

# Perendoscopic Placement of Palliative Stent for Obstructive Jaundice Caused by Head of Pancreas Malignancy in Dr Moewardi General Hospital-Surakarta

*Aritantri Darmayani, Triyanta Yuli Pramana, Paulus Kusnanto*

Division of Gastroentero-hepatology, Department of Internal Medicine,  
Dr. Moewardi General Hospital, Surakarta

## **Corresponding author:**

*Aritantri Darmayani. Division of Gastroentero-hepatology, Department of Internal Medicine, Dr. Moewardi General Hospital. Jl. Kol. Sutarto No. 132 Surakarta Indonesia. Phone/facsimile: +62-271-663177. E-mail: dr.aritantri@gmail.com*

## **ABSTRACT**

*Pancreatic cancer is difficult to diagnose in early stage. Malignant bile duct obstruction is a severe complication of pancreatic cancer, which can lead to poor outcomes including cholangitis, delayed treatment, reduced quality of life, and increased mortality. Perendoscopic placement of stents is a method widely used in the management of various malignant and benign pancreatobiliary abnormalities. A 70-year-old woman came to Dr Moewardi General Hospital in Surakarta with the chief complaint of yellowish skin and eyes since one month before hospital admission. Patient was diagnosed with obstructive jaundice due to suspected of advanced stage pancreatic cancer. Subsequently, patient underwent endoscopic retrograde cholangiopancreatography (ERCP) which revealed an intrahepatic and extrahepatic bile ducts dilatation due to pancreatic tumor which infiltrated common bile duct, thus self expandable metallic stent (SEMS) placement was performed. Furthermore, patients received palliative therapy due to inadequate chemotherapy requirement.*

**Keywords:** *pancreatic cancer, biliary obstruction, self-expandable metallic stent (SEMS)*

## **ABSTRAK**

*Kanker pankreas sulit didiagnosis pada tahap awal penyakit. Obstruksi duktus bilier merupakan komplikasi tingkat lanjut dari kanker pankreas yang dapat menyebabkan hasil yang buruk termasuk kolangitis, penundaan terapi, penurunan kualitas hidup dan peningkatan mortalitas. Pemasangan stent perendoskopik adalah metode yang banyak digunakan dalam manajemen obstruksi bilier-pankreas baik maligna maupun benigna. Seorang wanita berusia 70 tahun datang ke Rumah Sakit Umum Dr Moewardi di Surakarta dengan keluhan kulit dan mata kuning sejak satu bulan sebelumnya. Pasien didiagnosis menderita ikterus obstruktif et causa karsinoma pankreas stadium lanjut. Kemudian, pada pasien dilakukan endoscopic retrograde cholangiopancreatography (ERCP) yang menunjukkan adanya dilatasi duktus biliaris intrahepatal dan extrahepatal et causa tumor pankreas yang menginfiltrasi duktus koledokus. Oleh karena itu, dilakukan pemasangan self expandable metallic stent (SEMS). Selanjutnya, pasien mendapat terapi paliatif karena persyaratan kemoterapi yang tidak memadai.*

**Kata kunci:** *kanker pankreas, obstruksi bilier, self expandable metallic stent (SEMS)*

## INTRODUCTION

Although the number of pancreatic cancer patients is only about 3% of all cancers in the United States, it is the fourth leading cause of death in both men and women, and it is responsible for 7% of all cancer-related deaths.<sup>1</sup> Pancreatic cancer is difficult to diagnose in early stage. At the time of diagnosis, 52% of all patients having distant metastatic disease, and 26% have regional distribution. The survival rate in 5 years and a year of pancreatic cancer is low.<sup>2,3</sup>

Malignant bile duct obstruction is a severe complication of pancreatic cancer which can lead to poor outcomes including cholangitis, delayed treatment (chemotherapy or surgery), reduced quality of life and increased mortality. For palliative purposes, biliary decompression may improve patients' comfort by alleviating jaundice and pruritus.<sup>4</sup>

Perendoscopic placement of stents is a method widely used in the management of various malignant and benign pancreatobiliary abnormalities.<sup>5</sup> Stent strategies and selection may differ based on clinical scenario and disease stage.<sup>4</sup> In this case report, we reported a geriatric patient who presented with typical obstructive jaundice caused by head of pancreas malignancy.

## CASE ILLUSTRATION

A 70-year-old woman came to Dr Moewardi General Hospital in Surakarta with the chief complaint of yellowish skin and eyes eye complaints since one month before hospital admission. There was significant weight loss and decreased appetite with full stomach complaint and also nausea-vomit. She also mentioned abdominal pain especially in the epigastric and right hypochondriac region. During the episode of illness, there was no fever. History of vomiting blood or black starry stool was denied. No pale (clay) colored stool was found. Previously, the patient was admitted to a private hospital and had an abdominal ultrasound examination. She denied history of diabetes or hypertension. Physical examination found weak general condition and composmentis awareness. There was no abnormality in vital signs. From physical examination of the eye, pale conjunctiva and icteric sclera was found. Further, lung and heart were within normal limits with no hepatosplenomegaly. There was positive Murphy sign, palpable vesica fellea in the right hypochondriaca region (positive courvosier sign), no peripheral lymphadenopathy and no edema of the legs.

Laboratory results showed mild anemia (9.8 g/dL),

normal leukocyte count (9200 u/L), normal platelet count (455000 u/L), with slightly elongated bleeding time (INR 1.59). There were hyperbilirubinemia with dominance of direct bilirubin (initial total bilirubin level was 40 mg/dL then 32.74 mg/dL, direct bilirubin 21.28 mg/dL, indirect bilirubin 11.46 mg/dL), increased alkali phosphatase (964 u/L), increased gamma glutamyl transferase (490  $\mu$ /L), increased transaminase enzymes (AST 164 u/l, ALT 82 u/L), normal urea and creatinine level, mild hypokalemia (3.1 mmol/L). Examination of tumor markers showed normal limit of alpha feto protein (AFP) and significant increase of Cancer Antigen (CA) 19-9 >500 U/mL.

The abdominal ultrasound examination performed in the previous hospital described intrahepatic biliary obstruction caused by suspect of cholangitis, dilated vesica fellea with cholecystitis and sludge in it. A thoracic photo revealed aortosclerosis. Magnetic resonance imaging (MRI) and magnetic retrograde cholangiopancreatography (MRCP) showed that pancreatic head mass suspicion of malignancy which attached to the surrounding tissue and caused obstruction of intrahepatic and extrahepatic obstruction of biliary system; blood vessel supply was derived from branches of the superior and inferior pancreaticoduodenal artery; lymphadenopathy in the paraaortic and parailiac regions; hydrops vesica fellea accompanied with cholangitis, cholelithiasis and multiple choledocolithiasis. Examination of esophagogastroduodenoscopy showed gastritis and duodenal bulbus ulcer (Forrest III).

Patient was diagnosis with obstructive jaundice due to suspected of advanced stage pancreatic cancer. Subsequently, patient underwent endoscopic retrograde cholangiopancreatography (ERCP) which revealed intrahepatic and extrahepatic bile ducts dilatation due to pancreatic tumor which infiltrated the common bile duct. Further, self-expandable metallic stent (SEMS) Boston Wallflex Uncovered 10 mm 8 cm placement was performed.

After undergoing therapeutic ERCP patient did not experience any post-ERCP side effects such as pancreatitis, bleeding or infection. Furthermore, patients received palliative therapy. One week evaluation of post-insertion of SEMS showed significant decrease of bilirubin (total bilirubin 22 mg/dL then 10 mg/dL, direct bilirubin 7.31 mg/dL and indirect bilirubin 2.69 mg/dL). Finally, the patient was allowed to be outpatient with performance status score 3 of Eastern Cooperative Oncology Group (ECOG).

## DISCUSSION

Pancreatic cancer is the fourth cause of death in the world.<sup>1,2</sup> The average of new case is 28,000 per year with most cases are found at a later stage. Whereas in developing countries, it is ranked as the fifth cause of death after lung cancer, stomach cancer, colon cancer, and breast cancer. Most cases were often found (approximately 80%) in the age between 60-80 years old, while case in the age < 40 years old is rare. These cases are more common in men than women. The location of pancreatic cancer was found to be at most 65-75% in the head, 15-20% in the body, and only 5-10% in the tail.<sup>2,6</sup> The 5-years survival rate in the overall stage is 5-7% while the survival rate in 1 year is only 28%.<sup>2,3</sup>

Stomachache is the most common complaint in patient with pancreatic cancer, which account for approximately 80%. The area of pain depends on the location of the lesion. Most of pain radiates to the back. Other symptoms include yellowish eyes and skin (jaundice), anorexia, weight loss, diarrhea and pale stool. The presence of bloody stool shows the presence of tumor erosion to the duodenum. History associated with diabetes mellitus, symptoms of chronic pancreatitis, obesity, smoking, long-term medication consumption, alcohol consumption, daily habits in processed food and diet, history of genetic and other factors are useful to retrieve. The presence of diabetes mellitus with symptoms of pain, anorexia, and weight loss are present in 70% of pancreatic cancer cases. Acute pancreatitis might occur as an effect of the pressure in the pancreatic duct.<sup>7</sup>

The patient was a 70-years-old woman with suspected pancreatic cancer, this way in accordance with the epidemiology of the disease. Upon admission, patient's chief complaints were yellowish skin and eyes accompanied with significant weight loss. Patient also complained of indigestion in the form of decreased appetite, nausea and occasional vomiting. This was in accordance to the findings of MRI-MRCP investigation results that indicated the presence head of pancreas mass attached to surrounding tissue which caused biliary obstruction.

Clinical symptoms of pancreatic cancer are not specific in the early stage. Whereas, if there are any signs of biliary system blockage, especially if the location of lesion is on the pancreatic head, physical examination of the patient shows yellowish eyes and skin (jaundice) with pruritus, cachexia, and sometimes enlarging gallbladder (Courvosier sign) in 20-25% of cases. The presence of ascites, hepatomegaly,

Virchow's nodes (Left supraclavicular adenopathy), Sister Mary Joseph's node (periumbilical adenopathy) suggest metastases, whereas stomach blockage indicated advanced stage and poor prognosis.<sup>2,7</sup> Non-complicated obstructive jaundice is largely due to pancreatic head lesions.<sup>8</sup> Head of pancreas is a common site for carcinoma. Most of these cases arise in the head of the pancreas from ductular epithelium, but may also develop from pancreatic acinar cells, the lining of the low bile duct, the ampulla of Vater (papilla) or rarely the duodenum. Five-year survival following resection is 40-70% for ampullary and only 10-20% for pancreatic carcinoma.<sup>9</sup>

The effects of carcinoma in the ampullary region consists of: (1) General effects of malignant disease-weakness, weight loss; (2) Obstructed common bile duct; dilated gallbladder and bile ducts-jaundice, pruritus; (3) Obstructed pancreatic duct-steatorrhea, diabetes; (4) Local invasion: blood vessels (portal, superior mesenteric)-encasement, thrombosis; nerves-back and epigastric pain; (5) Duodenal invasion-occasional duodenal obstruction, positive occult blood; (6) Tumor metastases-regional glands, liver, lungs, peritoneum.<sup>9</sup>

Patients who have mass in the pancreatic capillary (part of the periampullary region carcinoma) experience symptoms and signs corresponding to the extra and intrahepatic biliary obstruction, accompanied by vesicofellea dilatation (positive Courvisier sign). There was no invasion to celiac vessels, superior mesenteric, portal to the inferior cava vein. The pancreatic mass was supplied by the superior and inferior pancreaticoduodenal artery branches. However, patients could be categorized as having advanced stage disease because of the presence of metastases into non-regional lymph nodes (paraortic and parailiac lymph nodes). The presence of typical features of symptoms, signs, imaging and significant increase of CA 19-9 (typical tumor marker) could strengthen the suspicion of advanced stage pancreatic cancer (stage IV) according to the American Joint Committee on Cancer (AJCC). Based on that stadium, the prediction of this patient's survival in 5 years was only 2%.

Tumor marker is one of the investigations performed for identifying or screening for cancer. Cancer antigen (CA) 19-9 is the only tumor marker recommended by the National Academy of Chemical Biochemistry (NACB), European Group on Tumors and American Gastroenterological Association (EGTM) to screen for pancreatic cancer. CA 19-9 is also used to assess the prognosis and monitor the response of the treatment

that had been given. The sensitivity of CA 19-9 is 70-90% and specificity is 90%. The combination of CA 19-9 and the imaging diagnostic examination raise the suspicion of pancreatic cancer.<sup>2</sup>

Only 10% of patients with non-metastatic local disease are allowed for resection surgery. Outcome is better in patients with small tumors (< 3 cm), well-differentiated tumors and with no lymph node involvement. Approximately 30% of locally advanced patients can not be resected although having no metastasis. Approximately 60% of patients have metastases. Patients with poor performance status do not get benefit from chemotherapy.<sup>7</sup> The definition of patient which can be resected or not is considered by the presence of involvement of the celiac artery, superior mesenteric artery, portal vein or inferior vena cava and the presence of distant metastases (including non-regional lymph node metastasis).<sup>10</sup>

The management of pancreatic cancer patients with distant metastases is placement of SEMS in the presence of jaundice. If the patients have good performance status, they can get various chemotherapy options. However, if the patients have bad performance status, they can get chemotherapy with gemcitabine or receive palliative therapy.<sup>10</sup>

Because there were an unresectable advance stage disease due to the involvement of distant lymph nodes and an obstructive biliary system, we performed ERCP and SEMS placement to the patient. The patient had symptomatic ECOG 3 score, where more than 50% of her activity was in bed, but not bed-bound (still limited to own limited requirement, 50% confined to bed or chair). Furthermore, patient was given palliative management and did not receive chemotherapy due to inadequate chemotherapy requirement (such as still had hyperbilirubinemia).

Appropriate ERCP indications are jaundice caused by biliary obstruction (appropriate therapeutic maneuvers performed during the procedure) and pancreatic duct disorders.<sup>11</sup> In his review, Higuera et al conclude that treatment of pancreatic cancer at old age patient with score of ECOG > 2 is palliative therapy. Biliary obstruction was observed in more than 70% pancreatic cancer patients and most of them had perendoscopic stents placement and resolution is obtained in 90% of cases. Biliary bypass surgery was an advanced option in patients who were not effective with stent.<sup>12</sup>

To achieve a longer duration for patency of the stent, SEMS is preferred than plastic stents. Based on previous study, it is said that plastic stents had more complications and higher rate of hospitalization

compared with metallic stent. Although SEMS is more expensive than plastic stents, the existing data indicates its superiority in the patency and outcome of patients (safer and more cost effective).<sup>4</sup>

More recent literatures had focused on comparing the different types of SEMS used in patients undergoing neoadjuvant therapy or in palliative cases. Major categories of SEMSs include uncovered (USEMSs) and covered (CSEMSs) groups. USEMSs have a mesh design that allows them to embed in the biliary duct wall but it also makes them susceptible to tissue ingrowth, which can lead to occlusion in as many as 20% of patients. CSEMSs are designed to prevent tissue ingrowth, but because of this they are known to have increased rates of migration.<sup>4</sup>

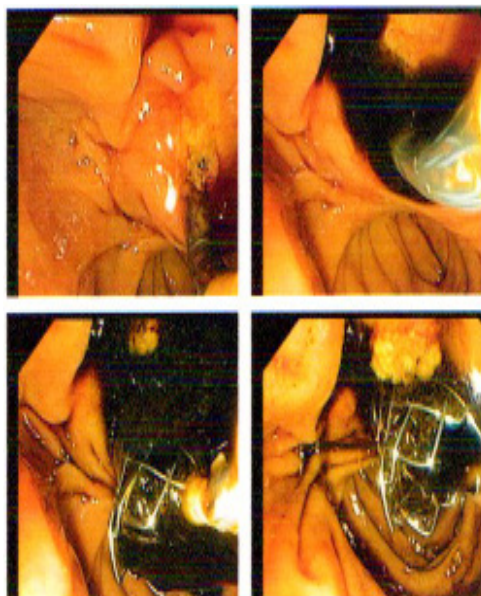
To our patient, we performed stent placement using SEMS Boston® Wallflex Uncovered 10 mm 8 cm, thus the possibility for migration from SEMS was less. As for reocclusion causing biliary reobstruction might happen in the future, the patient required to be re-observed.

Another focus in the management of malignant biliary obstruction is the placement of stents for palliative purposes in non-curable pancreatic cancers. The rationales for stent placement occurs in patients with neoadjuvant therapy are reducing jaundice and pruritus, normalizing bilirubin levels for palliative chemotherapy and preventing other complications such as cholangitis, recurrent hospitalization, and overall quality of life improvement. However in patients with advanced disease and short life expectancy, using SEMS because long-term stent patency is not an objective in this case. Plastic stents will be more effective in cost in patients with distant metastases and short-life expectancy.<sup>4,13</sup>

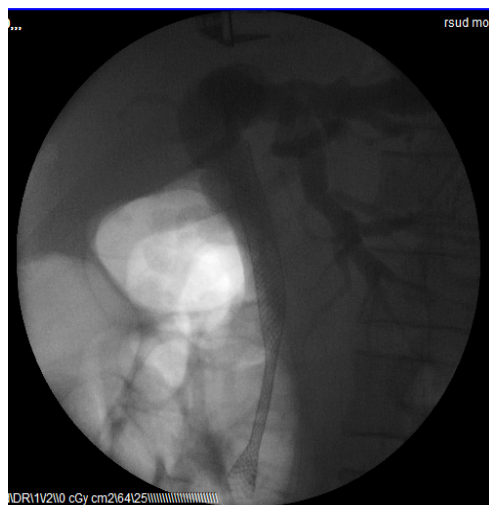
A meta-analysis study showed that SEMS is only cost-effective if patient survival is > 4 months (studies show that patients with liver metastases have a median survival time of 2.7 months compared with 5.3 months in patients without liver metastases). Other study concluded that SEMS should be useful in patients with no distant metastases.<sup>4</sup> According to Sperti et al, although the involvement of paraaortic lymph nodes was one form of distant metastases, but paraaortic lymph node metastases was only associated with short survival rates in univariate analysis. Sperti et al concluded that paraaortic lymph node metastases was not an independent prognostic factor.<sup>14</sup>

Patients obtained palliative SEMS insertion in accordance to NCCN guideline. Based on the AJCC criteria the patient had entered at stage IV disease due to metastases to the paraaortic and parailiaca

lymph nodes. In general, the prediction of survival in 5 years of stage IV is 2%, but this might be different because paraaortic lymph nodes were not independent prognostic factors.



**Figure 1. Perendoscopic placement of SEMS in pancreatic head malignancy**



**Figure 2. Fluoroscopy of SEMS in pancreatic head malignancy**

## CONCLUSION

Malignant biliary obstruction due to pancreatic cancer is associated with poor outcomes and low survival rate. Biliary decompression can improve the quality of life and mortality of patients. The role of stent placement in biliary decompression is more pronounced in locally advanced disease and patients with incurable for palliative purposes. Several studies had demonstrated the superiority of SEMS compared to plastic stents in long-term stent patency and improvement in patient outcomes.

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