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Case Series

Clinical Impact of Biliary Candidiasis in Pancreatoduodenectomy: A Series of Cases

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ARTICLE INFO

Article history:

Received: 7 May, 2021

Accepted: 22 May, 2021

Published: 8 June, 2021

Keywords:

Candidiasis

pancreatectomy

postoperative complications

antifungal agents

ABSTRACT

Infectious complications play a prominent role in postoperative outcome of pancreatoduodenectomy. The analysis of the microorganisms responsible for these complications has focused on bacteria, and there is little documentation regarding the role of fungi. We present a case series with 8 patients who underwent pancreatoduodenectomy with positive bile cultures for *Candida* spp., in order to analyse the postoperative outcome.

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Introduction

Infectious complications play a prominent role in postoperative outcome of pancreatoduodenectomy. Surgical site infection (SSI) and sepsis are some of the most frequent complications and have important clinical repercussions. Among the factors related to its occurrence, the existence of microorganisms in bile at the time of the surgery is of particular importance, a circumstance favoured by the performance of endoscopic retrograde cholangiopancreatography (ERCP) [1-3]. Thus far, the analysis of the microorganisms responsible for these complications has focused on bacteria, and there is little documentation regarding the role of fungi [2]. Although there are publications suggesting their association with the development of SSI and even pancreatic fistula, their impact on postoperative complications of pancreatoduodenectomy is not yet well understood [4, 5].

Case Series

In this case series we report patients who underwent pancreatoduodenectomy with positive bile cultures for *Candida* spp. The patients were treated in a third-level hospital between 2015 and 2018. Microbiological sampling was performed by puncturing the common

hepatic duct with a subcutaneous needle before sectioning the same. Once the culture result was obtained, targeted treatment was administered according to the findings. If biliary candidiasis was detected, antifungal treatment was initiated even in the absence of symptoms. Of the total number of patients who underwent pancreatoduodenectomy (60), biliary candidiasis was detected in 13.3% (8 cases). All of them had a history of preoperative biliary drainage (PBD), 87.5% (7 cases) by ERCP and 12.5% (1 case) by cholecystostomy.

Table 1 shows the demographic variables, as well as the most relevant medical history of each patient. Median and mean age were 66 years. It is noteworthy that 75% of the patients (6 cases) had received prolonged antibiotic treatment (more than 7 days) in the weeks prior to the surgery. It is also worth highlighting the history of neoadjuvant treatment and admission to the intensive care unit, both of which appeared in 12.5% (1 case) of the patients. All patients underwent surgery for malignant disease, with pancreatic adenocarcinoma in 87.5% (7 cases) and distal cholangiocarcinoma in 12.5% (1 case). Median time from PBD to surgery was 45 days and mean time was 32 days. The antibiotic therapy and the antifungal treatment administered in each case according to the microbiological culture are also recorded.

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Table 1: Descriptive table.

CASE	1	2	3	4	5	6	7	8
Age (years)	55	75	77	67	65	60	61	74
Sex	Female	Female	Female	Male	Male	Female	Female	Male
ATB>7 days	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
ICU admission previous weeks	Yes	No	No	No	No	No	No	No
Neoadjuvant	No	No	Yes	No	No	No	No	No
Tumor	Pancreatic adenocarcinoma	Pancreatic adenocarcinoma	Pancreatic adenocarcinoma	Distal cholangiocarcinoma	Pancreatic adenocarcinoma	Pancreatic adenocarcinoma	Pancreatic adenocarcinoma	Pancreatic adenocarcinoma
PBD	ERCP	ERCP	ERCP	ERCP	ERCP	Cholecystostomy	ERCP	ERCP
PBD to surgery (days)	90	32	100	13	21	14	18	42
Surgical technique	Cephalic pancreato-duodenectomy	Cephalic pancreato-duodenectomy	Total pancreato-duodenectomy	Cephalic pancreato-duodenectomy	Cephalic pancreato-duodenectomy	Cephalic pancreato-duodenectomy	Cephalic pancreato-duodenectomy	Cephalic pancreato-duodenectomy
Pancreatic anastomosis	Pancreatico-gastrostomy	Pancreatico-jejunostomy	No	Pancreatico-jejunostomy	Pancreatico-jejunostomy	Pancreatico-gastrostomy	Pancreatico-jejunostomy	Pancreatico-jejunostomy
Antibiotherapy	Piperacillin – Tazobactam, Linezolid	Piperacillin-Tazobactam	Piperacillin-Tazobactam, Linezolid	Piperacillin-Tazobactam	Piperacillin-Tazobactam	Vancomycin	Piperacillin-Tazobactam	Piperacillin-Tazobactam, Linezolid
Antifungal treatment	Fluconazole	Fluconazole	Fluconazole	Fluconazole	Fluconazole	Fluconazole	Fluconazole	Itraconazole

*ATB: Antibiotherapy

*ICU: Intensive Care Unit

*PBD: Preoperative Biliary Drainage

*ERCP: Endoscopic Retrograde Cholangiopancreatography

Table 2: Postoperative morbidity.

CASE	1	2	3	4	5	6	7	8
Superficial incisional SSI	No	No	No	No	No	No	No	No
Deep incisional SSI	No	No	No	No	No	No	No	No
Organ /space SSI	No	No	No	No	No	No	No	No
Sepsis	No	No	No	No	No	No	No	No
Septic shock	No	No	No	No	No	No	No	No
Pancreatic fistula	No	No	No	No	No	No	No	No
Bile leak	No	No	No	No	No	No	No	No
Hemorrhagic complications	No	No	No	Upper digestive bleeding	No	Bleeding from hepatic artery pseudoaneurysm	No	No
Need for re-laparotomy	No	No	No	No	No	Yes	No	No
Hospital readmission	No	No	No	Yes	No	Yes	No	No
Hospital stay	6	6	7	17	9	35	5	17
Mortality	No	No	No	No	No	No	No	No

*SSI: Surgical Site Infection

Table 2 shows the postoperative complications for each patient. The absence of infectious complications and postoperative mortality in our series is noteworthy. Regarding other complications, 25% (2 cases) of the patients presented postoperative hemorrhagic events. One patient had self-limited upper gastrointestinal hemorrhage. The other case presented intra-abdominal hemorrhage secondary to a hepatic artery

pseudoaneurysm. It required urgent surgery with vascular reconstruction, showing good clinical evolution. Median hospital stay was 12.7 days and mean hospital stay was 8 days. A figure illustrating the bacterial species detected in bile fluid cultures along with *Candida* species is attached hereto (Figure 1).

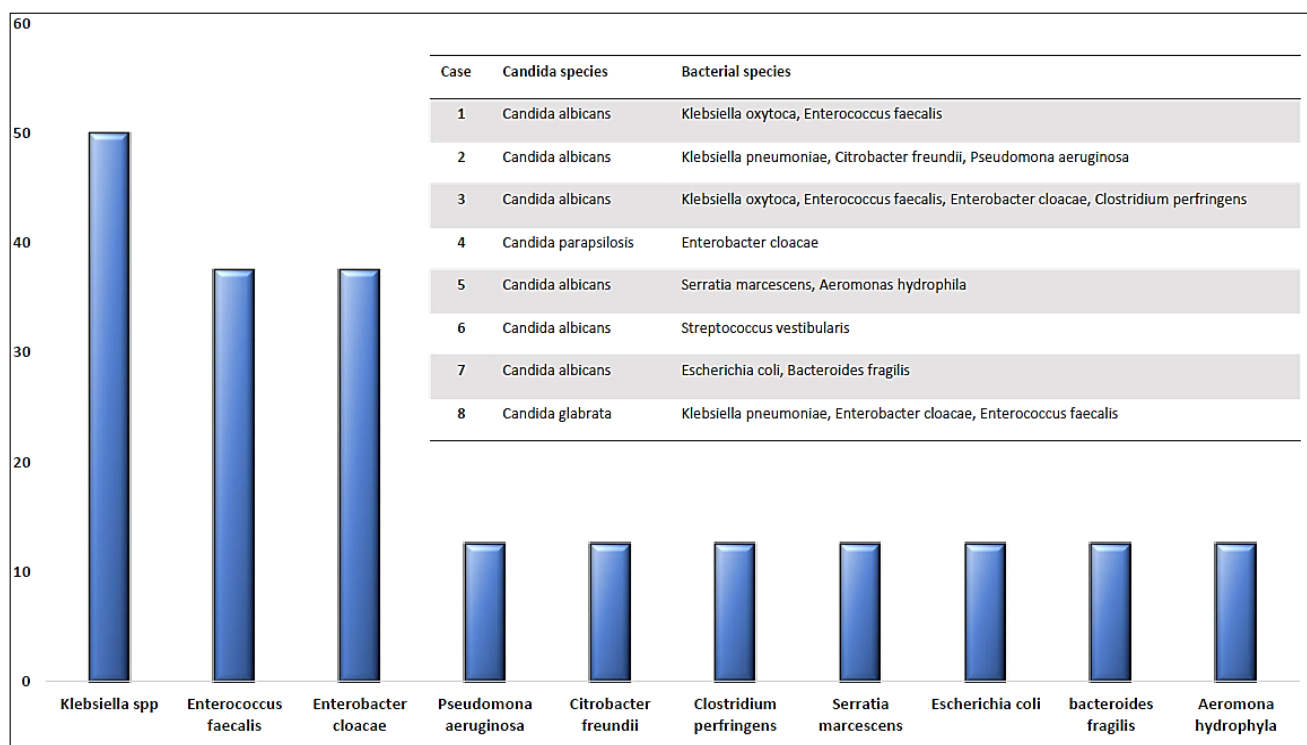


Figure 1: Bacterial species isolated with *Candida* spp.

Discussion

Candida infections are of increasing interest due to their role in the development of nosocomial infections, mainly in intensive care units. Similarly, although documentation of biliary candidiasis in literature has been scarce in previous years, an increasing number of articles address the subject [6-8]. Since different fungal species are part of the microbiota of different regions of the body, one of the most important aspects is how to differentiate infection from colonisation. It is well known that various *Candida* species are part of the microbiota of the oral cavity and digestive tract, acting as commensal bacteria [7]. However, the biliary tract is a sterile compartment and the presence of *Candida* at this level should be considered as a pathological finding [7-9]. These microorganisms can infect the bile upstream from the intestinal tract, particularly in cases with a history of preoperative endoscopic biliary drainage [10-12]. In fact, ERCP has been recognised as an independent risk factor for the development of biliary candidiasis [6]. Also, a high correlation between *Candida* spp. detected in bile fluid and those present in the intestinal tract has been documented [7].

In addition to the upstream, there is a possibility of infection via the haematogenous route in cases of fungaemia and sepsis [7]. Other possible risk factors for the development of biliary candidiasis are prolonged antibiotherapy (more than 7 days) in the weeks prior to surgery, immunosuppression and advanced age [6, 7]. In accordance

with these findings, 87.5% of the cases in our series had a history of ERCP and had received long-term antibiotic treatment in the weeks prior to surgery. The clinical impact of ERCP in the postoperative period following pancreatoduodenectomy, mainly in relation to the development of infectious complications, has been analysed in several articles [2, 13]. The alteration of the sphincteric mechanism of the bile duct caused by ERCP leads to the passage of enteric microorganisms, including *Enterococcus* spp., *Klebsiella* spp., *Escherichia coli* and *Enterobacter* spp. [2, 14-17]. Their presence in bile at the time of surgery is considered a risk factor for the development of postoperative infectious complications [1-3].

One of the findings in favour of this statement is the correlation between the micro-organisms present in bile and those detected in wound cultures upon the emergence of SSI [2, 18]. Although bacteria have been well analysed, so far there are not a large number of studies assessing the role of fungi in postoperative infectious morbidity in pancreatoduodenectomy. In this regard, Kato *et al.* reported that the presence of biliary candidiasis was significantly linked to the occurrence of SSI, is noteworthy [4, 5]. One characteristic of *Candida* spp. to consider is their ability to support bacterial growth. *Candida* spp. infection causes tissue damage that facilitates co-infection by bacteria. In addition, it can directly stimulate the growth of *Staphylococcus aureus*, *Serratia marcescens* and *Streptococcus faecalis* [19]. This may be linked to the high incidence of SSI in cases of biliary candidiasis [5].

In view of the foregoing, it is considered that biliary candidiasis should be treated whenever it is detected, even in cases without apparent symptoms [4]. In our clinical practice, we start antibiotic and antifungal treatment as soon as the bile culture result is available. To the best of our knowledge, it helps to avoid postoperative infectious complications. This is particularly important in immunocompromised patients, where early diagnosis and initiation of antifungal treatment is crucial [20].

In conclusion, although more studies are needed to provide further evidence, biliary candidiasis is an issue to be considered in patients undergoing pancreatoduodenectomy, especially in cases with ERCP or prolonged antibiotic therapy. Although it is just a case series, we believe that, given its possible relationship with the development of infectious complications, antifungal treatment should be considered whenever detected.

Conflicts of Interest

None.

Funding

None.

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