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Pancreatic Neuroendocrine Tumor Associated with Pancreatic Adenocarcinoma: A Case Report and Review of the Literature

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Pancreatic adenocarcinoma (PAC) is a high mortality cancer. Age, nicotine exposure, obesity, old-onset type 2 diabetes and chronic pancreatitis are identified risk factors for PAC. The Peutz-Jeghers Syndrome, Atypical Familial Syndrome of Multiple Moles and Melanomas (AFSMMM), Hereditary Ovarian and Breast Cancer, HNPCC and Familial Adenomatous Polyposis are the major genetic syndromes at high risk for pancreatic cancer. Neuroendocrine tumours (NETs) are defined by the expression of structural proteins and hormonal products common to neurons and endocrine cells. There is no identified risk factor for pancreatic NETs other than genetic predisposition syndromes (multiple endocrine neoplasia type 1 [MEN1], von Hippel-Lindau syndrome, tuberous sclerosis [TBS]). In this article we present a case of pancreatic neuroendocrine tumor associated with pancreatic adenocarcinoma and we discuss in light of the data in the literature, the risk factors that expose to both types of pancreatic tumors).

Keywords: Risk factors; Pancreatic Adenocarcinoma (PAC); neuroendocrine carcinoma of the pancreas; multiple endocrine neoplasia [NEM1].

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1. INTRODUCTION

Pancreatic cancer is a malignant proliferation at the expense of pancreatic cells. It is of ductal origin in the majority of cases.

Pancreatic cancer is rare before the age of 45; its incidence increases with age and the maximum frequency is around 75-80 years of age.

There are two histological types of pancreatic cancer: Exocrine cancer at the expense of the exocrine pancreas, and endocrine cancer at the expense of the endocrine pancreas.

Adenocarcinoma of the pancreas still has a very poor prognosis despite recent therapeutic progress. In the operable forms, about 1 in 5 patients survive in the long term. In inoperable forms, chemotherapy only prolongs survival by a few months and most patients die within a year.

Pancreatic neuroendocrine tumours (PNET) are rare tumours, but their incidence is increasing. They are characterized by a high rate of metastases (50%), mainly liver metastases. Due to their relatively slow tumour growth, they are nevertheless associated with prolonged survival rates (approximately 50% at 5 years).

2. CASE PRESENTATION

Mr. 60 years old, with no notable pathological history, presents with epigastralgia evolving 3 months before his admission without any sign of clinical cholestasis, evolving in a context of conservation of the general state of health. At the abdominal exam: Epigastric tenderness, no palpable mass, no hepatomegaly, the rest of the exam is unremarkable. At the ABDOMINAL CT scan: Cystic corporo-caudal pancreatic cystic formation of 47 mm partitioned, communicating with the wirsung canal which is dilated, corresponding to a TIPMP, without tissue component.

Tumor markers: CA19.9 =78835 U/l ACE: 261.4 ng/l

The patient underwent a central pancreatectomy, on exploration: presence of a cystic tumor with a regular wall mesuring 5 cm on the body of the pancreas without invasion of the mesenteric vessels, without hepatic metastasis. The post-operative follow-up: was simple. On the Anapath: Infiltrating pancreatic adenocarcinoma with a cystic appearance of 4.5 cm, healthy resection limit.

The evolution was marked by the accidental discovery 3 months later during a control abdominal CT scan: the presence at the caudal portion of the pancreas of an exophytic cystic formation mesuring 45*25 mm associated with a dilatation of the remaining Wirsung canal.

The patient underwent caudal splenopancreatectomy with gastric banding and suturing of the gastric wall. On exploration: presence of a 4 cm tumour of the tail of the pancreas invading the posterior face of the stomach with celiac trunk adenopathy. Anapath: G1 neuroendocrine tumor of the pancreas measuring 3.5 cm, invading peripancreatic fat tissue, limit of pancreatic resection is normal, PT2 stage. The post-operative suites marked by the appearance at Day Three after surgery of hyperglycemia for which the patient was put on insulin therapy.

3. DISCUSSION

Pancreatic cancer is the fifth leading cause of cancer death. More than 80% of pancreatic cancers are not amenable to curative surgery at the time of diagnosis.

The risk factors are age, smoking, obesity. Type 2 diabetes. Genetic predisposition includes familial pancreatic cancer, certain syndromes associated with an increased risk of pancreatic cancer and hereditary pancreatitis.

3.1 Risk Factors for Exocrine Pancreatic Cancer

The risk factors for exocrine pancreatic cancer are either poorly known or account for only a small proportion of pancreatic cancers.

The indisputable risk factors are advanced age. Tobacco with a relative risk of 2.2. There is a dose-response relationship and the relative risk is multiplied by 5 when cigarette consumption is greater than 30 per day. Obesity is a risk factor for pancreatic cancer. A recent study [1] found an association between increased body mass index and pancreatic cancer in women but not in men.

3.1.1 Diabetes

At the time of diagnosis of pancreatic cancer, between 40% and 60% of patients have

diabetes. Thus, a meta-analysis [2] has shown a relative risk of cancer in type 2 diabetics about 2 times higher than in non-diabetics.

3.1.2 Chronic pancreatitis

There is a risk of degeneration that is difficult to estimate because cancer can, at the time of diagnosis, mimic chronic pancreatitis. Moreover, histologically, there are often histological signs of pancreatitis prior to cancer. In most studies, the risk is 4 times higher than in patients without chronic pancreatitis.

3.1.3 Genetic predisposition to exocrine pancreatic cancer

3.1.3.1 Familial pancreatic cancer [3]

It is defined by the presence of at least two or three cases of pancreatic cancer in first- or second-degree relatives. There is no underlying chronic pancreatitis and no other associated cancer. Its frequency among all pancreatic cancer cases ranges from 1 to 8%. The risk of pancreatic cancer is increased with a family history of pancreatic cancer compared to the general population.

The age of familial ADKP is certainly lower than that of sporadic ADKP: 58-68 years versus 61-78 years [4].

The prognosis does not seem to be very different between familial and sporadic forms. However, in at-risk families, the risk of developing ADKP is higher (RR: 9.3) if at least one case occurred before the age of 50 and can reach 32 when three first-degree family members have pancreatic cancer [4].

However, more recently, mutations in the palladin gene have been identified [5]. This gene encodes a protein that is a component of the actin network of the cytoskeleton. The palladin gene is over-expressed in these cancers in favor of its role as a proto-oncogene [6].

3.1.3.2 Hereditary pancreatitis

It is a rare condition characterized by flare-ups of acute pancreatitis beginning in childhood. Half of the patients develop chronic pancreatitis. These patients have a 40% risk of cancer [7].

It is due to mutations in the cationic trypsinogen gene (PRSS1). Approximately 25 mutations are known to date. The two most frequent mutations, R122H and N29I, account for 70% of cases.

3.1.3.3 Several syndromes associated with an increased risk of pancreatic cancer [8,9]

Peutz-Jeghers syndrome, characterized by hamartoma-like gastrointestinal polyps and pigmented Skin-mucosal lesions, is associated with a relative risk of pancreatic cancer of 132;

Familial atypical multiple mole melanoma (familial atypical multiple mole melanoma) (FAMMM), is a rare condition in which there is a risk of malignant melanoma, with pancreatic cancer being the second reported cancer.

Pancreatic cancer also occurs in some families with breast cancer with BRCA2 mutations. These mutations, transmitted in an autosomal dominant manner, predispose to breast and ovarian cancer and increase the risk of ADKP by a factor of 2 to 10 depending on the age of onset. The presence of at least one ADKP in a BRCA 1/2 family further increases the risk of ADKP in exposed women. The absolute risk of ADKP at age 70 is in the range of 2-10% and vice versa [10].

3.1.3.4 Precancerous lesions

Mucinous cystadenomas and mucinous and papillary intracanal tumours of the pancreas (TIPMP) are at risk of degeneration.

3.2 Risk Factors for Endocrine Pancreatic Tumours

The rarity of TNEPs makes it difficult to identify risk factors. However, a meta-analysis has identified the following risk factors: family history of first-degree cancer (HR, 2.19), smoking (HR, 1.34), significant chronic alcoholism (HR, 2.44) and diabetes (HR, 2.76) [11].

Although most PNETs are sporadic, approximately 5% of PNETs occur in the context of an inherited predisposition, primarily multiple endocrine neoplasia type 1 (MEN1) and von Hippel-Lindau disease (VHL). They are then usually multiple and less aggressive than sporadic TNEP, but may recur after resection as new lesions. There are a few rare situations of endocrine hyperplasia, such as

microadenomatoses, characterized by the presence of multiple endocrine nodules consisting only of insulin or glucagon cells, some of which evolve into true NETs. Approximately 5-10% of NETs in the pancreas are multiple without an identified predisposition syndrome [12–14].

4. CONCLUSION

Pancreatic cancer remains a cancer with a unfavourable prognosis, survival is very poor as it is usually diagnosed at a late stage and therefore unsuitable for surgery.

The known risk factors for pancreatic cancer are multiple: alcohol, tobacco, cholecystectomy, diabetes, obesity, genetic factors, hepatitis and chronic pancreatitis but which have not been proven to have a direct causal effect except for smoking. Pancreatic neuroendocrine tumours (NETs) account for 5% of NETs and less than 5% of pancreatic tumours. They are characterized by variable differentiation in anatomopathology, their capacity for hormonal secretion and the potential association with an hereditary predisposition syndrome.

CONSENT

As per international standard or university standard guideline participant consent and has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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