Human Pathology (2017) 65, 71–78

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

SLC2A1/GLUT1 expression in mural nodules of intraductal papillary mucinous neoplasm of the pancreas☆,☆☆

Yasunori Oda MD, PhD[a], Shinichi Aishima MD, PhD[a,*], Koji Shindo MD, PhD[a], Minoru Fujino MD[a], Yusuke Mizuuchi MD, PhD[a], Masami Hattori MD[a], Tetsuyuki Miyazaki MD[a], Masao Tanaka MD, PhD[b], Yoshinao Oda MD, PhD[a]

[a]*Department of Anatomic Pathology, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan*
[b]*Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan*

Received 30 May 2016; revised 3 March 2017; accepted 12 March 2017

Keywords:
Intraductal papillary mucinous neoplasm;
Glucose transporter;
Mural nodule;
Positron-emission tomography;
Endoscopic ultrasonography;
EUS

Summary In intraductal papillary mucinous neoplasms (IPMNs), the presence of a mural nodule showing a papillary or nodular proliferation of tumor cells in the dilated pancreatic duct is an indication for resection of IPMN. Solute carrier family 2, facilitated glucose transporter member 1, known as glucose transporter type 1 (SLC2A1/GLUT1) mediates cellular glucose uptake in many carcinomas and is correlated with increased ^{18}F-fluorodeoxyglucose (^{18}F-FDG) uptake. We examined SLC2A1/GLUT1 expression in the mural nodules of 180 IPMN specimens to distinguish malignant/benign tumors. A mural nodule was detected in 80 (44.4%) of the IPMNs, and was detected in 18.6% (13/70) of the IPMN-low (dysplasia) specimens, 36.1% (13/36) of the IPMN-int, 93.3% (28/30) of the IPMN-high, and 59.1% (26/44) of the IPMN-inv (with an associated invasive carcinoma) specimens. The sensitivity for detecting mural nodules was 81.7% by endoscopic ultrasonography, 70% by contrast-enhanced computed tomography and 54% by endoscopic retrograde cholangiopancreatography. SLC2A1/GLUT1 expression in the mural nodules was recognized in the basal and basolateral cytomembrane of tumor cells and was expressed in 15.4% (2/13) of the IPMN-low, 15.4% (2/13) of the IPMN-int, 71.4% (20/28) of the IPMN-high and 84.6% (22/26) of the IPMN-inv groups. The SLC2A1/GLUT1 expression was significantly higher in the IPMN-high and IPMN-inv mural nodules than in those of the IPMN-low and IPMN-int groups. Our findings suggest that SLC2A1/GLUT1 is expressed late in the adenoma-carcinoma sequence during carcinogenesis in IPMN, and SLC2A1/GLUT1 act as therapeutic target for malignant IPMN.

1. Introduction

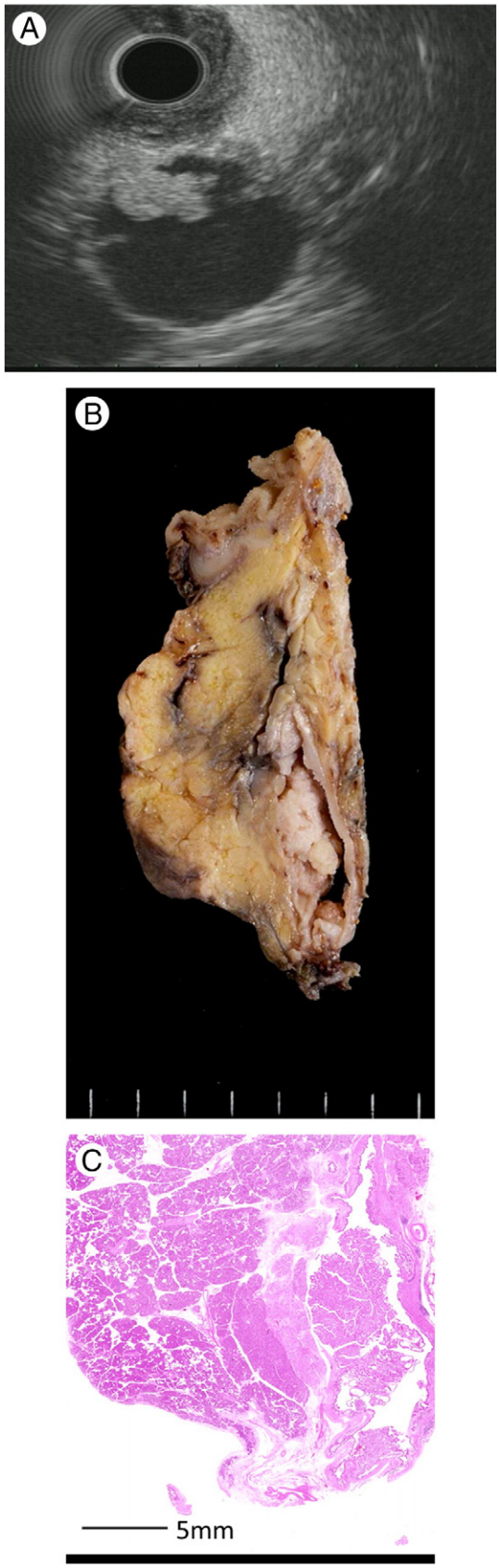
Intraductal papillary mucinous neoplasms (IPMNs) are characterized by intraductal papillary growth and mucin secretion in the dilated pancreatic ducts [1,2]. Many reports of IPMNs have been published since the first report in 1982 [3]. The incidence of IPMN is 1% to 3% of exocrine pancreatic neoplasms and 20% of pancreatic cystic lesions [4]. According

☆ Disclosures: The authors declare no conflict of interest associated with this manuscript.

☆☆ This study was supported by a Grant-in-Aid for Scientific Research (KAKENHI: 23590399) and the Japan Society for the Promotion of Science (JSPS).

* Corresponding author: Department of Anatomic Pathology, Graduate School of Medical Science, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan.
E-mail address: saish@surgpath.med.kyushu-u.ac.jp (S. Aishima).

http://dx.doi.org/10.1016/j.humpath.2017.03.008
0046-8177/



to the World Health Organization (WHO) classification, IPMNs can be histologically classified into the following 4 groups: IPMN with low-grade dysplasia (IPMN-low), IPMN with intermediate-grade dysplasia (IPMN-int), IPMN with high-grade dysplasia (IPMN-high), and IPMN with an associated invasive carcinoma (IPMN-inv). In 2012, international consensus guidelines for the management of IPMN and mucinous cystic neoplasm (MCN) of the pancreas were published [5]. The presence of mural nodules that show a papillary or nodular proliferation of tumor cells in the dilated pancreatic duct is an indication for the resection of the IPMN. Several studies showed that the mural nodule size of IPMN is a predictor of malignancy [6,7].

Positron-emission tomography (PET) using 18F-fluorodeoxyglucose (^{18}F-FDG) is useful for detecting primary and recurrent cancers. Increased ^{18}F-FDG uptake is correlated with the expression of solute carrier family 2, facilitated glucose transporter member 1, known as Glucose transporter type 1 (SLC2A1/GLUT1)—a trans-membrane protein that mediates cellular glucose uptake—in many carcinomas such as pancreatic, colorectal, ovarian, and non–small cell lung cancers and squamous cell carcinoma of the cervix [8-12].

Here we used immunohistochemical staining to investigate the SLC2A1/GLUT1 expression in mural nodules of IPMNs and to distinguish malignant IPMNs from benign IPMNs, This distinction is critical to the decision whether to proceed with surgical resection or observe the IPMN by cytology and biopsy.

2. Materials and methods

2.1. Patients

We obtained 180 surgically resected IPMNs, which had been diagnosed at the Department of Anatomic Pathology of Kyushu University (Fukuoka, Japan) between January 2000 and June 2012. The specimens were fixed by formalin and cut vertically to cross the main pancreatic duct into approximately 5-mm-thick sections. All of the sections were routinely examined microscopically by hematoxylin and eosin staining. The 180 cases were histologically classified into 70 IPMN-low, 36 IPMN-int, 30 IPMN-high and 44 IPMN-inv cases. Based on their morphological features and MUCs staining, the IPMNs were also classified into 4 IPMN subtypes: 99 gastric-type, 38 intestinal-type, 32 pancreatobiliary-type, 7 oncocytic-type, and 4 unclassified-type [13].

Because IPMNs have various atypia within the same samples, we evaluated the SLC2A1/GLUT1 expression in both

Fig. 1 EUS shows a large mural nodule (17 mm) in the dilated main pancreatic duct of the pancreatic head (A). Macroscopic finding indicating an intraductal tumor, which was yellow to white, occupying the dilated main pancreatic duct (B). The mural nodule shows a papillary proliferation of atypical cells (C).