Case Series

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Pancreatic Adenocarcinoma and Other Tumors: Incidental Association or Common Oncogenic Mechanism? Report Of Three Cases

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1. Abstract

The synchronous development of pancreatic adenocarcinoma and other tumors has rarely been reported in the literature. In this article, we report three observations of such an association. One concerns a 51-year-old woman with an adenocarcinoma of the head of the pancreas associated with a papillary tumor of the gallbladder. The other concerns a 68-year-old woman with adenocarcinoma of the head of the pancreas associated with squamous cell carcinoma of the oesophagus. The third concerns a 57-year-old woman with cancer of the body of the pancreas and squamous cell carcinoma of the lung. Is this the case? A chance association, especially in countries with a high incidence of cancer, or a genetic mutation with an oncogenic mechanism capable of inducing histopathologically different tumors?

2. Introduction

The occurrence of synchronous tumors in the same patient represents a major therapeutic challenge, as multidisciplinary therapeutic approaches have to be applied [1,2]. Most often requiring mutilating, cumbersome and time-consuming surgical techniques. Recently, the number of patients diagnosed with multiple primary cancers has increased. This trend can be attributed to improved diagnostic techniques, longer life expectancy and increased incidence of long-term survival in patients with malignancies [3,4]. Synchronous cancers are defined as malignant tumors appearing within the first six months following the first primary cancer), or metachronous cancers (defined as malignant tumors appearing beyond the first six months). In our study, we report 3 cases of pancreatic cancer associated with other organs.

3. Observation 1

Patient B.A., aged 67, with a medical history of hypertension, diabetes and asthma under treatment, and surgical history of cholecystectomy and hysterectomy, presented with cholestatic jaundice. Clinical examination revealed an average general condition with asthenia and anorexia, generalized mucocutaneous jaundice and slight tenderness in the right hypochondrium. Biological workup revealed anemia with cholestasis. MRI revealed double dilatation of the biliary-pancreatic ducts upstream of a nodular formation of the head of the pancreas deemed resectable(Fig. 1. C). Endoscopic biliary drainage in our patient was difficult, if not impossible, due to an impassable narrowing of the thoracic oesophagus, for which an upper gastrointestinal fibroscopy was performed, revealing an oesophageal stenosis approximately 25 cm from the dental arches. The anatomopathological study was in favour of esophageal squamous cell carcinoma. A complementary exploration by an oeso-gastro-duodenal Transit (TOGD) found a tight stenosis of the middle third of the thoracic oesophagus, and a thoraco-abdominal CT showed a tumoral thickening of the middle third of the oesophagus(Fig. 1. D), multiple pulmonary nodules with a tumoral process of the pancreatic uncus (Fig. 1. A). The therapeutic decision was to perform an internal biliary drainage with a choledoco-duodenal anastomosis.

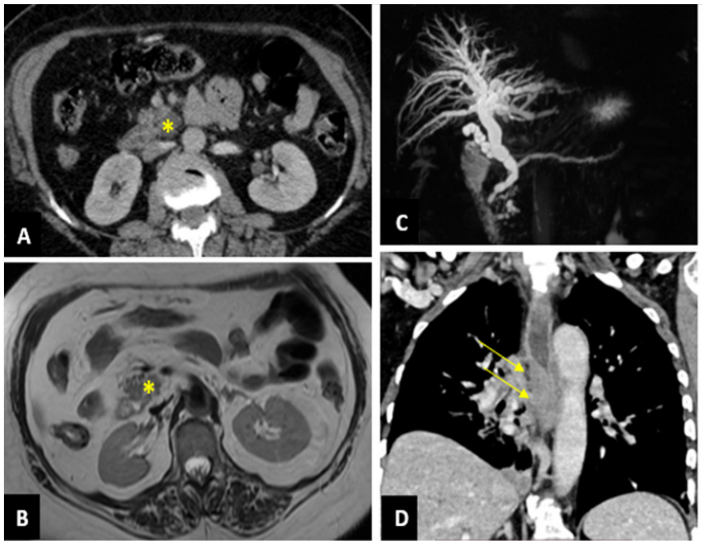

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Fig. 1: Pancreatic adenocarcinoma (*) in CT (A) and MRI (B) with double duct sign (C), associate with esophageal cancer (D, arrows).

4. Observation 2

Patient M. H, 50 years old, diabetic, on oral antidiabetic medication for 3 years, who presented with hepatic colic. Clinical examination revealed slight tenderness in the right hypochondrium, abdominopelvic ultrasound and MRI were performed, revealing a vesicular tumour process at the junction of its body-bottom portions, measuring 17 x 13 mm, associated with multiple adenopathies located at the caecaeliac level, on the hepatic pedicle and retro-portal level, sheathing and stenosing the hepatic artery, and confluent, creating a lymph node-tumour process. A thoraco-abdomino-pelvic CT scan was performed, and the patient underwent an IV b and V bisegmentectomy. Anatomical pathology examination of the surgical specimen showed a papillary tumour of the gallbladder. Two months later, the patient returned with an altered general condition and frank generalized mucocutaneous jaundice associated with excruciating epigastralgia. Biologically, a cholestasis syndrome was present, and lipasemia was negative. MRI revealed a well-limited, irregularly contoured cephalic pancreatic tissue mass, heterogeneous with a central zone of necrosis, measuring 53x35x57 mm, with bi-channel dilatation of the pancreatic duct and intra- and extra-hepatic bile ducts (Fig. 2). This mass infiltrated the retroportal lamina, in direct contact with the celiac trunk over 180° and completely obstructed the portal trunk: thus deemed unresectable. The patient underwent endoscopic biliary drainage with a plastic prosthesis and was referred to the oncology department for possible palliative chemotherapy after biopsy of the pancreatic mass (adenocarcinoma).

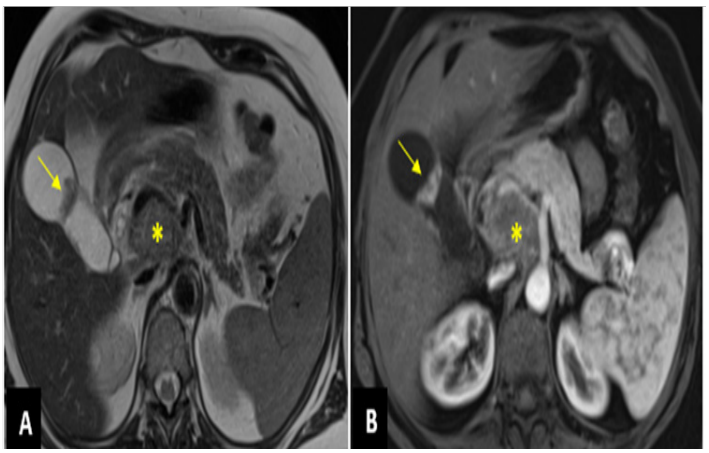


Fig. 2: MRI of intracystic papillary neoplasm of the gallblpadder (arrow) associated with pancreatic ductal adenocarcinoma (*) on T2 (A) and T1 with injection (B) sequences.

5. Observation 3:

Mrs F . DJ, aged 51, with a history of cancer of the right breast for infiltrating ductal carcinoma successfully operated on in 2012, having presented a nodular mass of the head of the pancreas on MRI in 2019 (Fig. 3), for which a series of radiological and biological examinations were carried out, a cephalic duodenopancreatectomy was performed, the pathological examination of which concluded in an adenocarcinoma of the pancreas head, in 2021 the patient presented an infiltrating ductal carcinoma of the left breast for which a second mastectomy was performed, the patient was referred to the oncologists for adjuvant chemotherapy.

Fig. 3: MRI of resectable cephalic pancreatic adenocarcinoma (arrow) in arterial (A) and venous phase (B).

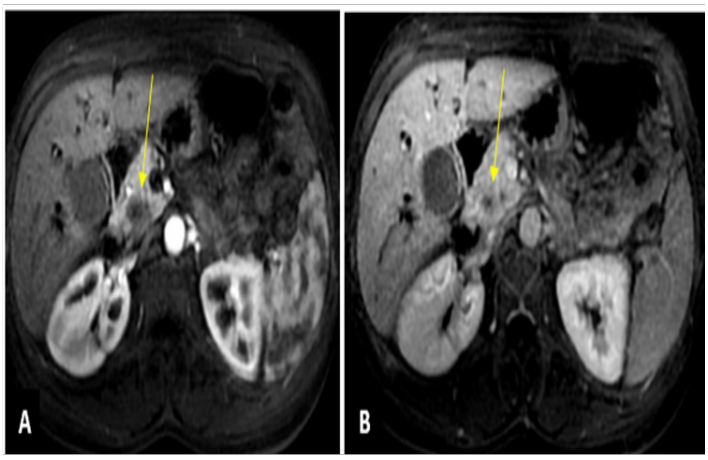
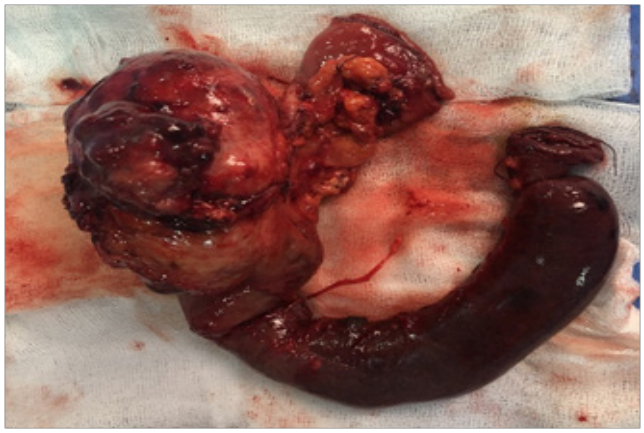


Fig .3: duodenopancreatectomy



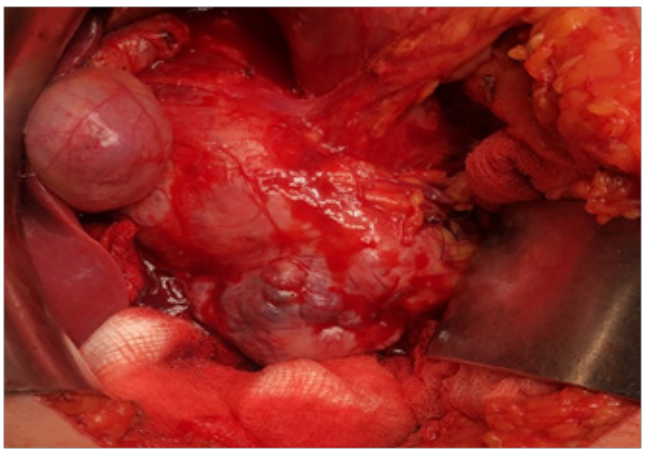
6. Discussion

The incidence of multiple primary cancers is on the rise, and more and more cases are being reported in the literature, which may be explained by improved diagnostic methods. Interestingly, patients with pancreatic cancer often have a multiple history of primary cancer, and their relatives are at increased risk of developing solid malignancies, a predisposition attributed to a hereditary component [5]. The hypothesis of chance as the origin of multiple primary cancers is the most widely accepted, but various mechanisms have been suggested as being involved in multiple primary cancers, such as family history, immunological and genetic abnormalities,

prolonged exposure to carcinogens, radiotherapy and chemotherapy for the primary cancer, and carcinogenesis in the field.[1,6-8] Previously reported cases of multiple primary cancers are mainly described in the respiratory, gastrointestinal and genitourinary systems.

Although few cases of bilio-digestive cancers have an underlying genetic predisposition, most authors point out that molecular genetic studies could identify dependencies that are not yet certain. Even if we consider the occurrence of synchronous pancreatic and digestive cancers to be sporadic (excluding, of course, the two intraductal mucinous neoplasms of the pancreas, whose association with colorectal cancer is greater than that of invasive ductal carcinoma [9] and Lunch syndrome), genetic studies could finally influence our therapeutic decisions. Unfortunately, no genetic studies have been carried out in our patients. With regard to therapeutic strategy, most authors agree that the most advanced cancers should be treated first. The association of gallbladder cancer and pancreatic cancer is very rare in the literature, until 2017 only 5 cases have been reported [10-13]. The association of pancreatic cancer and esophageal cancer has only rarely been described in the literature, with only a few isolated cases. This association poses an enormous surgical and technical challenge, requiring rapid management. The present study suggests the need for a complete and precise diagnosis with meticulous clinical, biological and radiological examination, in order to establish a detailed lesion map for each patient and choose the best therapeutic option without delay [14]. It is estimated that up to 10% of pancreatic cancer patients are associated with hereditary syndromes [15-16], including hereditary breast and ovarian cancer syndrome, Lynch syndrome, Peutz-Jeghers syndrome, atypical familial multiple melanoma syndrome and hereditary pancreatitis. These syndromes increase the risk of pancreatic cancer associated with malignancies originating in other organs. Previously reported primary pancreatic cancers with dual primary tumors from other organs are rare. Synchronous or metachronous malignancies commonly associated with other organs include cancers of the stomach, colon, thyroid and genitourinary tract [17, 18]. However, the clinicopathological features of pancreatic cancer with dual primary tumors have not yet been systematically studied.

Fig.4: peroperat photo of pancreatic cancer



7. Conclusion

In conclusion, we note the importance of performing an adequate preoperative workup and follow-up in every patient to exclude the possibility of a second synchronous tumor. Although it seems excessive to suggest a complete investigation in all patients with a primary cancer, clinicians must be aware of the possibility of multiple primary tumors in the same patient and subsequently optimize their investigative plans, as personalized treatment for each patient becomes inescapable.

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