Original Paper

Upper Gastrointestinal Bleeding -Initial Manifestation of Pancreatic Head Carcinoma

C.V. OBLEAGĂ¹, C.C. VERE², S.Ş. MOGOANȚA¹, C. FIRUȚ¹, C. MEȘINA¹, M.C. CIORBAGIU¹, C.S. MIREA¹, I.D. VÎLCEA¹

¹Department of Surgery, University of Medicine and Pharmacy Craiova, Romania

²Department of Gastroenterology, University of Medicine and Pharmacy Craiova, Romania

ABSTRACT: Pancreatic head carcinomas are a rare cause of upper digestive bleeding and the diagnosis and the treatment of these pose particular problems. We selected 6 cases from a number of 283 patients who were hospitalized for surgery between January 2014 and December 2016 with signs of upper digestive bleeding with no varicose origin who were subsequently diagnosed with pancreatic head carcinomas. The diagnosis was established by endoscopic and surgical methods. The evolution of these patients was influenced by whether there was active digestive bleeding or history of digestive bleeding and the possibility of tumor resection. Four patients needed emergency surgery due to continuous bleeding or rebleeding. The resectability of the cephalo-pancreatic tumor was determined and then subsequently performed in two patients who had a favorable postoperative outcome, while in two patients the tumor resection was impossible. The other two patients with upper digestive haemorrhage responded favorable to drug therapy, and digestive endoscopy and CT explorations were negative. After a 5-month interval they presented with clinical signs of a pancreatic neoplasm with invasion into the common bile duct, unwanted weight loss, abdominal pain, and icterus of the sclera and skin. The surgical intervention resulted in the confirmation of locally advanced pancreatic head carcinomas and the performing of bilio-digestive derivations. Pancreatic head carcinomas may be associated with upper digestive tract haemorrhage due to duodenal or bile duct invasion. The clinical picture of these patients can vary from occult haemorrhage to severe upper digestive tract haemorrhage accompanied by hypovolemic shock.

KEYWORDS: upper gastrointestinal bleeding, pancreatic head carcinomas, melena

Introduction

Pancreatic head carcinomas are a rare cause of upper digestive bleeding, and a primary diagnosis by endoscopic or radiological techniques can be unsuccessful. A small number of patients with cephalic pancreatic neoplasms have upper digestive bleeding as the initial clinical manifestation [1]. Abdominal pain, jaundice, nausea and vomiting are general symptoms caused by pancreatic neoplasm and can be controlled by medical or surgical treatment. Instead, upper digestive tract bleeding manifested by hematemesis, melena or hematochezia due to invasion in neighboring organs such as the bile duct, duodenum, stomach, jejunum and colon pose difficult treatment problems. From these symptoms, bleeding from the duodenum or the bile duct is the most difficult to control. Approximately 35.7% of patients with pancreatic neoplasm have duodenal invasion [2] and 2.6% of patients with pancreatic cancer have an upper gastrointestinal bleeding episode [3]

Pancreatic head carcinomas is a rare cause of digestive haemorrhage exteriorized by melena or hematochezia and it is extremely rare for hematemesis to be the initial manifestation of invasive pancreatic cancer [4]. In general, haemostatic methods for haemorrhage of the duodenal mucosa includes endoscopic haemostasis, arterial embolization and surgery. Failure of hemostasis results in an extremely poor prognosis and surgical intervention poses particular problems with a high mortality rate [5]

Cases reports

In our study we have 6 cases of upper digestive bleeding exteriorized through hematemesis. melena or hematochezia. accompanied in some cases by haemorrhagic shock, having a pancreatic neoplasm as the primary lesion. The 6 cases (2.12%) were selected from a group of 283 patients who were admitted in the Surgery Department of Craiova County Emergency Hospital from January 2014 to December 2016 who showed signs of nonvaricose digestive tract bleeding, who were subsequently diagnosed with pancreatic head carcinomas. The treatment of these cases were influenced by the evolution of the upper digestive haemorrhage. We established the final diagnosis through imaging techniques, surgery and by necropsy. The patients included in this study were fully informed about the aims and purpose of future medical publications and agreed to offer their case data towards publishing. For the patients that were

unconscious and needed urgent surgery we obtained the written agreement from their family.

The rarity of cases limits our ability to study these aspects of upper digestive haemorrhage. Even in bigger departments there are a small number of cases where upper digestive haemorrhage is the first symptom of a pancreatic head carcinomas. The mean age of our patients was 68.1 years, with a range between 45 and 78 years. Four cases presented with melena at admission, not accompanied by other clinical and biochemical samples showed signs, moderate anemia (Hgb: 8g/dl). One patient presented with hematemesis accompanied by melena, and one patient with hematochezia; both of whom had hypovolemic shock and severe anemia, which indicated emergency surgery. All cases received drug therapy specific to the upper digestive bleeding with PPI's and fluid/electrolyte resuscitation. Upper digestive endoscopy was performed on 4 patients who were hemodynamically stable and responded to drug therapy. For upper digestive endoscopy, PENTAX EG-290 and ELVIS EXERA III OLYMPUS endoscopes were used. In two cases the source of the bleeding was discovered,

bleeding through the duodenal papilla, in two cases the hemorrhagic lesion was not seen. Patients who were assessed via endoscopic procedures where the source of bleeding was identified required surgical treatment. Re-bleeding indicated surgical intervention. Patients who were not investigated by endoscopic procedures received emergency surgery when they were diagnosed with upper digestive bleeding and hypovolemic shock. The most important time of the intervention was represented by intraoperative exploration and assessing the resection criteria for the tumor. In cases of upper digestive tract bleeding accompanied by hypovolemic shock, we found pancreatic tumors (head of the pancreas) that invaded the duodenal mucosa, but without extension to surrounding organs (stomach, upper mesenteric vessels. colon and transverse mesocolon). The duodenal invasion was found is sections I and II of the duodenum. Cephalic duodenopancreatectomy was practiced with abandoned pancreatic stump. The postoperative outcome was slowly favorable. The pancreatic fistula had a long evolution (on average 60 days) and required daily dressing. Hospitalization lasted about 15 days.



Fig. 1. Resection sample: antrum, duodenum, pancreatic head with haemorrhagic Cephalo-pancreatic tumor with invasion in sections I and II of the duodenum. Cephalic duodenopancreatectomy

For patients with biliary tract bleeding, surgery was performed at 4 and 8 hours after the first medical examination.

In both cases, drug-specific therapy for upper gastro-intestinal bleeding had a favorable outcome, but bleeding relapse required surgical intervention. Blood samples also showed a decrease in Hgb and Hct with an increase in total bilirubin (3.2mg/dl) due to increase of direct bilirubin (2.5mg/dl). In both cases, the intraoperative exploration showed a large pancreatic tumor which invades n the upper mesenteric pedicle, the portal vein and the celiac trunk; multiple lymphnode metastasis (hepatic pedicle) and hepatic liver metastases. The ligature of vascular pedicles was impossible. The prognosis was poor.



Fig. 2. Intra-operative aspect: voluminous tumor of the pancreas which invades the transverse colon and transverse mesocolon

In the case of patients with upper gastrointestinal bleeding in whom the haemorrhagic lesion was not seen via endoscopic procedures; abdominal CT scan was performed and abdominal pathology was not found.

During hospitalization patients no longer had clinical signs of digestive haemorrhage.

After a period of 5 months, patients presented with jaundice, and diagnostic imaging, respectively scan/MRI detected CT а cephalo-pancreatic tumor with secondary hepatic metastasis.

Intraoperative exploration revealed pancreatic tumors and secondary liver metastasis in both lobes. In both cases palliative surgery and biopsies were performed which confirmed the malignancy of the tumor. Long term survival in such cases is limited.

Discussions

Pancreatic head carcinomas is a rare cause of upper digestive tract haemorrhage, clinically represented by hematemesis, melena or hematochezia [6,7].

Pancreatic tumors in the cephalic region may be associated with signs of upper digestive tract haemorrhage due to the invasion of the duodenum, stomach and the bile duct.

An important feature is the variability of the symptoms of these pancreatic tumors [3] which were manifested as an episode of upper gastrointestinal bleeding with serious bleeding, or mild bleeding that later worsened or occult bleeding.

Clinicians should be aware that pancreatic malignancy may have a wide range of gastrointestinal bleeding ranging from occult hematemesis to hypovolemic shock or exsanguination [3].

In the cases where endoscopic exploration did not reveal bleeding lesions and imaging (computer tomography) did not capture abdominal tumors, they followed a typical continuation of evolution in pancreas neoplasia; although, the onset of upper occult digestive haemorrhage is not typical for this type of malignancy. The appearance of jaundice by invasion of the bile duct required surgical procedures to drain the main biliary tract. In 4 cases where emergency surgery was needed, the decision to surgically intervene was determined by the evolution of the digestive haemorrhage, respectively the continuation or relapse of stopped bleedings.

Upper digestive tract endoscopy in such cases has more of a diagnostic rather than therapeutic role. In the case of upper digestive haemorrhage due to a pancreatic neoplasm, where bleeding is minimal and can be stopped by drug therapy; upper digestive endoscopy cannot detect the source of bleeding [8]. The most important step of surgery is represented by intraoperative exploration and the determination of resectability of the pancreatic tumor [9]. Tumor resection was performed in 2 patients (cephalic duodenopancreatectomy) with postoperative evolution immediately favorable. Local development without the invasion in neighboring structures was also the decision of tumor resection. We decided in the case of the two patients with resected cephalo-pancreatic conducting cephalic tumors. а duodenopancreatectomy without anastomosis of the remaining pancreatic stump. This decision was taken because of the real anastomotic leakage risk, given that the patients are anemic and with multiple electrolyte and protein deficiencies [10]. In one case, we performed a duodenopancreatectomy cephalic with preservation of the pylorus (Transverso-Longmire), and in another case the gastric section was at the level of the antrum. The resection of the pylorus was determined by the presence of tumor invasion into the pyloric wall. Restoration of the digestive tract was accomplished by gastro-jejunal anastomosis and hepatico-jejunal anastomosis "Y a la Roux". The biliary anastomosis was performed in both cases on a tutor tube due to the normal size of the main bile duct. In these patients, pancreatic fistula was the norm with an average evolution time of 60 days. Anatomic pathology and immunohistochemistry examinations confirmed

the pancreatic origin and established the malignancy of the tumor. Both patients received chemotherapy. If a case had a favorable evolution at over time (6 and 12 month evaluations did not show signs of further progression), in the second case (where the pylorus was not preserved), evolution was influenced by the occurrence of liver metastases. We appreciate that the presence of metastasis in these cases was influenced by the tumor size.

In the other two cases, where the tumor couldn't be surgically removed due to advanced extension and invasion (the upper mesenteric pedicle, the portal vein and the celiac trunk), the evolution was unfavorable. Concomitant arterial embolization techniques may be a temporary or permanent option for haemostasis [11].

In patients without a positive endoscopic or imagistic diagnosis for the source the haemorrhage who developed obstructive jaundice due to bile duct invasion, without indication of tumor resection (advanced locoregional invasion and secondary hepatic metastasis), palliative bilio-digestive derivatives (cholecysto-gastric were performed anastomosis). In these patients imaging did not incipient lesions. Nowadays. reveal а combination of imaging methods is used for a correct and early diagnosis, investigations such as ERCP, Colangio MRI, CT scan and exploratory laparotomy or laparoscopy for patients with high risk [12,13]. In these cases, serologic biomarkers may be very useful in early detection, and histology-based markers may have an important role in differentiating benign lesions from those pre-malignant and malignant [14].

Conclusions

Pancreatic head carcinomas may be associated with signs of upper digestive tract haemorrhage, and the progression of these patients is determined by the evolution of the digestive bleeding. Initial conventional diagnostic evaluation by endoscopic and radiological techniques may be unsuccessful. Patients with upper digestive haemorrhage episodes who responded to primary drug therapy and whose source of bleeding is not determined may have a pancreatic head neoplasm. The treatment of complicated pancreatic head carcinomas with upper digestive haemorrhage is complex, and haemostasis surgery procedures have a high mortality. Blood embolization techniques may be a temporary or permanent way of obtaining haemostasis in such cases.

Acknowledgments

This study was financially supported by the project: "The role of Helicobacter pylori infection in upper gastrointestinal non-variceal bleedings. An endoscopic, serological and histopathological study" sponsored by "The Medical Center Amaradia" (Contract No. 723/25.06.2014, partner of University of Medicine and Pharmacy of Craiova).

References

- 1. Ryoji Takada, Tatsuya loka, Hironari Sueyoshi, Ishida, Takuo Yamai, Nobuyasu Nobuko Fukutake, Reiko Ashida, Hiroyuki Uehara, Akemi Takenaka, Tomita. Yasuhiko Kazuhiro Katayamaa. Duodenal Hemorrhage from Pancreatic Cancer Infiltration Controlled through Combination Therapy with Gemcitabine and S-1. Case Rep Gastroenterol; 2014; 8(2):221-226.
- 2. Tanaka M. Pancreatic Cancer Report, Suizou; 2007; 22:86-88.
- 3. Lee P, Sutherland D, Feller ER. Massive gastrointestinal bleeding as the initial manifestation of pancreatic carcinoma. Int J Pancreatol; 1994;15:223-227.
- Tomita H, Osada S, Matsuo M, Shimokawa K. Pancreatic cancer presenting with hematemesis from directly invading the duodenum: report of an unusual manifestation and review. Am Surg; 2006; 72(4):363-366.
- Yueh-Hung Lin, Chih-Yen Chen, Chih-Ping Chen, Tien-Yin Kuo, Full-Young Chang, Shou-Dong Lee. Hematemesis as the initial complication of pancreatic adenocarcinoma directly invading the duodenum: A case report. World J Gastroenterol; 2005; 11 (5):767-769.

Moosa AR, Levin B. The diagnosis of "early"

- pancreatic cancer. Cancer. 1981; 147: 1688-1697.
 6. Fernandez del Castillo A, Warshaw AL. Diagnosis and preoperative evaluation of pancreatic cancer with implications for management, disorders of the pancreas. Sternberg W, ed: WB Saunders, Philadelphia. 1990; 915-933.
- 7. Forsmark GC, CM Wilcox, Grendel JH. Endoscopy-negative upper gastrointestinal bleeding in a patient with chronic pancreatitis. Gastroenterology; 1992; 102:320-329.
- Bachmann J, Michalski CW, Martignoni ME, Büchler MW, Friess H. Pancreatic resection for pancreatic cancer. The Official Journal of the International Hepato Pancreato Biliary Association; 2006; 8(5):346-351.
- Cosmin Vasile Obleagă, Cristin Constantin Vere et al. Severe upper gastrointestinal bleeding determined by a gastric lymphoma associated with Helicobacter pylori positive atrophic gastritis. Rom J Morphol Embryol; 2017; 58(2):611-617
- Steckman ML, Dooley MC, Jaques PF, Powell DW. Major gastrointestinal hemorrhage from peripancreatic blood vessels in pancreatitis. Treatment by embolotherapy. Dig Dis Sci; 1984; 29(6):486-497.
- 11. McSweeney SE, O'Donoghue PM, Jhaveri K. Current and emerging techniques in gastrointestinal imaging. J Postgrad Med; 2010; 56:109-116.
- Galasso D, Carnuccio A, Larghi A. Pancreatic cancer: diagnosis and endoscopic staging. Eur Rev Med Pharmacol Sci; 2010; 14:375-385.
- Vasco Eguia, Tamas Adam Gonda, Muhammad Wasif Saif. Early Detection of Pancreatic Cancer: ASCO Gastrointestinal Cancers Symposium 2012. J Pancreas; 2012; 13(2):131-134.

Corresponding Author: C.V. Obleaga, Department of Surgery, University of Medicine and Pharmacy Craiova, Romania, SCJU Craiova, Clinic II of Surgery, Tabaci Street No.1, Craiova, (200642); e-mail: cosmin.obleaga@gmail.com