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Pancreatic Serous Cystadenocarcinoma: Are You Really So Malignant?

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Abstract

In 2010 the World Health Organization described pancreatic serous cystadenocarcinoma (SCAC) as a serous cystadenoma that presents metastases or invasion of adjacent organs. Although a handful of cases have been described in literature, this entity shows some discrepancies. The dilemma can arise starting on the concept of "metastases" and "invasion": any of reported SCAC shows clear histopathological features of malignancy. Moreover no patient deceased for reasons specifically related to SCAC, even those with metastatic disease. For these reasons, several cases defined as SCACs are not convincing.

Keywords: Serous cystic neoplasm; Pancreas; Metastases

Introduction

In 1989 George et al. firstly described a case of a 70-year-old man with an 11 cm cystic lesion in the pancreatic tail, presenting with gastrointestinal bleeding [1]. The histology of the lesion after resection showed invasion of the stomach, spleen and gastric wall. Liver metastases and a neoplastic thrombus in the splenic vein were also observed. The authors called it "serous cystadenocarcinoma" (SCAC) and the question was: "is it a new entity?" Up to now, about 25 years after, the answer is still controversial.

In 2010 the World Health Organization described SCAC as a serous cystadenoma (SCA) that presents metastases or invasion of adjacent organs [2]. So far, at least 29 cases of SCAC have been reported in the literature, with synchronous or metachronous liver metastases in 12 patients (Table 1) [3-6]. The majority of these patients were symptomatic and/or with giant cysts (>10 cm), suggesting that this tumor acquire malignant potential with the growth. However, the interpretation of these cases as malignant is debated [7]. In particular, the dilemma can arise on the concept of "metastases" and "invasion".

Vascular and perineural invasion and local invasion into the stomach and duodenum are not sufficient criteria for diagnosis of a malignant variant [8]. On the other hand, even SCAs do not always show the histopathological features of benign neoplasms, i.e. non infiltrative growth and clear demarcation from the surrounding tissue [3]. Indeed, a distinct wall or capsule is not always described, as well as nerves, blood vessels or pancreatic structures were often found in or adjacent to the tumor [3].

Some patients with SCAC developed liver metastases in the absence of local invasion [9]. In these cases pancreatic lesions were well-demarcated, sometimes with central scar as it appears in benign SCA. In other cases, distant metastases have been reported to occur several years after the primary surgery. The possibility that the metastasis represents a metachronous neoplasm is difficult to exclude. Multifocal SCAs has been described, suggesting displaced primitive cells or dislocated embryonic rests [10]. Diffuse involvement of pancreatic tissue may be also present in patients with Von Hippel-Lindau syndrome. The cysts observed in these patients are virtually indistinguishable from those of SCAs [11]. Moreover, examples of metastatic ovarian clear-cell adenocarcinoma and clear renal cell carcinoma were mistaken for SCAC [12].

Conclusion

Finally, most of the reported SCACs were microscopically identical to SCA, and no morphologic findings have been found to distinguish them from their benign counterparts [1]. Indeed, in all reported cases cytohistological preoperative diagnosis of serous cystodenocarcinoma was never made [4], except for the very recent case of Bassam et al. [13] where the first preoperative diagnosis is described (after percutaneous biopsies of a pancreatic and a liver lesion). Consequently, in these cases EUS-FNA has no-value [14], since the benign and malignant variants appear histological identical and immunohistochemistry, although under study [9], cannot yet provide definitive answers.

For these reasons, several cases defined as SCACs are not convincing. To increase the doubts, if needed, there is the fact that no patient deceased for reasons specifically related to SCAC [4].

In conclusion, we cannot yet say whether SCAC is a distinct entity. Diagnosis of SCAC is impossible without gross evidence of invasiveness and/or in the presence of distant metastases. However, even in these cases clear criteria to define malignancy are not well established. To better define and characterize SCAC, further cases and longer follow-up are needed, possibly under the aegis of pancreatologic scientific society that should collect adequate numbers to answer question posed.

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Cases number	Author (year)	Age	Metastases and Invasion	Outcome	Preoperative diagnosis
1	George (1989)	70	SM in stomach and liver. Invasion of stomach and spleen.	Operative death due to hemorrhage	No
2	Friedman (1990)	74	SM in liver, lungs, bone marrow, adrenal glands, LN	NA	No
3	Kamei (1991)	72	No	NA	No
4	Okada (1991)	63	MM in liver	Alive 1 year later	No
5	Yoshimi (1992)	63	MM in liver	Alive 3 years later	No
6	Ohta (1993)	64	No	Alive 9 months later	No
7	Widmaier (1996)	71	SM in LN	Alive 1 year later	No
8	Ishikawa (1998)	63	MM in liver	NA	No
9-10	Siech (1998)/2 cases	NA	NA	NA	No
11	Eriguchi (1998)	65	SM and MM in liver	Alive 10 years later	No
12	Abe (1998)	71	SM in LN	Alive 2 years later	No
13-16	Schmidt-Rohlfing (1998) /4 cases	52-74	NA	NA	No
17,18	Kimura (1999)/2 cases	53, 66	NA	NA	No
19	Horvath (1999)	81	NA	NA	No
20	Wu (1999)	57	SM and MM in liver	NA	No
21	Strobel (2003)	56	MM in liver	Alive 3 years later	No
22	Shintaku (2005)	85	Invasion of spleen	Alive 10 months later	No
23	Friebe (2005)	80	Invasion of spleen	Alive 1 year later	No
24,25	Galanis (2007)/2 cases	NA	SM and MM in liver	NA	No
26	King (2009)	70	Invasion of duodenum	Alive 7 years later	No
27	Cho (2011)	64	Invasion of colon	Alive 1 year later	No
28	Bramis (2012)	86	Invasion of stomach, SM in liver	NA	No
29	Bassam (2013)	68	SM in liver	NA	Yes

NA: Not Available. SM: Synchronous Metastases. MM: Metachronous Metastases

Table 1: Characteristics of 29 reported cases of pancreatic serous cystadenocarcinoma.