Experimental and Molecular Pathology 93 (2012) 345–349

Contents lists available at SciVerse ScienceDirect

Experimental and Molecular Pathology

journal homepage: www.elsevier.com/locate/yexmp

Invasive mucinous cystic neoplasms of the pancreas

Michael L. Baker [a,*], E. Scott Seeley [b], Reetesh Pai [b], Arief A. Suriawinata [a], Mari Mino-Kenudson [c], Giuseppe Zamboni [d], Günter Klöppel [e], Daniel S. Longnecker [a]

[a] Department of Pathology, Dartmouth Hitchcock Medical Center and Dartmouth Medical School, Lebanon, NH 03756, USA
[b] Department of Pathology, Stanford Hospitals and Clinics and Stanford University School of Medicine, Stanford, CA, USA
[c] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[d] Department of Pathology, Ospedale S.Cuore-Don Calabria and University of Verona, Italy
[e] Departments of Pathology, Technical University of Munich and University of Kiel, Germany

ARTICLE INFO

Available online 10 August 2012

Keywords:
Mucinous cystic neoplasm
Intraductal papillary mucinous neoplasm
Mucinous cystadenoma
Mucinous cystadenocarcinoma
Colloid carcinoma
MUC2
CDX2
Pancreas

ABSTRACT

Mucinous cystic neoplasms (MCN) and intraductal papillary mucinous neoplasms (IPMN) of the pancreas both appear to have been included and intermixed in some early reports of pancreatic cystic neoplasms. Recognition of their distinguishing features evolved during the last decade of the twentieth century. One legacy of the early period is the statement that mucinous cystic neoplasms sometimes progress to invasive colloid carcinoma. It is now recognized that colloid carcinomas characteristically arise from IPMN. We set out to see if we could find MCN that invaded as colloid carcinomas and found no examples in MCN collected in two academic medical centers. We then sought to expand the number of MCN by evaluating series from additional centers. This yielded no examples of colloid carcinomas associated with 291 MCN, however one MCN exhibited a minor component with colloid (non-cystic mucinous) growth pattern within the fibrous wall of the neoplasm. The expression of CDX2, a marker of intestinal differentiation that is found in colloid carcinomas was examined by immunostaining in the original MCN series and in the MCN with the intratumoral colloid growth pattern. Focal expression of CDX2 was found in 22 of 43 MCN including the MCN that exhibited the intratumoral colloid growth pattern. Overall, the data suggest that MCN rarely, if ever, invade as colloid carcinoma but the expression of CDX2 by some MCN and the observation of intratumoral colloid growth pattern in one MCN seems to leave open the possibility that MCN might rarely invade as colloid carcinoma.
The majority of malignant MCN invade with a tubular (ductal) pattern, and rarely the invasive component was anaplastic.

© 2012 Elsevier Inc. All rights reserved.

Introduction

[1]Pancreatic mucinous cystic neoplasms (MCN) were first characterized as distinct from serous neoplasms by Compagno and Oertel (1978, 573–580) over thirty years ago, initially as an all-inclusive category of mucin-producing cystic neoplasms. MCN have since been distinguished from intraductal papillary-mucinous neoplasms (IPMN) and well-characterized with respect to clinical presentation and behavior in many excellent series and reviews. Difficulties in discriminating the two entities persist.

MCN are clinicopathologically defined as mucinous cysts occurring preferentially in the body and tail of the pancreas in pre-menopausal women. Although a recent report (Masia et al., 2011, 264–267) describing a case of MCN involving the main pancreatic duct, and other rare exceptions (Hruban et al., 2007, 422; Yamao et al., 2003, 142–146) illustrate otherwise, it has been established that MCN do not generally communicate with the pancreatic ducts, a macroscopic feature used in many series as a factor to discriminate MCN from IPMN (Adsay, 2008, 401–404; Reddy et al., 2004, 1026–1031).

MCN are histologically defined as well-demarcated cysts lined by a mucin-producing columnar epithelium overlying an ovarian-type stroma that has been established as the sole requisite criterion for diagnosis of MCN in some reports (Luttges et al., 2002, 466–471; Tanaka et al., 2006, 17–32; Zamboni et al., 1999, 410–422). In addition to the inconsistent application of this criterion, the ovarian-type stroma may only have a weak or focal presence (Reddy et al., 2004, 1026–1031; Zamboni et al., 1999, 410–422), lending to the diagnostic confusion between MCN and IPMN, especially with sub-optimally sampled resection specimens. Epithelial dysplasia is graded as mild, moderate, or severe, corresponding to low-, intermediate-, and high-grade dysplasia (carcinoma *in situ*) respectively in the current World Health Organization (WHO) classification system (Zamboni et al., 2010). Low grade

* Corresponding author at: Department of Pathology, Texas Children's Hospital, 6621 Fannin Street, Suite AB1195, Houston, TX 77030, USA. Fax: +1 832 825 0164.
E-mail address: bakerm10@lsus.edu (M.L. Baker).

[1] MCN Mucinous cystic neoplasm; IPMN intraductal papillary mucinous neoplasm; CC colloid carcinoma; WHO World Health Organization; AFIP Armed Forces Institute of Pathology.

0014-4800/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.yexmp.2012.07.005

MCN are generally regarded to be at risk for progression to higher grade lesions and to invasion; therefore, complete resection is recommended for patients who are fit for surgery, with thorough sampling and histological examination of the resected neoplasm to evaluate for dysplastic and invasive foci (Crippa et al., 2008, 571–579; Tanaka et al., 2006, 17–32; Thompson et al., 1999, 1–16; Zamboni et al., 1999, 410–422; Zamboni et al., 2010).

The current consensus in the international community of pathologists with an interest in the pancreas is that MCN presenting with invasion do so most commonly with a tubular (ordinary ductal) invasive pattern. However, some authors have indicated that a small fraction of MCN invaded as colloid carcinoma (CC, aka mucinous noncystic carcinoma)(Adsay, 2007, S71-S93; Adsay et al., 2001, 26–42; Japan Pancreas Society, 2003; Klimstra, 2005, 318–329; Odze and Goldblum, 2009). CC in the pancreas is usually associated with invasive IPMN in the head of the gland and is characterized by extracellular (stromal) pools of mucin containing floating malignant epithelial cells that comprises more than 50% of the tumor volume(Odze and Goldblum, 2009; Seidel et al., 2002, 56–63; Zamboni et al., 2010); however, some authors have recommended a diagnostic criterion requiring that more than 80% of the tumor volume be composed of malignant epithelium and mucin (Adsay et al., 2001, 26–42; Hruban et al., 2007, 422). Contact with one of the authors cited above, who reported a single case of MCN invading as CC, revealed that the reported tumor lacked characteristic ovarian-type stroma, suggesting that this most likely reflected misdiagnosis of IPMN as MCN (personal communication, N. Volkan Adsay). Although the report of this case is cited in the current Armed Forces Institute of Pathology (AFIP) fascicle, neither the latest WHO classification of tumors nor the fascicle directly mentions a CC pattern of invasion associated with MCN (Hruban et al., 2007, 422; Zamboni et al., 2010). The question of whether MCN invade as CC is clinically relevant since CC in the pancreas has recently been described as having a more favorable clinical course than invasion with a conventional tubular (ductal) type (Hruban et al., 2007, 422; Mino-Kenudson et al., 2011, 1712–1720; Odze and Goldblum, 2009).

Our goals were primarily to evaluate the prevalence and patterns of invasion associated with MCN, and secondarily to assess the accuracy of our separation MCN from IPMN.

Material and methods

This study began with evaluation of 22 MCN resected at the Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire (Dartmouth) and 20 MCN from the Stanford University Hospitals & Clinics in Stanford, California (Stanford). Due to the small number of MCN with invasion in these series, we sought to increase the number of invasive MCN evaluated in regard to the pattern of invasion by embracing a published series of 163 MCN reported from Massachusetts General Hospital, Boston, Massachusetts and the University of Verona, Italy (Crippa et al., 2008, 571–579), plus 31 additional cases from the Massachusetts General Hospital and 55 cases from the University of Kiel in Kiel, Germany (Kiel). The report published by Crippa et al. (2008, 571–579) did not include a description of associated invasive patterns.

The MCN from Dartmouth were accessioned between the years 1992 and 2009. The H&E stained glass slides were evaluated by four reviewers independently and in consensus for diagnostically challenging cases. Current WHO classification guidelines (Zamboni et al., 2010) for MCN were applied as diagnostic criteria. Electronic medical records were retrieved and reviewed as appropriate. Immunohistochemical studies were performed for MUC1, MUC2, and CDX2 to characterize the immunophenotype of the neoplastic epithelium, and for ER, PR and inhibin to evaluate the ovarian-type stroma and support the diagnosis of MCN. Similar examination of the MCN from Stanford was conducted by co-authors at that center.

All immunostained glass slides were evaluated by two reviewers and graded according to established criteria, with interobserver disagreement arbitrated by a third reviewer.

Results

From a total of 291 cases of MCN that were evaluated in regard to invasion, 38 were classified as invasive (13.4%), including 3 cases from Dartmouth (13.6%), 1 from Stanford (5.0%), 6 from Boston (6.5%), 11 from Kiel (20%), and 17 from Verona (16.6%). Of these cases, none was classified as a colloid carcinoma. All invasive cases included from Dartmouth and Stanford did so with a tubular (ductal) pattern. All invasive cases except one in the series published by Crippa et al. exhibited a tubular (ductal) pattern. One case (described below) exhibited apparent intratumoral invasion with a colloid growth pattern. Since that report was published in 2008, an additional 4 cases of invasive MCN have been seen in Boston, none of which was associated with invasion as CC. Invasive cases from the Kiel series did so most commonly with a tubular (ductal) pattern, and otherwise with an anaplastic (3 cases, 27%) or adenosquamous (1 case, 9%) component. All patients were female, with the exceptions of a single male case (1.8%) included in the data from Kiel, and eight male cases (5%) included in the series from Crippa et al. (2008, 571–579).

All of the cases from Dartmouth and Stanford ($n=42$) were women ranging in age from 23 to 76 years (average age 49 years, SD $\pm$ 14 years). All but two tumors were located in the body or tail of the pancreas, with sizes ranging from 0.9 to 11 cm (average size 5.0 cm, SD 2.7 cm).

All of the invasive cases from Dartmouth ($n=3$) showed positive immunoreactivity for MUC1 and negative staining for MUC2, with only one case moderately immunoreactive for CDX2. One of the invasive cases was a 5.8 cm tumor located in the distal pancreas of a 66 year old woman, featuring intermediate-grade dysplasia in the lining epithelium and, focally, an unusual muconodular pattern of invasion with dissecting mucin pools and scant floating malignant epithelial cells in the invasive component. The major portion of the invasion occurred with a tubular pattern with focal lymphovascular space invasion and extensive perineural involvement. The area with distinct mucinous architecture composed 5% or less of total tumor volume, and was most often seen immediately adjacent to a frank tubular (ductal) invasive pattern. Immunohistochemistry showed positive immunoreactivity for MUC1, and negative staining for MUC2 and CDX2 (Fig. 1), as well

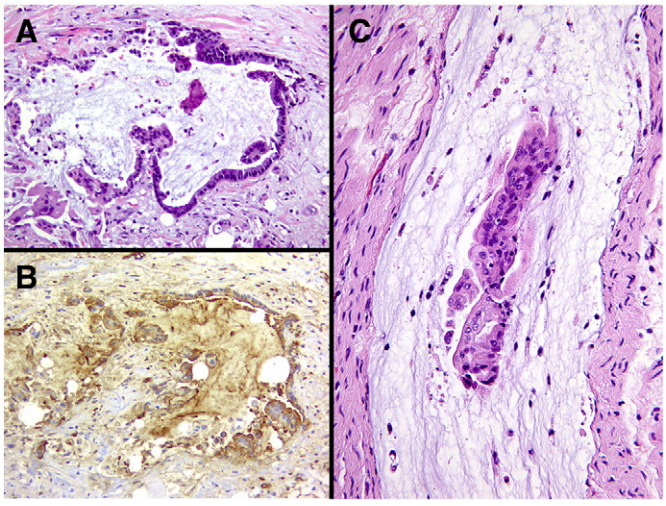

Fig. 1. A) An invasive MCN with scant malignant epithelium floating in mucin pools dissecting desmoplastic stroma (H&E), with B) positive immunoreactivity for MUC1 in goblet cells and C) malignant epithelial cells floating in an intraneural mucin pool (H&E). All panels 200×.

Download English Version:

https://daneshyari.com/en/article/2775177

Download Persian Version:

https://daneshyari.com/article/2775177

Daneshyari.com