Case Report
Extensively Invasive Gallbladder Cancer from Intracholecystic Papillary Neoplasm Treated with Pylorus-Preserving Pancreaticoduodenectomy and Extended Cholecystectomy: A Case Report and Literature Review

Hideki Kumagai,1 Akira Umemura,1 Hiroyuki Nitta,1 Hirokatsu Katagiri,1 Masao Nishiya,2 Noriyuki Uesugi,2 Tamotsu Sugai,2 and Akira Sasaki1

1Department of Surgery, School of Medicine, Iwate Medical University, 2-1-1 Idaidori, Yahaba, Iwate 028-3695, Japan
2Department of Molecular Diagnostic Pathology, Iwate Medical University, 2-1-1 Idaidori, Yahaba, Iwate 028-3695, Japan

Correspondence should be addressed to Hideki Kumagai; hishioka@iwate-med.ac.jp

Received 9 November 2022; Revised 26 April 2023; Accepted 13 June 2023; Published 24 June 2023

Copyright © 2023 Hideki Kumagai et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. Intracholecystic papillary neoplasm (ICPN) is a rare tumor first classified by the World Health Organization in 2010. ICPN is a counterpart of the intraductal papillary mucinous neoplasm of the pancreas and intraductal papillary neoplasm of the bile duct [1]. Tumors are considered premalignant lesions [2, 3].

ICPN is rare, accounting for 0.4–1.5% of cholecystectomies and 6.4% of gallbladder cancers [1–3]. Therefore, there are limited previous studies on the diagnosis or surgical management of ICPN, and the prognosis of ICPN remains controversial.

1. Introduction

Intracholecystic papillary neoplasm (ICPN) is a relatively new concept established by the 2010 World Health Organization (WHO) classification [1]. According to this classification, ICPN is recognized as a counterpart of intraductal papillary mucinous neoplasm in the pancreas and intraductal papillary neoplasm of the bile duct [1]. Tumors are considered premalignant lesions [2, 3].
Here, we report a rare case of extensively invasive gallbladder cancer arising in ICPN treated with pylorus-preserving pancreaticoduodenectomy (PPPD) and extended cholecystectomy and review the previous literature.

2. Case Presentation

A 75-year-old man presented to the hospital with jaundice that had been present for 1 month. He had a medical history of hypertension and non-tuberculosis mycobacterial infection but no surgical history. Laboratory findings showed elevated levels of serum bilirubin and liver enzymes: total bilirubin, 10.6 mg/dL; aspartate aminotransferase, 68 IU/L; alanine aminotransferase, 119 IU/L; and gamma-glutamyl transpeptidase, 393 IU/L. Serum carbohydrate antigen 19-9 was also elevated (54.8 U/mL), though carcinoembryonic antigen was within the normal range. Enhanced computed tomography (CT) revealed a well-enhanced tumor in the distal bile duct and dilation of the hepatic-sided bile duct (Figure 1(a)). In addition, the gallbladder mucosa was thickened, with a homogeneous contrast effect (Figure 1(b)).

Endoscopic retrograde cholangiopancreatography (ERCP) showed a filling defect of the distal bile duct and dilation of the hepatic-sided bile duct seen from the tumor (Figure 1(b)).

Figure 1: Enhanced CT findings. (a) A well-defined tumor from a cystic duct to a distal bile duct was observed (yellow arrow), and a hepatic-sided bile duct seen from the tumor was dilated. (b) Gallbladder mucosa was well-contrasted, and the wall was thickened (yellow arrow). CT: computed tomography.

Figure 2: MRI and MRCP findings. (a) The tumor located in the distal bile duct had a low T2 signal (yellow arrow). (b) MRCP showed a filling defect of the distal bile duct and dilation of the hepatic-sided bile duct seen from the tumor (yellow arrow). MRCP: magnetic resonance cholangiopancreatography; MRI: magnetic resonance imaging.

2 Case Reports in Surgery
Figure 3: ERCP and IDUS findings. (a) ERCP showed a filling defect of the distal bile duct; the cystic duct was invisible. (b) IDUS showed that the tumor had invaded the bile duct subserosa (yellow arrow). (c) The patient’s distal bile duct was almost obstructed by the tumor. ERCP: endoscopic retrograde cholangiopancreatography; IDUS: intraductal ultrasonography.

Figure 4: Macroscopic findings. (a) Macroscopic findings revealed a papillary tumor that had invaded the common bile duct. The distal bile duct lumen was severely constricted by the tumor invasion (yellow arrow). (b) Cross section of the resected specimen revealed that the white tumor extensively invaded the liver (white arrow), cystic duct (red arrow), common bile duct (yellow arrow), and pancreas (pink arrow). Black arrows point to the papilla of Vater.
revealed a filling defect in the distal bile duct, and the cystic duct was invisible (Figure 3(a)). Moreover, intraductal ultrasound (IDUS) showed a papillary tumor in the common bile duct and indicated invasion of the bile duct subserosa (Figures 3(b) and 3(c)). Subsequent bile duct brushing cytology on ERCP and IDUS revealed adenocarcinoma, and the patient was diagnosed with distal bile duct cancer associated with adenomyomatosis of the gallbladder.

The patient was referred to our hospital for surgical treatment, and we planned to perform PPPD for distal bile duct cancer with curative intent. Intraoperative findings revealed a thickened and indurated gallbladder wall, suggesting the coexistence of gallbladder cancer; thus, we performed PPPD and extended cholecystectomy. Intraoperative frozen-section analysis of the cut end of the hepatic bile duct was negative for the tumor. A macroscopic examination of the resected specimen revealed a papillary tumor that had extensively invaded the liver, cystic duct, bile duct, and pancreas (Figures 4(a) and 4(b)). Permanent histopathological findings indicated that the tumor was papillotubulary and had broad-based growth of columnar cells with mucus production in the gallbladder (Figures 5(a) and 5(b)). In addition, metastasis to the lymph nodes of the hepatoduodenal ligament was observed. Immunohistochemical analysis revealed that the tumor cells were positive for mucin (MUC5AC) staining (c), but negative for MUC2 (d) and p53 (e) (all 100×).

**Figure 5:** Histopathological images showed that the tumor was papillotubulary and had broad-based growth of columnar cells with mucus production in the gallbladder; hematoxylin and eosin staining: (a) 20× and (b) 100×. Immunohistochemical analysis showed the tumor cells were positive for mucin (MUC5AC) staining (c), but negative for MUC2 (d) and p53 (e) (all 100×).

3. Discussion

We report the case of a patient with extensively invasive gallbladder cancer originating in ICPN treated with PPPD and extended cholecystectomy. Adsay et al. reported that invasiveness was observed in 55% of ICPN cases [1]; however, most patients with ICPN are found at an early stage incidentally by imaging studies, as mentioned below, and reports on advanced cases are limited [4–7]. We searched for previous reports on ICPN in PubMed using the keywords “intracholecystic papillary neoplasm” or “intracystic papillary neoplasm”
Table 1: Overview of the recent literature on ICPN.

<table>
<thead>
<tr>
<th>Case</th>
<th>First author</th>
<th>Age (year)</th>
<th>Gender</th>
<th>Symptom</th>
<th>Imaging findings</th>
<th>Preoperative diagnosis</th>
<th>Surgical procedure</th>
<th>Invasive component</th>
<th>Lymph node metastasis</th>
<th>Adjuvant therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sato [8]</td>
<td>77</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>SC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 10 months</td>
</tr>
<tr>
<td>2</td>
<td>Dettoni [9]</td>
<td>62</td>
<td>Female</td>
<td>Abdominal pain</td>
<td>Gallbladder tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 29 months</td>
</tr>
<tr>
<td>3</td>
<td>Meguro [10]</td>
<td>54</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Papillary tumor</td>
<td>Gallbladder tumor</td>
<td>EC, extrahepatic bile duct resection, and choledochojunostomy</td>
<td>Yes (complicated with mixed adenoneuroendocrine carcinoma)</td>
<td>No</td>
<td>No</td>
<td>Alive 24 months</td>
</tr>
<tr>
<td>4</td>
<td>Hashimoto [4]</td>
<td>58</td>
<td>Female</td>
<td>Jaundice</td>
<td>Papillary tumor</td>
<td>Gallbladder cancer</td>
<td>EC, PD</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Recurrence 16 months after surgery</td>
</tr>
<tr>
<td>5</td>
<td>Michalinos [11]</td>
<td>28</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Dilation of common bile duct</td>
<td>Choleodochal cyst</td>
<td>SC, extrahepatic bile duct resection, and choledochojunostomy</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>6</td>
<td>Sato [12]</td>
<td>64</td>
<td>Male</td>
<td>Epigastric pain</td>
<td>Cystic tumor</td>
<td>Not mentioned</td>
<td>SC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 8 months</td>
</tr>
<tr>
<td>7</td>
<td>Páez Cumpa [13]</td>
<td>39</td>
<td>Male</td>
<td>Epigastric pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>SC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Alive 6 months</td>
</tr>
<tr>
<td>8</td>
<td>Unno [14]</td>
<td>74</td>
<td>Male</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 3 months</td>
</tr>
<tr>
<td>9</td>
<td>Mizobuchi [15]</td>
<td>74</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>10</td>
<td>Mizobuchi [15]</td>
<td>61</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>11</td>
<td>Mizobuchi [15]</td>
<td>83</td>
<td>Male</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>Not mentioned</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>12</td>
<td>Sakai [5]</td>
<td>74</td>
<td>Male</td>
<td>Jaundice</td>
<td>Papillary tumor</td>
<td>Gallbladder cancer</td>
<td>EC, extrahepatic bile duct resection, and choledochojunostomy</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>13</td>
<td>Muranushi [16]</td>
<td>70</td>
<td>Male</td>
<td>No</td>
<td>Gallbladder tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Alive 42 months</td>
</tr>
<tr>
<td>14</td>
<td>Hara [17]</td>
<td>71</td>
<td>Male</td>
<td>No</td>
<td>Papillary tumor</td>
<td>ICPN</td>
<td>SC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>15</td>
<td>Fujii [6]</td>
<td>59</td>
<td>Male</td>
<td>Fatigue</td>
<td>Papillary tumor</td>
<td>ICPN</td>
<td>SSPPD after SC</td>
<td>Yes</td>
<td>No</td>
<td>Tegafur/gimeracil/oteracil</td>
<td>Alive 2 months</td>
</tr>
<tr>
<td>16</td>
<td>Yokode [18]</td>
<td>58</td>
<td>Female</td>
<td>Fever</td>
<td>Papillary tumor</td>
<td>ICPN</td>
<td>EC and SSPPD</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 6 months</td>
</tr>
<tr>
<td>Case</td>
<td>First author</td>
<td>Age (year)</td>
<td>Gender</td>
<td>Symptom</td>
<td>Imaging findings</td>
<td>Surgical procedure</td>
<td>Preoperative diagnosis</td>
<td>Adjuvant therapy</td>
<td>Invasive component</td>
<td>Lymph node metastasis</td>
<td>Outcome</td>
</tr>
<tr>
<td>------</td>
<td>--------------</td>
<td>------------</td>
<td>--------</td>
<td>---------</td>
<td>------------------</td>
<td>------------------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>---------</td>
</tr>
<tr>
<td>17</td>
<td>Saritas [19]</td>
<td>52</td>
<td>Female</td>
<td>Right upper quadrant pain</td>
<td>Gallbladder tumor</td>
<td>SC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>18</td>
<td>Park [20]</td>
<td>78</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>19</td>
<td>Fraga [21]</td>
<td>85</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>Yes (complicated with angiosarcoma)</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>20</td>
<td>Sciarrino [22]</td>
<td>66</td>
<td>Female</td>
<td>Abdominal pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>ICPN</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>21</td>
<td>Oh [23]</td>
<td>79</td>
<td>Female</td>
<td>Abdominal pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>SC</td>
<td>Yes (complicated with NEC)</td>
<td>No</td>
<td>No</td>
<td>Alive 5 months</td>
</tr>
<tr>
<td>22</td>
<td>Iwasaki [24]</td>
<td>52</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>SC</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 5 months</td>
</tr>
<tr>
<td>23</td>
<td>Oba [25]</td>
<td>78</td>
<td>Male</td>
<td>Jaundice and epigastric pain</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>No (complicated with MiNEN)</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>24</td>
<td>Logrado [26]</td>
<td>71</td>
<td>Female</td>
<td>Epigastric pain</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>ICPN</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>25</td>
<td>Iseki [27]</td>
<td>83</td>
<td>Male</td>
<td>No</td>
<td>Wall thickness of the gallbladder</td>
<td>Not mentioned</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>26</td>
<td>Kuniyoshi [28]</td>
<td>86</td>
<td>Female</td>
<td>Jaundice</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>ICPN</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>27</td>
<td>Ismail [29]</td>
<td>48</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>IC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>28</td>
<td>Aida [30]</td>
<td>65</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>SC</td>
<td>No (complicated with xanthogranulomatous cholecystitis)</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Dör [31]</td>
<td>77</td>
<td>Female</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>30</td>
<td>Shimada [32]</td>
<td>69</td>
<td>Male</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>31</td>
<td>Wong [33]</td>
<td>49</td>
<td>Male</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>32</td>
<td>Trisal [34]</td>
<td>48</td>
<td>Male</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>33</td>
<td>Watanabe [35]</td>
<td>79</td>
<td>Female</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Case</td>
<td>First author</td>
<td>Age (year)</td>
<td>Gender</td>
<td>Symptom</td>
<td>Imaging findings</td>
<td>Preoperative diagnosis</td>
<td>Surgical procedure</td>
<td>Invasive component</td>
<td>Lymph node metastasis</td>
<td>Adjuvant therapy</td>
<td>Outcome</td>
</tr>
<tr>
<td>------</td>
<td>--------------</td>
<td>------------</td>
<td>--------</td>
<td>---------</td>
<td>-----------------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>------------------</td>
<td>---------------------</td>
<td>-----------------</td>
<td>---------</td>
</tr>
<tr>
<td>34</td>
<td>Oishi [35]</td>
<td>60s</td>
<td>Female</td>
<td>No</td>
<td>Papillary tumor</td>
<td>ICPN</td>
<td>EC and resection of the extrahepatic bile duct</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Alive 24 months</td>
</tr>
<tr>
<td>35</td>
<td>Limaiem [36]</td>
<td>76</td>
<td>Male</td>
<td>Right upper quadrant pain</td>
<td>Papillary tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>36</td>
<td>Scarola [37]</td>
<td>80</td>
<td>Male</td>
<td>Fatigue</td>
<td>Gallbladder tumor</td>
<td>Not mentioned</td>
<td>EC</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Alive 6 months</td>
</tr>
<tr>
<td>37</td>
<td>Mruthyunjayappa [38]</td>
<td>70s</td>
<td>Male</td>
<td>Right upper quadrant pain</td>
<td>Gallbladder tumor</td>
<td>Gallbladder tumor</td>
<td>EC</td>
<td>Yes (complicated with NEC)</td>
<td>No</td>
<td>No</td>
<td>Death 50 months after surgery</td>
</tr>
<tr>
<td>38</td>
<td>Koike [39]</td>
<td>44</td>
<td>Male</td>
<td>No</td>
<td>Gallbladder tumor</td>
<td>Cholesterol polyp or pyloric-type adenoma</td>
<td>SC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>39</td>
<td>Our case</td>
<td>75</td>
<td>Male</td>
<td>Jaundice</td>
<td>Papillary tumor</td>
<td>Distal bile duct cancer</td>
<td>PPPD and EC</td>
<td>Yes</td>
<td>Yes</td>
<td>Tegafur/gimeracil/oteracil</td>
<td>Alive 12 months</td>
</tr>
</tbody>
</table>

**Summary**

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>No symptom</th>
<th>Papillary tumor</th>
<th>ICPN</th>
<th>SC</th>
<th>Yes</th>
<th>Yes</th>
<th>Tegafur/gimeracil/oteracil</th>
<th>Follow-up duration, Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>66.3</td>
<td>17</td>
<td>17 (43.6)</td>
<td>22 (56.4)</td>
<td>6 (15.4)</td>
<td>14 (35.9)</td>
<td>22</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Abdominal pain</td>
<td>Gallbladder tumor</td>
<td>12 (30.8)</td>
<td>13 (33.3)</td>
<td>21 (53.8)</td>
<td>17</td>
<td>38</td>
<td>Alive 24</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>16 (41.0)</td>
<td>Wall thickness of the gallbladder</td>
<td>3 (7.8)</td>
<td>4 (10.3)</td>
<td>Resection of the extrahepatic bile duct</td>
<td>5 (12.8)</td>
<td>PD</td>
<td>5 (12.8)</td>
</tr>
</tbody>
</table>

Data are expressed as the mean (range) or number (%).

ICPN: intracholecystic papillary neoplasm; SC: simple cholecystectomy; EC: extended cholecystectomy; PD: pancreaticoduodenectomy; SSPPD: subtotal stomach-preserving pancreaticoduodenectomy; PPPD: pylorus-preserving pancreaticoduodenectomy; NEC: neuroendocrine carcinoma; MiNEN: mixed neuroendocrine-non-neuroendocrine neoplasm.
and reviewed 39 cases [4–39], including the present case diag-
nosed as ICPN histopathologically (Table 1). The mean age of
patients with ICPN was 66.3 years, and female patients out-
numbered male patients, as previously reported [3]. Approx-
imately half of the ICPNs have invasive components, as found
by Adsay et al., however, our patient was the only patient with
lymph node metastasis in our review.

Moreover, Adsay et al. reported that approximately half
of the ICPNs develop in the right upper abdominal region,
and the other half are incidentally found by imaging studies
[1], which is similar to our findings summarized in Table 1.
Conversely, jaundice is an uncommon symptom in ICPN,
and there are few previous reports in the literature [4, 5,
25, 27]. Of the four patients, two patients suffered from jaun-
dice resulting from a protruding tumor from the gallbladder
to the common bile duct [4, 5]. Interestingly, the other two
developed jaundice due to mucus production from the
tumor [25, 27]. In the present case, histopathological find-
ings revealed that the tumor had extensively invaded the bile
duct; thus, the patient had obstructive jaundice owing to
vibration of the common bile duct rather than a pro-
truding tumor from the gallbladder. Protruding or advanced
tumors associated with ICPN can cause obstructive jaundice;
mored, mucus production from ICPN can lead to jaundice.

Distinguishing between ICPN and other gallbladder
tumors using imaging studies is difficult. In our review, only
15.8% of patients with ICPN were diagnosed accurately
before surgery. According to previous reports, ICPN is
well-defined on enhanced CT and presents high or low T2
signal intensity and high diffusion-weighted imaging signal
intensity on MRI [4, 7]. Fluorodeoxyglucose (FDG) accumu-
lation in ICPN has been observed on FDG-positron emis-
tion tomography [5, 28]. However, these are non-specific
findings that can be observed in other gallbladder tumors.
Moreover, histopathological examinations, including cytology
and biopsy are not diagnostic in terms of distinguishing
between ICPN and other types of gallbladder carcinomas
[4–7]. However, endoscopic ultrasound (EUS), including
IDUS or peroral cholangioscopy (POCS) has shown the
presence of a papillary tumor in most patients diagnosed
with ICPN preoperatively [4–6, 25, 27]. EUS and POCS
may provide a better definition of ICPN compared with
other imaging modalities. In the present case, IDUS revealed
a papillary tumor in the common bile duct. Therefore, clini-
cians should be familiar with ICPN, and make an effort to
accurately diagnose it using multiple imaging techniques.

The treatment for ICPN is oncological resection; how-
ever, the selection of the optimal surgical procedure is often
challenging. Simple cholecystectomy is sufficient for ICPN
limited to the gallbladder mucosa without invasion. How-
ever, approximately half of the ICPN cases have an invasive
component [1]. Moreover, some patients have ICPNs sus-
ppected of common bile duct invasion due to a protruding
tumor from the gallbladder to the common bile duct [4, 5].
In the present case, CT, MRI, and ERCP findings indicated
that the tumor was located in the distal bile duct, and IDUS
suggested that the tumor had invaded the subserosa of the
bile duct; therefore, we decided to perform PPPD. Moreover,
 intraoperative findings showed a thickened and indurated
gallbladder wall, suggesting advanced gallbladder carcinoma;
thus, we performed an extended cholecystectomy in addition
to PPPD. Intraoperative frozen-section analysis of the cut
end of the hepatic-sided bile duct confirmed no evidence of
a tumor. To select the optimal surgical procedure, a com-
prehensive evaluation that considers preoperative imaging
studies and intraoperative findings is essential. Notably,
EUS, including IDUS, can be a useful tool for assessing
tumor extension of ICPN.

Some studies have reported that ICPN with or without
invasive carcinoma has a good prognosis, in contrast to
other types of gallbladder carcinoma [1, 40, 41]. Adsay
et al. reported that the 1-, 3-, and 5-year overall survival rates
of non-invasive ICPN were 90%, 90%, and 78%, respectively
[1]. In addition, the percentages of invasive ICPN were 69%,
60%, and 60%, respectively [1]. These overall survival rates
are much better than those of other types of gallbladder car-
cinomas, which have an 18–30% 5-year survival rate [1, 42].
In contrast, a recent study reported that in a stage-matching
analysis of gallbladder carcinoma, there was no difference
between the prognosis of invasive carcinoma and other types
of gallbladder carcinoma [43]. In our review, most ICPN
patients had a good prognosis. We speculate that this was
due to most ICPNs being resected at an early stage. How-
ever, our patient had advanced cancer originating from an
ICPN with lymph node metastasis. Therefore, our patient
was closely followed up with adjuvant chemotherapy.

The optimal choice of surgical procedure, including
extended cholecystectomy, bile duct resection, and pancre-
atico-duodenectomy is essential for achieving complete
oncological resection of the tumor. In addition, close post-
operative follow-up is crucial for patients with ICPN, espe-
cially those with advanced cancer arising from the tumor,
in accordance with other types of gallbladder carcinoma.

4. Conclusions

Accurate preoperative diagnosis of ICPN, including the
extent of tumor invasion, is challenging; however, both
EUS and POCS are effective tools for resolving these chal-
lenges. ICPN has been recognized as a tumor with a better
prognosis compared with other types of gallbladder carci-
noma; however, a recent study reported that the prognosis
of these tumors is equivalent. The optimal choice of surgical
procedure and close postoperative follow-up are essential for
patients with ICPN, especially those with advanced cancer
arising from the tumor.

Data Availability

Data supporting this research article are available from
the corresponding author or first author upon reasonable
request.

Consent

Written informed consent was obtained from the patient for
publication of the case details.
Conflicts of Interest
The author(s) declare(s) that they have no conflicts of interest.

References


