Case Series

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

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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 choledochostomy.

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 |
| 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 |
| Pancreatic anastomosis | Pancreatico-gastrostomy | Pancreatico-jejunostomy | No | Pancreatico-jejunostomy | Pancreatico-jejunostomy | Pancreatico-gastrostomy | Pancreatico-jejunostomy |
| Antibiotherapy | Piperacillin-Tazobactam, Linezolid | Piperacillin-Tazobactam, Linezolid | Piperacillin-Tazobactam | 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

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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).

| Case | Candida species | Bacterial species |
|------|----------------|------------------|
| 1    | Candida albicans | Klebsiella oxytoca, Enterococcus faecalis |
| 2    | Candida albicans | Klebsiella pneumoniae, Citrobacter freundii, Pseudomonas aeruginosa |
| 3    | Candida albicans | Klebsiella oxytoca, Enterococcus faecalis, Enterobacter cloacae, Clostridium perfringens |
| 4    | Candida parapsilosis | Enterobacter cloacae |
| 5    | Candida albicans | Serratia marcescens, Aeromonas hydrophila |
| 6    | Candida albicans | Streptococcus vanus |
| 7    | Candida albicans | Escherichia coli, Bacteroides fragilis |
| 8    | Candida glabrata | Klebsiella pneumoniae, Enterobacter cloacae, Enterococcus faecalis |

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 antibiotic therapy (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 [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.

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