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Mini Review

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Intraductal papillary mucinous neoplasms of the pancreas; a mini review of diagnosis, treatment and outcomes

Abstract

The rate of diagnosis of pancreatic IPMNs has significantly increased today owing to widespread use of radiological imaging techniques. These cases can be seen in a broad range of stages, from early neoplastic changes to invasive carcinoma (e.g., IPMN associated with low grade-intermediate dysplasia, high grade dysplasia, or invasive carcinoma). IPMNs have a better prognosis than classical pancreatic ductal adenocarcinoma. A multidisciplinary approach is highly important for the diagnosis and treatment of these cases and identification of prognostic factors. The treatment should be individually tailored, taking into account the prognostic characteristics of the case and life expectancy. Moreover, considering the molecular analysis approach used today, we can assume that different and more appropriate treatment models will be available in the future.

Keywords: pancreas, intraductal papillary mucinous neoplasms (IPMN), pancreatectomy

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Introduction

Due to technological advances in imaging, cases of cystic pancreatic lesions are now more commonly encountered.[1] The history of these lesions, which dates back to the time of Becourt, one of the founders of modern surgery, revealed that their classification was put forward only toward the end of the 20th century.[2] Currently, pancreatic cystic lesions are divided into two main categories: neoplastic and nonneoplastic. There are many entities and factors that need to be considered during classification, such as pseudocysts due to damage and inflammation; cysts related to infection and paraduodenal wall cysts; serous type cysts of ductal origin; mucinous type cysts; unclassified cysts of endocrine, acinar, endothelial, mesenchymal origin, which are observed in rare instances; and congenital cysts due to duplication and duodenal diverticula.[3] While nonneoplastic pancreatic cystic lesions constitute approximately one-third of all pancreatic cystic lesions, neoplastic lesions are more commonly observed and have been reported in about 60-70% of cases.[3] Entities under the main category of mucinous cystic neoplasms include intraductal papillary cystic neoplasms (IPMN), mucinous cystic neoplasms, intraductal oncocytic papillary neoplasms, retention cysts (mucocele or mucinous nonneoplastic cysts), ductal type adenocarcinoma, or cystic changes of other carcinoma variants.[3]

In the neoplastic category, IPMN is a mucinous type lesion of ductal origin that has been thoroughly studied in recent years.[1] IPMN is a neoplastic process that needs to be evaluated in a broad spectrum ranging from early neoplastic changes to invasive carcinoma[4,5] and differently evaluated from pancreatic intraepithelial neoplasms (PanINs). PanINs lead to pancreatic ductal adenocarcinoma, while IPMN can be clinically detected at an earlier stage and are good examples of preinvasive neoplasms.[1,6] IPMN is reported to constitute about 5% of all pancreatic neoplasms. Histopathologically, it involves a proliferation with papillary configuration, composed of neoplastic mucinous cells toward the intraductal area.[7] It frequently has a multiloculated appearance, and occasionally, small papillary proliferations might be observed macroscopically (Figure 1). Clinically, it is slightly more common in males than females, and is reported to be identified at around the age of 70 years on average. Approximately one-third of these cases are detected incidentally, following admissions to clinics for complaints in other organs.[8–10] Endoscopically, mucin outflow from the ampulla of Vater might be seen in these cases, while radiologically, a large number of dilated cysts might be observed in the main pancreatic duct or dilated branch ductus. Nowadays with the increasing use of screening programs, cases usually present a small cyst that is usually detected incidentally via computed tomography (CT).[11]

Figure 1 Pancreatectomy specimen with IPMN diagnosis shows multiloculated cystic lesions sampled with a megablock and bright cross-section due to mucin (slide stained with surgical boundary stain).

The following methods can be preferred in the diagnosis of these cases:[12,13]

1. CT (In IPMNs originating from the main ductus, dilatation can be noted in the main pancreatic duct, while multiocular, grape-like cystic lesions of branch ductus type can also be observed)
2. Endoscopic ultrasound (EUS) (this method might be preferred as it allows fine needle aspiration (FNA) and cytological examination of cystic fluid)
3. Endoscopic retrograde cholangiopancreatography (ERCP) (dilatation of the pancreatic duct can be observed along with filling defects)
4. Magnetic resonance cholangiopancreatography (MRCP) (this method might be preferred to reduce radiation exposure)

In IPMN cases, approximately two-thirds of the masses tend to be localized at the head of the pancreas, while full involvement of the entire ductal system is rare. It is important to macroscopically show that the lesion originates from the ductal system. In some less commonly observed cases, the main pancreatic duct is involved, while in other and more commonly observed cases, lesions can be identified in the branch ductus. Especially in younger cases, it has been reported that IPMN shows a more frequent involvement of the pancreatic uncinate process in the posterior part of the vena porta (14). In the treatment of these cases, surgical resection should be performed in all cases with main ductus type IPMN. In branch ductus type IPMNs, surgery is recommended if the case is symptomatic, if there is an accompanying mural nodule around the cyst, and if there are positive cytological findings in EUS-FNA.[15]

Macroscopically, the head of the pancreas is primarily affected in main ductus type IPMNs, while involvement along the main duct may also be observed. Mucin outflow from the major and minor papillae is also notable. Dilated, irregular, and mucin-filled main duct is generally observed. In addition, the surrounding pancreatic tissue is atrophic due to occlusions in main ductus type IPMNs. In branch ductus type IPMNs; multiloculated, grape-like cystic lesions localized in the uncinate process are generally observed. Usually, the surrounding pancreatic tissue is normal. Macroscopically, in the presence of bright mucinous areas in the surrounding pancreas, it is necessary to focus on the possibility of an invasion.[16,17] In both types of IPMN, a high number of careful macroscopic sampling is important for excluding any possible IPMN-related invasive carcinoma.[18–20] Molecularly, the presence of GNAS, KRAS, and RNF43 mutations are often mentioned in IPMN-related invasive carcinoma.[21] Furthermore; CRAS, TP53, and CDKN2A (p16) mutations are reportedly among mutations that increase the dysplasia grade in the mucinous epithelium of IPMN cases.[22]

Conclusion

In conclusion, the rate of diagnosis of IPMNs has significantly increased today owing to widespread use of radiological imaging techniques. These cases can be seen in a broad range of stages, from early neoplastic changes to invasive carcinoma (e.g., IPMN associated with low grade-intermediate dysplasia, high grade dysplasia, or invasive carcinoma). IPMNs have a better prognosis than classical pancreatic ductal adenocarcinoma. A multidisciplinary approach is highly important for the diagnosis and treatment of these cases and identification of prognostic factors. The treatment should be individually tailored, taking into account the prognostic characteristics of the case and life expectancy. Moreover, considering the molecular analysis approach used today, we can assume that different and more appropriate treatment models will be available in the future.

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Conflicts of interest

Authors declare that there is no conflicts of interest.

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