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Synchronous manifestation of colorectal cancer and intraductal papillary mucinous neoplasms

Synchronous manifestation of CRC and IPMN

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Abstract

+ADw-html+AD4APA-p+AD4-High rates of extrapancreatic malignancies, in particular colorectal cancer (CRC), have been detected in patients with intraductal papillary mucinous neoplasm (IPMN). So far, there is no distinct explanation in the literature for the development of secondary or synchronous malignancies in patients with IPMN. In the past few years, some data related to common genetic alterations in IPMN and other affiliated cancers have been published. This review elucidated the association between IPMN and CRC, shedding light on the most relevant genetic alterations that may explain the possible relationship between these entities. In keeping with our findings, we suggested that once the diagnosis of IPMN is made, special consideration of CRC should be undertaken. Presently, there are no specific guidelines regarding colorectal screening programs for patients with IPMN. We recommend that patients with IPMNs are at high-risk for CRC, and a more rigorous colorectal surveillance program should be implemented.+ADw-/p+AD4APA-/html+AD4-

Key Words: Colorectal cancer; Intraductal papillary mucinous neoplasm; Genetic alterations; Extrapancreatic malignancies; Synchronous neoplasms

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Core Tip: In this mini-review, we highlighted the genetic alterations that occur in intraductal papillary mucinous neoplasm (IPMN) and colorectal cancer to understand common genetic or epigenetic risk factors that could explain their synchronous manifestation. The process of malignant transformation in both entities is complex, but some distinctive features of IPMN lesions are linked with their genetic heterogeneity. Specific mutations in *GNAS* and *KRAS* are mainly expressed in IPMN.

A significantly lower frequency of mutations is detected in other cancer-related genes, such as *SMAD4*, *PI3KCA*, *PTEN*, and *BRAF*.

INTRODUCTION

Intraductal papillary mucinous neoplasm (IPMN) of the pancreas is characterized histologically by a broad spectrum of transformation starting from low-grade dysplasia, moderate dysplasia, high-grade dysplasia, and invasive pancreatic carcinoma (PC)[1]. Depending on the epithelial type, IPMN has a variable prognosis with the unambiguous potential to transform to invasive PC[2]. IPMN is characterized by intraductal papillary growth and mucous secretion, which lead to ductal dilatation of the pancreas. IPMN is classified into main duct IPMN, branch duct IPMN, or mixed type IPMN based on anatomical involvement of the pancreatic ductal system[3]. It was estimated that the main duct type IPMN has a higher malignancy potential, with a range of 36%-100%[4]. It is important to note that even malignant IPMN could be resected and has a better prognosis compared with pancreatic ductal adenocarcinoma[5]. In the last few decades, many studies have been published representing an interesting correlation between IPMN and other malignancies, which emerge before or simultaneously with the diagnosis of IPMN. It was estimated that in patients with

IPMN, the incidence of additional malignancy is in the range of 10%-52%[6]. Typically the gastrointestinal (GI) tract is involved, with a prevalence of colon polyps and colorectal cancer (CRC) in Western countries and gastric cancer in Asian countries[7]. The incidence of synchronous CRCs and IPMN is about 3%-12% in Western countries[8]. In some publications, it was pointed out that the frequency of colonic adenomas was uncommonly higher in patients with IPMN than in those with pancreatic ductal adenocarcinoma[9]. In the last two decades, a unique carcinogenesis model for CRC has been revealed with a detailed analysis of underlying genetic and epigenetic alterations[10]. On the contrary, the mechanisms of malignant transformation in IPMN remain poorly understood. It is believed that IPMN is fundamentally characterized by a genetic lesion and that an accumulation of somatic mutations drives the histologic progression, ultimately leading to malignant transformation[11]. So far, there is no distinct explanation in the literature for the development of secondary or synchronous malignancies in patients with IPMN. In the past few years, data were published related to common genetic alterations between IPMN and other affiliated cancers[12,13]. This review elucidates the association between IPMN and CRC. We also discuss the most relevant information concerning the molecular mechanism of genetic alterations leading to the synchronous development of IPMN and CRC.

CONCLUSION

There is a significantly increased prevalence of CRC in patients with IPMN compared to the average population. Unfortunately, there are scarce data aimed at elucidating the molecular mechanisms leading to CRC development among patients with IPMN. More studies are needed to clarify the underlying pathophysiology and common genetic events shared between these two lesions.

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