

Synchronous double cancers of the colon and the pancreas: a case report

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Abstract. – The authors report a clinical case of a synchronous double cancer of the colon and pancreas. Having carefully examined the scarce literature, they dwell on the incidence of this disease referring to frequencies that in the literature range from 0.06% and 0.55% while considering that some series do not show any association between the two neoplasms. The authors analyze the role of the colorectal follow-up. In fact, such a follow-up, even if only providing a relative improvement in disease-free survival, has allowed for a treatment of the two certainly not-advanced tumors ensuring the patient a good prognosis. Finally, the authors analyze how endoscopic ultrasound-guided fine-needle aspiration made possible a preoperative diagnosis of small pancreatic cancer, and show that, the positive predictive value (PPV) of this method was 100%.

Key Words:

Double cancer, Colorectal cancer, Pancreatic cancer, Endoscopic ultrasound, Fine-needle aspiration, Follow-up.

Introduction

The incidence of either synchronous or metachronous second primary tumors in cancer survivors is between 2 and 10%^{1,2}. Taking into consideration only colorectal cancer, the incidence is instead between 1.2 and 8.7% with the stomach being the most commonly involved localization^{3,4}. In our series of colorectal carcinomas, the incidence of either synchronous or metachronous second primary tumors is 4.75%, if the metachronous tumor of the large intestine itself is listed as a second localization; if it is not, the incidence is 2.26% (Table I).

In this context, the association between pancreatic cancer and colorectal cancer is almost anecdotal especially if we only consider the synchronous tumors as well as stage II of Moertel

neoplasia, a tumor which arises in different organs or tissues, both histologically independent and not related to a genetic abnormality or multicentric origin. In fact, our research of the literature on the topic has resulted in very few findings, even after cross-searching the words “double cancer”, “synchronous”, “pancreatic cancer”, “colorectal cancer”, and “multiple primary cancers” in the main databases (PubMed, Scopus, Web of Knowledge).

We report the case of a patient with two synchronous adenocarcinomas of the colon and pancreas, which offered us an opportunity carefully to do a review on this topic.

Case Report

F.S. 68 years old, male. In April of 1991, the patient was subjected to a right hemicolectomy for a colon adenocarcinoma whose staging was T2N0M0, moderately differentiated and re-evaluated as stage I, according to the AJCC 2010. The patient was regularly subjected to follow-up, according to a previously described schedule⁵, for 10 years. During this period of time, the patient had undergone 22 determinations of carcino-embryonic antigen (CEA), 4 ultrasounds of the abdomen, 12 colonoscopies, 4 of which were performed with polypectomy, 7 computed tomographies (CTs) of the abdomen and 8 chest X-rays. The patient, tumor-free, was then asked to be submitted exclusively to a colonoscopy every 3-4 years.

In October of 2012, a colonoscopy, performed with no clinical symptoms, showed at 40 cm from the anal sphincter, a plaque proliferative lesion with a major diameter of 40 mm. The biopsy results showed an adenocarcinoma. For staging purposes, we performed a contrast-enhanced CT (Figure 1), which highlighted at the head of the pancreas an uneven area of about 1 cm, not related to the superior mesen-

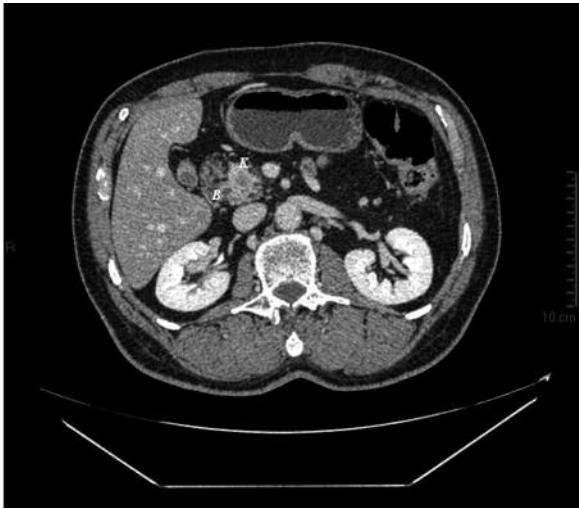


Figure 1. Abdominal contrast-enhanced CT. Cancer (A) of the head of pancreas and common bile duct (B) physiological in size.

teric vessels and the wall of the duodenum. The common bile duct appeared to be physiological in size. Following this, the patient was first subjected to an endoscopic-ultrasound, which confirmed the lesion, and subsequently to an endoscopic ultrasound-guided fine-needle aspiration biopsy. Using a 25-gauge needle and performing three subsequent passes provided us with the diagnosis of “*fragments of the cylindrical epithelium of sure neoplastic nature significant for adenocarcinoma*”.

In November of 2012, the patient was subjected to a pancreaticoduodenectomy and a total colectomy with ileo-rectal anastomosis.

A histological examination, which excluded mutual dependence by immunohistochemistry, staged both the colic tumor (22 lymph nodes examined) and the pancreatic tumor (10 lymph nodes examined) as T2 N0 M0.

At 12 months after surgery, the patient is currently free of any cancer recurrence.

Discussion

Eriguchi⁶ and Kahn⁴, reviewing Japanese (2,898 patients) and Korean (2,112 patients) case studies of pancreatic carcinoma, have reported the incidence of a second colorectal cancer, respectively, in 0.55% and 0.33% of cases. In Italy, Minni et al² reported a 0.11% incidence on 867 pancreatic carcinomas. In these cases, however, the synchronous or metachronous nature of these double cancers is unknown.

In our experience, we can not report case studies on pancreatic cancer because of the incompleteness of the data. We can, however, through a prospective audit of patients with colorectal cancer, record 40 double cancers (4 synchronous and 36 metachronous) out of 842 patients (4.75%) treated with radical surgery, and among these, 2 cases (one synchronous and one metachronous) of association between colon cancer and invasive ductal pancreatic cancer with a frequency of 0.24% (Table I). This percentage is similar to those described above^{1,2,6}, which, instead, refer to case studies of carcinoma of the pancreas with a second neoplasia on the colon-rectum. Minni et al² report an even smaller percentage in his series of colorectal carcinomas with a second cancer on the pancreas (0.06%, 1 metachronous neoplasia out of 1,742) while other similar colorectal cancer case studies do not report any second tumor in the pancreatic area^{4,7,8}.

From these data we can, therefore, infer that the incidence of synchronous pancreatic cancer and colorectal cancer is sporadic, especially if we exclude both the intraductal pancreatic mucinous neoplasm (IPMN), whose association with colorectal cancer is greater than an invasive ductal carcinoma⁹ and double cancers which are due to a genetic syndrome such as Peutz-Jeghers syndrome¹⁰.

If in this latter case the genetic origin is evident, it is less clear when referring to the simultaneous presence of two occasional biologically in-

Table I. Second primary tumors in 842 colorectal cancer (personal series).

2° site	Colon	Breast	Lung	Stomach	Small B.	Pancreas	Others	Total
Metachronous	21	5	3		1	1	5	36
Synchronous				2	1	1		4
Total	21	5	3	2	2	2	5	40

dependent carcinomas, even if mutations in the p-53 and K-ras are reported in the case of multiple primary carcinomas involving the colorectum and pancreas^{9,11}. Environmental factors, infections of unknown origin, or chemotherapy (in the case of metachronous tumors) were other reasons taken into consideration to explain the simultaneous presence of the two tumors¹.

The main goal of the colorectal follow-up is to improve patient survival by early diagnosis of recurrence during the asymptomatic stage when radical surgical treatment is more viable. In a previous study we calculated that the incidence of follow-up on a 5-year disease free interval was only 2.6%, and other authors have reported similar findings⁽⁵⁾. Such unimpressive data has brought about an extensive debate in the literature on whether to continue the colorectal follow-up since costs are not secondary. Our opinion was to continue the follow-up while tailoring it in relation to the “evidence-based medicine”⁵. We were able to diagnose, as previously stated, out of our 842 patients (Table I) 36 new metachronous cancers and we performed an R0 surgery on almost 80% of them (28/36). In our clinical case both the sigmoid colon carcinoma and the tumor of the pancreas, both asymptomatic, were histologically classified as T2N0M0, which is a certainly not an advanced staging. We agree, however, with Eriguchi⁶ when he asserts that an abdominal CT, routinely performed as part of a follow-up, can not always lead to a diagnosis of a not-advanced pancreatic cancer. In fact, this proved to be true in our experience, especially if we consider that our diagnosis, for the only patient who developed pancreatic cancer during a constant colorectal follow-up, was late and a palliative intervention was the only option. Eriguchi⁶, in his experience, reports two cases of synchronous double cancers of the colon and pancreas, and both reported a palliative intervention with a mortality rate of 4 and 12 months.

The diagnosis of a synchronous pancreatic lesion with a maximum diameter of about 1 cm made by a careful abdominal CT, was confirmed preoperatively by an endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) performed by a physician of our team (Bonanno G)¹². He cites, in his series, a sensitivity and specificity of EUS-FNA in the solid pancreatic lesions of, respectively, 95% (95% CI: 88.59-99.16) and 100% (95% CI: 47.83-100) with a positive predictive value (PPV) of 100 % and a negative predictive value (NPV) of 62%. Therefore, based on these

data, a negative pancreatic biopsy does not allow us to exclude the presence of a neoplasm. Instead, the presence of neoplastic cells, obtained by 3-4 passes with a 25-gauge needle¹³, makes the presence of a pancreatic tumor certain. Other authors have recently reported similar data¹⁴⁻¹⁶.

Conclusions

We believe that: (1) Our instructing the patient to a colorectal follow-up, even 10 or more years after surgery, has allowed us to perform a radical intervention on both the carcinoma of the colon and the synchronous pancreatic cancer whose not-advanced staging guarantees a good prognosis; (2) Recent improvements in both radiological and endoscopic techniques and increasing longevity will allow for a greater diagnosis of both synchronous and metachronous double cancers; (3) Additional molecular genetic studies could allow us to find dependencies which are to date not certain, even if as of now the association of colorectal and pancreatic cancers can be considered occasional.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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