Human Pathology (2013) **44**, 503–511

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Diagnostic utility of von Hippel-Lindau gene product, maspin, IMP3, and S100P in adenocarcinoma of the gallbladder☆

Jianhui Shi MD, PhD, Haiyan Liu MD, Hanlin L. Wang MD, PhD, Jeffrey W. Prichard DO, Fan Lin MD, PhD*

Geisinger Medical Center, Danville, PA 17822

Received 17 February 2012; revised 26 June 2012; accepted 27 June 2012

Keywords:
Adenocarcinoma;
Gallbladder;
pVHL;
Maspin;
IMP3;
S100P

Summary Our recent study demonstrated the up-regulation of maspin, IMP3, and S100P and down-regulation of von Hippel-Lindau gene product (pVHL) in ductal adenocarcinoma of the pancreas. Distinction of adenocarcinoma of the gallbladder from benign/reactive glandular epithelium can be challenging if based on hematoxylin and eosin–stained sections alone. Immunohistochemical stains for pVHL, maspin, IMP3, and S100P were performed on 82 gallbladder specimens, including adenocarcinoma (n = 33) and normal/reactive gallbladder (n = 49). The results demonstrated (1) only 6.0% of adenocarcinoma cases were focally positive for pVHL, and all normal and most reactive cases (85%) were diffusely positive for pVHL; (2) maspin, IMP3, and S100P were positive in 100%, 81.8%, and 75.8% of adenocarcinoma cases, respectively; in contrast, 53.1%, 12.2%, and 30.6% of normal/reactive cases were only focally and weakly positive for maspin, IMP3, and S100P, respectively; and (3) 90.3% of adenocarcinoma cases were pVHL-negative and positive for 2 or more positive markers, whereas none of the benign/reactive cases showed this staining profile. This study demonstrates that the immunostaining profile of pVHL−/IMP3+/maspin+/S100P+ is useful in the distinction of adenocarcinoma of the gallbladder from normal/reactive conditions.
© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Although cholecystectomy specimens are among the most common specimens received in a surgical pathology grossing room, gallbladder adenocarcinoma is rare and accounts for only 0.49% of all cancers among women and 0.17% of all cancers among men [1–3]. It is often discovered incidentally during or after cholecystectomy. It is a highly aggressive malignancy with a 5-year survival rate of 13% [4]. Gross identification of gallbladder adenocarcinoma is difficult since only approximately 20% of gallbladder adenocarcinomas are associated with "porcelain-like" gallbladder [1,2], which usually raises suspicion for malignancy. Because of this and the very low incidence of gallbladder adenocarcinoma, limited tissue blocks are usually submitted for routine histological examination. The distinction between reactive glandular epithelial atypia and adenocarcinoma can be challenging if based on limited hematoxylin and eosin–stained sections alone.

☆ Partly presented at the United States and Canadian Academy of Pathology Annual Meetings in 2010 and 2011.

* Corresponding author. Department of Laboratory Medicine, MC 01–31, Geisinger Medical Center, Danville, PA 17822.
E-mail address: Flin1@geisinger.edu (F. Lin).

0046-8177/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.humpath.2012.06.010

To improve the diagnostic accuracy, numerous biomarkers have been investigated and reported in the literature, including P-cadherin, CD24 , p53, p16, CDX2, HepPar1 (hepatocyte paraffin-1), Reg IV (regenerating islet-derived family member 4), EGFR (epidermal growth factor receptor), EpCAM (epithelial cell adhesion molecule), Claudin 4, CD147, MMP2 (matrix metalloproteinase 2), N-cadherin, E-cadherin, GLUT-1 (glucose transporter-1), and maspin [5–18]; however, there is no single marker proven to be absolutely sensitive and specific for confirming the diagnosis of gallbladder adenocarcinoma.

Recently, we tested and refined a panel of immunohistochemical markers including von Hippel-Lindau gene product (pVHL), maspin, S100P, and IMP3 in diagnosis of pancreatic adenocarcinoma in both surgical and fine needle aspiration specimens [19–21]. Maspin (mammary serine protease inhibitor), also known as serpin B5, is a tumor suppressor gene expressed in some human epithelial cells. Maspin overexpression can be seen in carcinomas from various organs including adenocarcinoma of the gallbladder [17,18]; however, maspin overexpression was also reported in non-tumorous gallbladder epithelium in patients with cholelithiasis and intestinal metaplasia [17,18]. Therefore, maspin alone cannot be used as a reliable diagnostic marker to differentiate benign from malignant gallbladder glandular lesions. The biology and function of S100, pVHL, and IMP3 have been briefly reviewed in our previous publications [19,21,22]. Typically, pancreatic adenocarcinoma expresses maspin, S100P, and IMP3, but not pVHL; conversely, benign and reactive pancreatic ducts are positive for pVHL and negative for maspin, S100P, and IMP3 [21]. In addition, it has been demonstrated that a panel of IMP3, S100P, and pVHL is valuable in the detection of adenocarcinoma of the common bile duct, which frequently shows an immunoprofile of IMP3-positive/S100P-positive/pVHL-negative. In contrast, benign/reactive biliary epithelium frequently exhibits an IMP3-negative/S100P-negative/pVHL-positive staining pattern [22,23].

The potential utility of these 4 markers (pVHL, maspin, S100P, and IMP3) in differentiating gallbladder adenocarcinoma from benign/reactive gallbladder glandular epithelium has been studied, and the preliminary results were similar to those of pancreatic adenocarcinoma [24]. The aim of the current study is to further investigate the diagnostic value of these 4 markers in distinguishing adenocarcinoma of the gallbladder from benign/reactive gallbladder epithelium.

2. Materials and methods

2.1. Case selection

The study was conducted with approval from the institutional review board of Geisinger Health System. Eighty-two surgical gallbladder specimens from 1995 to 2011 were retrieved from the archives of the Department of Laboratory Medicine at Geisinger Medical Center. The 82 cases were divided into 4 groups: group 1, 33 cases of gallbladder adenocarcinoma (GBCA); group 2, 16 cases of normal gallbladder (NGB); group 3, 20 cases of chronic cholecystitis (CCGB) with one or more of these features: chronic inflammation, fibrosis, Rokitansky-Aschoff sinuses, and gastric or intestinal metaplasia; and group 4, 13 cases of active chronic cholecystitis (ACGB) with acute inflammation, mucosal ulceration, and reactive glandular atypia. The World Health Organization 3-tiered histologic grading system was applied, with grade I/well-differentiated (>95% glandular formation), grade II/moderately differentiated (40%-95% glandular formation), and grade III/poorly differentiated (<40% glandular formation). Among the 33 consecutive gallbladder adenocarcinomas from 1995 to 2011 with available tissue blocks, the grade I, II, and III adenocarcinoma cases numbered 6, 23, and 4, respectively.

2.2. Immunohistochemistry

Immunohistochemical stains with pVHL, maspin, IMP3, and S100P were performed on these 82 cases using the previously published protocol on a Dako staining system [19]. Detailed information about the antibodies and staining conditions is summarized in Table 1. Pancreatic adenocarcinoma was used as a positive control for S100P, maspin, and IMP3. Normal renal tissue was used as a positive control for pVHL.

The staining intensity for both tumor cases and normal/reactive gallbladder tissues was graded as weak or strong. The distribution was recorded as negative (<5% of tumor

Table 1 Summary of antibody information and staining conditions

Antibody	Vendor	Catalog no.	Approved use	Clonality	Host animal	Dilution	Incubation time/temp	AR method/time/temp/pH
Maspin	BD	554292	RUO	G167-70	Mouse	1:200	40 min/ambient	EDTA/15 min/100°C/8.0
IMP3	DAKO	M3626	IVD	69.1	Mouse	1:50	40 min/ambient	EDTA/15min/100°C/8.0
S100P	BD	610307	RUO	Clone 16	Mouse	1:100	30 min/ambient	ProtK/12 min/ambient/7.5
pVHL	SantaC	Sc-5575	RUO	Polyclonal	Rabbit	1:50	30 min/ambient	ProtK/9 min/ambient/7.5

Abbreviations: AR, antigen retrieval; RUO, for research use only; IVD, in vitro diagnostic use; BD, Becton Dickinson Immunocytometry Systems (BD Biosciences, San Jose, CA, USA); DAKO, Dako North America, Inc., Carpinteria, CA, USA; SantaC, Santa Cruz Biotechnology, Inc, Santa Cruz, CA, USA.

Download English Version:

https://daneshyari.com/en/article/4133446

Download Persian Version:

https://daneshyari.com/article/4133446

Daneshyari.com