an oral pro-drug that is converted to 5′-DFUR (5′- deoxy-5-fluorouridine) in the liver and tumor tissue. Saif *et al.*, 2007, reported capecitabine resulted in long-term survivals in two patients with metastatic PC after gemcitabine failure.[15] In this patient who has already treated with two lines of chemotherapy regimens and decreasing performance status capecitabine is an options to prolong survival.

CONCLUSION

Management strategy in advanced pancreatic carcinoma complicated with obstructive jaundice is important. Bile diversion method and prompt chemotherapy regimen choice can prolong survival and improve patient's quality of live.

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