REVIEW ARTICLE

A Star of Connection Between Pancreatic Cancer and Diabetes: Adrenomedullin

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ABSTRACT

Pancreatic cancer belongs to the most aggressive cancer types, with an incidence rate equallig mortality rate. It is well-known that type 2 diabetes is a significant risk factor for pancreatic cancer. Interestingly, several studies have shown that pancreatic cancer can also lead to type 2 diabetes, as part of the pancreatic cancer induced paraneoplastic syndrome. Multiple factors have been proposed to be involved in the interaction between pancreatic cancer and diabetes. Adrenomedullin, a multifunctional hormone, is nominated as a strong candidate influencing the connection of pancreatic cancer with diabetes. Evidence so far suggest that adrenomedullin upregulation is linked with pancreatic cancer growth, invasion, metastasis, and angiogenesis. Most importantly, adrenomedullin exerts paracrine effects on pancreatic β cells impairing insulin secretion, causing glucose intolerance, and thus leading to β cell dysfunction. This review will explain recent advances regarding the involvement of adrenomedullin in pancreatic cancer and pancreatic cancer-associated diabetes.

INTRODUCTION

Pancreatic cancer bears a poor prognosis and dismal survival rate representing the twelfth most common cancer in the world. Indeed, overall five-year survival rate of pancreatic cancer patients is below 5%, with a median survival of 4 to 6 months [1, 2]. Pancreatic cancer is typically diagnosed at an advanced stage, reducing efficient treatment strategies. An important risk factor for pancreatic cancer is type 2 diabetes. Interestingly, studies indicate that pancreatic cancer can also cause diabetes along with weight loss and cachexia, as part of the cancer-induced paraneoplastic syndrome. Pancreatic cancer-induced diabetes has been shown to be present in 34% of patients (177of 512) [3]. Even though, the pathogenesis of these cancer-associated metabolic syndromes is only beginning to be understood, they present potential avenues in enhancing the survival and growth of pancreatic cancer, especially as pancreatic cancer is characterized by an abundant and desmoplastic microenvironment. Adrenomedullin (ADM) is a multifunctional hormone, which is expressed in different tissues of the human body including the pancreas. Researchers have shown that ADM is involved in regulating growth of normal and carcinogenic cells, both with antiproliferative and mitogenic activities. Recently, ADM has been described as a candidate diagnostic marker of pancreatic cancer in association with diabetes mellitus. Furthermore, many studies have highlighted the importance of ADM in pancreatic cancer and diabetes. For a general overview on ADM function, see an informative review [4]. This review will describe the involvement of ADM in pancreatic cancer and pancreatic cancer-associated diabetes. For the literature research Pubmed was used, no restrictions were applied and the time frame covered was from 1994-2015. The keywords used for the research included “Adrenomedullin cancer”, “adrenomedullin pancreatic cancer”, “pancreatic cancer and diabetes”. In some cases, references from cited papers have been included in the analysis.

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Adrenomedullin and Its Role in Malignant Growth

Adrenomedullin (ADM) is a 52 amino acid peptide known to inhibit insulin secretion. Receptors of this pluripotent hormone are found on β cells in the pancreas. ADM expression is sighted particularly in the F cells of pancreatic islets. ADM expression has also been identified

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