Intraductal Papillary Mucinous Tumors
Non-Invasive and Invasive

Intraductal Tumor: Noninvasive and Invasive

Initial studies on premalignant lesions of pancreatic cancer showed that hyperplastic and metaplastic ductal proliferations, including papillary hyperplasia, are often found in association with pancreatic carcinoma [1, 2]. Although subsequent reports have confirmed these observations, it has been established that most of these lesions do not serve as cancer precursors [3–5]. In fact, papillary hyperplasia is now considered to be a nonspecific response of the ductal epithelium to various stimuli, especially ductal obstruction [6]. Only one case of papillary hyperplasia of the pancreas unassociated with preexisting chronic pancreatitis or pancreatic cancer has been reported [7]. Histologically, papillary hyperplasia may involve the intralobular, interlobar, and main ducts. Tall columnar mucin-secreting cells with regular basal nuclei line the papillary projections. Cytologic atypia and mitotic figures are not seen and, therefore, this lesion does not represent a diagnostic problem and should not be confused with intraductal papillary tumor.

Recent efforts to detect early pancreatic carcinoma by endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), and ultrasound (US), or by careful examination of the pancreas at autopsy have resulted in the characterization of papillary intraductal carcinoma.

Definition

Intraductal tumor corresponds well to a tumor of type III cancer of the pancreatographic classification proposed by Ohashi and Takagi [8] in 1980 (Fig. 1). Because they established clinical criteria for this cancer, much information concerning this type of cancer has accumulated and the definition of the tumor has been revised. Currently, the definition of this type of cancer is approached from two points of view: consideration from a clinical standpoint (narrow view) and from a pathological or clinicopathological context (broad view). The narrow view of this cancer was advocated by Ohashi et al. [9]. This definition is based on clinical concepts and, more specifically, on the characteristic features of the papilla of Vater (excretion of mucin through the patulous orifice and accumulation of mucin in the dilated pancreatic duct). The broad view of this cancer is defined pathologically by Kato and Yanagisawa [10] as a “pancreatic cancer with a large volume of extracellular mucin production or retention” or clinicopathologically by Yamao et al. [11] as a “pancreatic cancer in which the mucin produced by the tumor can be clinically or macroscopically recognized.” Intraductal mucin hypersecreting tumor is the clinical term (narrow view). The cancer that is defined by the clinicopathological concept (broad view) consists of intraductal papillary cancer of a mucin-producing type, mucinous cystadenocarcinoma, and mucinous adenocarcinoma.

By histology, immunohistochemistry, and intraductal growth pattern, two types of intraductal tumors can be distinguished: intraductal mucin hypersecreting and intraductal papillary neoplasms [12]. These two tumor types may be found together in a single tumor with varying degrees of each [13]. The criterion for a common classification of these tumors is their intraductal growth pattern. There-
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Fig. 1. New classification of endoscopic retrograde cholangiopancreatography findings of pancreatic cancer proposed by Ohashi and Takagi. (From [8], with permission)

Therefore, the intraductal mucin hypersecreting tumors, intraductal papillary neoplasms, and duct-ectatic type of pancreatic carcinoma [14] represent variants of intraductal tumors and not separate entities. However, most of the intraductal papillary neoplasms that were clinically diagnosed are mucin hypersecreting. Only a few cases with non-duct-ectatic type intraductal papillary tumors were reported [15].

To avoid confusion, the term “intraductal tumor” should be applied to both of these neoplasms and the presence of excess mucin or the predominance of papillary structures should be indicated as an additional characteristic (i.e., intraductal “papillary” and/or “mucin-hypersecreting” tumor). Because even benign-appearing tumors show focal atypia or malignant changes and because the unpredictable biological behavior of this tumor and the presence of c-Ki-ras mutation (even in benign-looking epithelia) [16, 17], the term “adenoma” should be reserved for only those intraductal lesions which do not show any cytomorphological and molecular biological evidence for malignancy.

Synonyms and Related Terms

Mucous-secreting cancer [9]; mucin-producing cystic adenocarcinoma [18]; duct-ectatic mucinous cystadenocarcinoma [10]; and mucin-hypersecreting cancer [19] are terms used to describe similar findings, and this has led to a certain amount of confusion.

The spectrum of tumors that show characteristic features of the papilla of Vater and pancreatogram include: mucin-producing tumor [20, 21]; intraductal mucin-hypersecreting neoplasms [13]; intraductal papilloma [12]; villous adenoma of the main pancreatic duct [22]; intraductal cystadenoma [23]; diffuse intraductal papillary adenocarcinoma [24]; diffuse villous carcinoma of the duct of Wirsung [25]; diffuse villous adenoma of the pancreatic duct [26]; and mucinous pancreatic duct ectasia [27].

Incidence

Intraductal tumor (IDT) accounts for 0.5% of pancreatic tumors found at autopsy, 7.5% of clinically diagnosed tumors, and 16.3% of tumors in resected cases [14]. With regard to only resected ductal cancers, IDT comprises from 5.8% [28] to 9.5% [29]. Until the first proposal on a detailed definition of this cancer was presented in 1982, only a few cases were reported in Japan and other countries; however, the number of documented cases has increased remarkably in recent years, especially in Japan. The reason for this increase is unknown, but it might be related to a better understanding of the characteristic clinical features of this tumor and improvement of diagnostic methods such as US, CT, and endoscopic retrograde cholangiopancreatography (ERCP).

Age and Sex

IDT is usually found in the 60–70 year age group. The tumors are most frequently found in the head of the pancreas in men [28, 29], while mucinous cystic neoplasms often occur in the body or tail of the pancreas in middle-aged women. Yamao et al. [29, 30] studied 34 cases with this tumor. The age of the 13 patients with this invasive type (9 men and 4 women) ranged from 50 to 87 years (mean age: 69 years); of 14 patients with noninvasive type (10 men and 4 women), the ages ranged from 47 to 74 years (mean age: 64 years); and of 7