

New-onset diabetes mellitus revealing pancreatic cancer in elderly woman

*Diabète inaugural révélant un cancer pancréatique chez une femme âgée*Samir Ait Abderrahmane¹, Djamel Aid², Amria Semara¹, Fadewa Boucelma¹, Soumia Abdelkrim¹, Imad Boulmarka¹, Mounira Chanegreha¹, Hamida Oumbiche¹, Nacer Boubendir², Brahim Oudjit¹

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RÉSUMÉ

L'adénocarcinome pancréatique a une incidence presque égale au taux de mortalité, ceci est dû principalement à l'apparition tardive des symptômes et au retard diagnostique. Des preuves convaincantes indiquent que le diabète d'apparition tardive chez le sujet âgé, peut-être une manifestation de la maladie. Le diagnostic précoce de ce cancer donne la possibilité d'une prise en charge précoce. Nous rapportons le cas clinique d'une patiente âgée de 78 ans qui s'est présentée au pavillon des urgences pour prise en charge d'un diabète inaugural par une hyperglycémie majeure. À la recherche d'un diabète secondaire, un cancer du pancréas a été confirmé par une biopsie pancréatique. Ce cas clinique souligne que le diabète chez le sujet âgé pourrait être un mode de révélation d'un cancer du pancréas.

Mots-clés : cancer du pancréas, diabète de type 2.

ABSTRACT

Pancreatic adenocarcinoma has an almost equal incidence to mortality, mainly due to late onset of symptoms and delayed diagnosis. There is convincing evidence that late-onset diabetes in the elderly may be a manifestation of cancer. Early diagnosis of this cancer gives the possibility of early management. We report case of a 78-year-old woman who presented to the emergency room for the management of inaugural diabetes with major hyperglycaemia. In search of secondary diabetes, pancreatic cancer was confirmed by pancreatic biopsy. This clinical case highlights the fact that diabetes in the elderly could be a way of revealing pancreatic cancer.

Keywords: pancreas cancer, type 2 diabetes.

Introduction

Pancreatic cancer (Pa C) carries a poor prognosis since cancer-specific symptoms occur only at an advanced stage. Pa C is associated with a diabetogenic state and evidence has emerged that new-onset diabetes mellitus (DM) may be a warning sign necessitating further investigation for occult Pa C [1,2]. Improvement of diabetes following resection of Pa C suggests that diabetes may be caused by cancer. Patients with new-onset DM have a 5–8 fold increased risk of being diagnosed with Pa C within 1–3 years of developing diabetes [3]. Although the association between new-onset DM and Pa C is established, the pathogenesis of Pa C-associated DM is not well understood. It has been postulated that Pa C-associated DM is a paraneoplastic phenomenon caused by diabetogenic tumor-secreted products [4]. Recognition of new-onset hyperglycemia as an early manifestation of Pa C could lead to diagnosis of Pa C at an early asymptomatic stage. The learning objective of the following report is to highlight that new-onset DM in the setting of suspicion or risk for Pa C may serve as a clue that the patient needs further workup for this malignancy [5].

Case report

A 78 years-old woman, with history of hypertension, syncopal complete atrioventricular block benefited from implementation of pacemaker, presented to the emergency unit with new onset osmotic symptoms and severe hyperglycemia. She had been experiencing polydipsia and polyuria for 2 months associated with asthenia and blurry vision. She lost about 9 kg weight over the last 3 months; her family history was negative for diabetes and/or cancer.

Clinical examination revealed overweight (body mass index: 27 kg/m²) and the absence of acantosis nigricans; a stage 2 dyspnea; systemic examination was unremarkable.

Laboratory finding on admission was as follows: random blood glucose 7 g/L, white blood cell counts 7.24 x 10³; osmolarity 297 mosmo/L, and negative urine ketones. Her glyated haemoglobin was 12.8 %.

Ultrasound of abdomen revealed a heterogeneous mass in the body of pancreas, the patient subsequently underwent a CT scan of the abdomen with IV contrast that showed a mass (34 mm) extending from head to the body of the pancreas. The duodenum, the inferior vena cava and the mesenteric artery were in close relation to the mass (figure 1). Biopsy per endoscopic ultrasound of the mass was performed and was suggestive of pancreatic adenocarcinoma.

Her diabetes was treated with multiple daily injections of insulin glargin and insulin aspart, and then switched to a double premix, twice a day before meal.

The patient was followed-up in oncology after confirmation of the diagnosis and was informed about the aggressive nature of the disease. She had a good functional status and was independent in activities of daily living without restriction. The patient and her family were informed that chemotherapy would be palliative to extend survival while preserving her quality of life as much possible; she then opted for chemotherapy after authorization of her cardiologist.



Figure 1. Abdominal CT. Cephalo isthmic tumor process of 34 mm long axis, irregular contours, hypodense enhances after injection of contrast product, with intimate relationship with the vascular and nerve neighboring structures, and invading the duodenal wall.

Discussion

The association between diabetes mellitus and PDAC is well-established epidemiologically. While long-standing type 2 diabetes mellitus is a modest risk factor for the development of PDAC, new-onset diabetes has also been observed to be an early manifestation of PDAC [6, 7].

About 80% of patients with PDAC have either impaired glucose tolerance or type 2 diabetes at the time of diagnosis. A meta-analysis conducted by Ben *et al.* in 2011 concluded that patients with diabetes had a 2-fold increased risk of developing PDAC compared to non-diabetics. However, the risk of PDAC was inversely proportional to the duration of diabetes and was highest among patients who were diagnosed with diabetes less than 1 year before the detection of PDAC (relative risk [RR] = 5.38) [8]. A prior meta-analysis conducted by Huxley *et al.* in 2005 showed similar results [9].

Patients who were diagnosed with diabetes less than 4 years earlier had a 50% higher risk of developing PDAC than patients who had diabetes for more than 5 years. The most recent meta-analysis by Batabyal in 2014 confirmed the aforementioned results, stating that although long-standing diabetes places patients at a risk of acquiring PDAC (RR = 1.36), the association is much higher for patients diagnosed with diabetes less than 1 year before diagnosis of PDAC (RR = 6.69). These studies suggest that new-onset diabetes mellitus or worsening glycemic control in a patient with previously controlled diabetes could be an indicator for PDAC [10].

This is further supported by the fact that patients with newly diagnosed diabetes mellitus who underwent surgery for PDAC had improvement in their blood glucose levels post resection. While still incompletely understood, there are many theories proposed explaining the association between diabetes and PDAC. These can be broadly classified as metabolic, hormonal, and immunological alterations. Insulin resistance is the hallmark of diabetes, specifically type 2 diabetes mellitus. In response to this resistance, there is an oversecretion of insulin, which leads to an increase in β -cell mass [11].

Experimental evidence suggests that insulin promotes cell proliferation through its mitogenic effects while simultaneously increasing glucose utilization by cells. Both these traits are inherent to tumor development. Thus, the exocrine pancreas in hyperinsulinemic patients is chronically exposed to high levels of this potential carcinogen. Furthermore, insulin, by its action on liver metabolism, upregulates levels of insulin-like growth factor-1 (IGF-1), which is known for its potent mitogenic and anti-apoptotic activities. While still incompletely understood, there are many theories proposed explaining the association between diabetes and PDAC. These can be broadly classified as metabolic, hormonal, and immunological alterations. Insulin resistance is the hallmark of diabetes, specifically type 2 diabetes mellitus. In response to this resistance, there is an over secretion of insulin, which leads to an increase in β -cell mass [12].

While no epidemiological evidence has irrefutably linked PDAC risk and plasma levels of insulin-like growth factors, a case control study indicated a possible association between polymorphic variants of the gene encoding IGF-1 and a risk of PDAC. More recent evidence suggests that inflammation plays an important role in the development of PDAC. Glucose and fat intake induce inflammation by increasing oxidative stress, which in turn increases insulin resistance [13].

Multiple genome studies have shown that some of the genetic variations and loci that modify the risk of diabetes mellitus have also been implicated in differentiation and cell development. A lower incidence of PDAC has been demonstrated in treated diabetic patients by metformin, as opposed to those treated with insulin. This is thought to be a consequence of hepatic glucose production by metformin and consequently circulating insulin levels [14].

While these theories attempt to explain how hyperglycemia predisposes to PDAC, the mechanism of diabetes development in patients with PDAC is still unknown. In vitro studies demonstrating intracellular defects in insulin action and a decrease in glycogen synthase activity resulting in impaired glucose removal were the suggested mechanisms for insulin resistance induced by insulin. the PDAC. Adrenomedullin is believed to be another protein secreted by cancer cells that causes β -cell dysfunction and thus leads to the development of diabetes in PDAC patients. However, studies with larger cohorts need to be conducted to confirm its diagnostic value. Since it is not yet possible to distinguish Diabetes Mellitus from Diabetes Mellitus with PDAC in its infancy, many studies are currently underway to identify biomarkers capable of identifying people at high risk of development of PDAC [15,16].

Conclusion

It should always be remembered the possible diagnosis of pancreatic cancer in diabetes of the elderly subject, although the relationship is complex and not fully understood, It is important to think about it.

Déclaration d'intérêts : les auteurs ne déclarent aucun conflit d'intérêt en rapport avec cet article.

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