Morphological Classification and Clinical Significance of the Papilla of Vater by Endoscopic Retrograde Cholangiopancreatography

Hiroyuki HANADA, Hiroshi ISHII, Kazushige Arai, Mitsuo KUSANO

Abstract: From May 1990 through April 1997, endoscopic retrograde cholangiopancreatography (ERCP) was performed in 1210 patients, of whom 652 were chosen as subjects of this study. We devised a new morphologic classification of the papilla of Vater. Forms of the protuberance of the major papilla were classified into three types: spherical type, flat type and irregular type. The opening of the pancreaticobiliary duct was classified into two types: spot type and elongated type. The epithelium around the opening was classified into two types: granular type and villous type. We studied these forms, separate openings of the pancreaticobiliary duct, the presence of oral protrusion and frenulum, presence of anomalous connections of the pancreaticobiliary ducts, abnormal adherence of the cystic duct, relation to cholangiopancreatic diseases in flat and irregular types. We conclude that a larger proportion of cases were of the elongated and villous types and were of separate openings in the flat and irregular types than the spherical type. All cases of the flat and irregular types tended to have oral protrusion and many cases of the irregular types did not have a frenulum. An anomalous connection of the pancreaticobiliary duct was noted in one case of the flat type, and abnormal adherence of the cystic duct was noted in no cases of either the flat or irregular type. An association with pancreas cancer was noted in cases of the flat and irregular types. Therefore, if an unusual form of the papilla of Vater is confirmed, it may be necessary to perform further examinations of the pancreaticobiliary tract such as computed tomography and magnetic resonance cholangiopancreatography.

Key words: Endoscopic retrograde cholangiopancreatography, papilla of Vater, morphologic classification

Introduction

Owing to the recent development and diffusion of various types of diagnostic imaging, cholangiopancreatic diseases have been diagnosed from multiple points of view and the certainty of diagnosis has increased. Endoscopic retrograde cholangiopancreatography (ERCP) is a safe and painless examination because of improvements in endoscopes and advances in technique. Many varied systems of classification of X-ray findings in the
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Fig. 1. Schematic diagram of the papilla of Vater

pancreaticobiliary tract have been devised. However, findings of the papilla of Vater on direct visual examination have not been described in detail. Various classifications are used for each site, and this classification confusion has been treated rather lightly; a conclusion has not been confirmed. We performed a morphologic study of the papilla with ERCP and studied the relationships of anatomic variants of the papilla to cholangiopancreatic diseases, anomalous connection of the pancreaticobiliary duct, and abnormal adherence of the cystic duct.

Subjects and methods

Of the 1210 patients who underwent ERCP from May 1990 through April 1997, 652 patients aged 16 years or older in whom the papilla was clearly observed and the pancreatic duct or the bile duct was imaged retrogradely, were selected as subjects of this study. The papilla was macroscopically observed from the front and the side. The findings of ERCP were studied from several points of view: frontal, lateral and oblique. In general, the papilla consists of an oral protrusion, a hooding fold, a major papilla, and a frenulum (Fig. 1).

For morphologic classification of the papilla, the methods of Nakayama et al. and Ohi and Takemoto are often used, but our study used the method of Arai and Koizumi. However, the major papilla exhibits various forms. The degree of protuberance and the epithelial forms at and around the opening of the bile and pancreatic ducts are often judged subjectively by the investigator. Therefore, to improve the objectivity of judgement, we devised a new morphologic classification (Fig. 2).

Forms of protuberance of the major papilla were classified into three types: spherical type for circular and oval protuberances; flat type for flat protuberances; and irregular type, for protuberances belonging to neither of the after two types. The openings of the bile and pancreatic ducts (opening form) were classified into two types: spot type for spot-like openings and elongated type for slit-like openings. The epithelium around the opening was classified into two types: granular type and villous type. Additionally, regarding the
number of openings at the papilla of the bile and pancreatic ducts, we also studied cases having separate openings\(^4\), a type of papilla often seen clinically. Typical examples of each form of papilla are shown (Fig. 3-5).

We studied opening forms, epithelial forms, separate openings, presence of oral protrusion, and the frenulum in flat and irregular types, which are unique forms of protuberance, and the presence of anomalous connections of the pancreaticobiliary duct, abnormal adherence of the cystic duct, and their relations to cholangiopancreatic diseases (Table 1).

**Results**

1. Detailed characterization of forms of protuberance (Table 2)

In the 652 cases examined, the spherical type was observed in 638 cases (97.9 %). The flat type and irregular type were noted in 8 cases (1.2 %) and 6 cases (0.9 %), respectively.

By sex, 326 men and 312 women had spherical type forms. Three men and 5 women had flat type forms, whereas 2 men and 4 women had irregular type forms. The average age was 59.8 years for the spherical type, 65.5 years for the flat type, and 64.5 years for the irregular type. The average age of men with the spherical types was 59.7 years; with the flat type, 75.7 years; and with the irregular type, 60.5 years. The average age of women with the spherical types was 59.8 years; with the flat type, 59.4 years; and with the irregular type, 66.5 years. Men with flat type protuberances tended to be older.

2. Relationships between forms of protuberance and opening forms (Table 3)

Among opening forms, 561 cases of the spot type (87.9 %) and 77 cases of the elongated type (12.1 %) were of the spherical type. The flat type included 5 cases of the spot type (62.5 %) and 3 cases of the elongated type (37.5 %). The irregular type included 4 cases of the spot type (66.7 %) and 2 cases of the elongated type (33.3 %). In the flat and
Form of protuberance: Spherical type
Opening form: Spot type
Form of epithelium around the opening: Granular type
Opening form of the choledochopancreatic duct: General type
Fig. 3. Typical example 1

Form of protuberance: Flat type
Opening form: Elongated type
Form of epithelium around the opening: Granular type
Opening form of the choledochopancreatic duct: General type
Fig. 4. Typical example 2

Form of protuberance: Irregular type
Opening form: Spot type
Form of epithelium around the opening: Villous type
Opening form of the choledochopancreatic duct: General type
Fig. 5. Typical example 3
irregular types, a larger proportion of cases were of the elongated type than of the spherical type.

3. Relationship between forms of protuberance and epithelial forms (Table 4)

Among epithelial forms, 626 cases of the granular type (98.1%) and 12 cases of the villous type (1.9%) were noted in the spherical type. Seven cases of the granular type (87.5%) and 1 case of the villous type (12.5%) were in the flat type, and 5 cases of the
Table 4  Relationship between forms of protuberance and epithelial forms

<table>
<thead>
<tr>
<th>Type</th>
<th>Spherical type</th>
<th>Flat type</th>
<th>Irregular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granular type</td>
<td>626 (98.1 %)</td>
<td>7 (87.5 %)</td>
<td>5 (83.3 %)</td>
</tr>
<tr>
<td>Villous type</td>
<td>12 (1.9 %)</td>
<td>1 (12.5 %)</td>
<td>1 (16.7 %)</td>
</tr>
<tr>
<td>Total (cases)</td>
<td>638</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 5-A  Relationship between forms of protuberance and separate opening

<table>
<thead>
<tr>
<th>Form of choledochopancreatic duct</th>
<th>Spherical type</th>
<th>Flat type</th>
<th>Irregular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Separate</td>
<td>78 (12.2 %)</td>
<td>3 (37.5 %)</td>
<td>2 (33.3 %)</td>
</tr>
<tr>
<td>General</td>
<td>560 (87.8 %)</td>
<td>5 (62.5 %)</td>
<td>4 (66.7 %)</td>
</tr>
<tr>
<td>Total (cases)</td>
<td>638</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 5-B  Relationship between forms of protuberance and presence of oral protrusion and frenulum

<table>
<thead>
<tr>
<th>Presence</th>
<th>Spherical type</th>
<th>Flat type</th>
<th>Irregular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral protrusion</td>
<td>+ 597 (93.6 %)</td>
<td>8 (100 %)</td>
<td>6 (100 %)</td>
</tr>
<tr>
<td></td>
<td>- 41 (6.4 %)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Frenulum</td>
<td>+ 503 (78.8 %)</td>
<td>8 (100 %)</td>
<td>4 (66.7 %)</td>
</tr>
<tr>
<td></td>
<td>- 135 (21.2 %)</td>
<td>0</td>
<td>2 (33.3 %)</td>
</tr>
<tr>
<td>Total (cases)</td>
<td>638</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

granular type (83.3 %) and 1 case of the villous type (16.7 %) were in the irregular type.

In the flat and irregular types, a larger proportion of cases were of the villous type than of the spherical type.

4. Presence of separate openings, oral protrusion, and the frenulum (Table 5)

Among the cases with separate openings, 78 cases (12.2 %) were of the spherical type. Three cases (37.5 %) were of the flat type, and 2 cases (33.3 %) were of the irregular type. A high proportion of cases of the flat and irregular types had separate openings. Oral protrusion was noted in 597 cases (93.6 %) of the spherical type and in all of the flat and irregular. A frenulum was noted in 503 cases of the spherical type (78.8 %), in all cases of the flat type, and in 4 cases of the irregular type (66.7 %). Many cases of the irregular type did not have a frenulum.

5. Presence of anomalous connections of the pancreaticobiliary duct and abnormal adherence of the cystic duct (Table 6)

Anomalous connections of the pancreaticobiliary duct were noted in 7 cases of the spherical type (1.1 %) and 1 case of the flat type (12.5 %) but such connections were not noted in any case of the irregular type. Abnormal adherence of the cystic duct was noted in 37 cases of the spherical type (5.8 %) but in no cases of either the flat or irregular type.

6. Relationship between forms of protuberance and cholangio-pancreatic disease (Table 7)

Thirty-three cases of cancer of the pancreas (5.2 %), 32 cases of chronic pancreatitis (5.0 %), 289 cases of cholecystolithiasis (45.3 %), 106 cases of choledocholithiasis (16.6 %), 3 cases of papillitis (0.5 %), and 175 cases of other diseases (27.4 %) were noted in cases of the spherical type. Three cases of cancer of the pancreas (37.5 %), 2 cases each of
Table 6  Relationship between forms of protuberance and the anomalous connection of the pancreatobiliary duct (ACPBD) and abnormal adherence of the cystic duct (AACD)

<table>
<thead>
<tr>
<th></th>
<th>Spherical type</th>
<th>Flat type</th>
<th>Irregular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACPBD</td>
<td>+ 7 (1.1%)</td>
<td>1 (12.5%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>− 631 (98.9%)</td>
<td>7 (87.5%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>AACD</td>
<td>+ 37 (5.8%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>− 601 (94.2%)</td>
<td>8 (100%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>Total (cases)</td>
<td>638</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 7  Relationship between forms of protuberance and diseases

<table>
<thead>
<tr>
<th></th>
<th>Spherical type</th>
<th>Flat type</th>
<th>Irregular type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic cancer</td>
<td>33 (5.2%)</td>
<td>3 (37.5%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>32 (5.0%)</td>
<td>0</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Cholecystolithiasis</td>
<td>289 (45.3%)</td>
<td>2 (25.0%)</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>106 (16.6%)</td>
<td>1 (12.5%)</td>
<td>1 (16.7%)</td>
</tr>
<tr>
<td>Papillitis</td>
<td>3 (0.5%)</td>
<td>2 (25.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>175 (27.4%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (cases)</td>
<td>638</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

papillitis and cholecystolithiasis (25 % each), and 1 case of choledocholithiasis (12.5 %) were noted in cases of the flat type. Two cases each of cancer of the pancreas and chronic pancreatitis (33.3 %) and 1 case each of cholecystolithiasis and choledocholithiasis (16.7 %) were noted in cases of the irregular type. Both the flat and irregular types tended to be associated with cancer of the pancreas.

Discussion

The papilla of Vater arises from the foregut with the stomach and the upper part of the duodenum when the fetus is approximately 4 cm long. The appearance of the papilla is almost complete at the 9 cm stage. Many of the openings of the duodenopapilla have a labial (spindle-shaped or oval) shape as a fissure of mucosa.

For the definition and discrimination of elements of the constitution of the papilla of Vater, there are numerous reports based on visual, radiologic, and endoscopic findings. Regardless of differences in definitions and terminology, there is little objection to the existence of four elements: a protuberance around the opening of the bile and pancreatic ducts, longitudinal folds at the oral and anal sides, and a horizontal fold at the bottom of the protuberance. They are referred to as the major papilla, longitudinal fold, frenulum and preputium, which together form the papilla of Vater. The macroscopic form of the major papilla has been studied numerous times and has been classified, for example, into 30 types, such as circular, oval, and triangular, on the basis of frontal imaging in autopsy cases; into 5 types on the basis of the forms of the opening. The major papilla has also been classified into protuberant and flat types. The protuberant type is further divided into 3 subtypes: hemispheric type with a clear boundary separating it from other elements; the rod-stick type with an unclear boundary with the frenulum; and the hairpin type, in which a horizontal fold surrounds the opening in a hairpin-like fashion. However, in our
investigation, some cases were judged by different persons to have different forms. In particular, the appearance of the major papilla and the form of protuberance were often confused, as were the form of the opening and the epithelial form. Therefore, to eliminate subjective differences, we established a classification based on the elements of constitution.

Ishikawa\(^6\) reported that the form of protuberance of the major papilla was the protuberant type in 95.3% of cases, the flat type in 2.7%; these percentages were almost the same as ours. However, Fujita et al.\(^12\) reported a rate of 87.5% for protuberant type and 12.5% for the flat type; corresponding rates of 78.0% for the protuberant type and 22.0% for the flat type were reported by Ogoshi et al.\(^13\); and 83.9% for the protuberant type and 16.1% for the flat type were reported by Kasugai et al.\(^14\). In particular, evacuation, cracks, and concentration of elastic fibers increase in severity in elderly persons and those with inflammatory conditions; fibrosis and hardening of the papilla exhibit marked increases in connective tissue. This fibrosis appears more in men and in elderly patients\(^8\). Regarding the form of protuberance, there are more cases of the protuberant type in young patients, and the degree of protuberance decreases with advancing age. Protuberance tends to change to the flat type or irregular type with aging.

The elongated type of the opening form increased in frequency with the decrease in protuberance to flat and irregular structures. The epithelial opening tended to have a villous shape. The duodenopapilla had a unique papillary fold. The shape varies, e.g., villous with single stem, horizontal folding, and others, which gives an unusual appearance to the duodenopapilla and results in many types of exterior shapes. This fold has an important role in protecting the pancreatic and bile ducts against reflux from the duodenum. Increased pressure in the duodenum can cause these folds to occlude the internal cavity\(^15\).

Maruoka et al.\(^16\) report that the papilla is protuberant in most children and that the frequency of the flat type increases with aging. They also report that the elongated type of opening becomes more frequent than the granular type with aging. These findings suggest that the opening and epithelial forms change with aging.

A classification have been proposed by Suda and Miyamoto\(^4\) opening forms at the papilla of Vater in the bile and pancreatic ducts. In addition, the frequency of separate openings, which is often seen clinically, was 16.7% among all cases. In our report, although the frequency of the protuberant type was almost the same, the frequencies of flat and irregular types tended to be higher. Langlet\(^17\) classified the exterior form of the duodenopapilla into seven types corresponding to the opening forms of the bile and pancreatic ducts, with the assumption that the exterior form of the duodenopapilla determines the opening form of the bile and pancreatic ducts. On the other hand, Tokuyama\(^8\) reported that distinguishing the opening forms of the bile and pancreatic ducts by the exterior form of the papilla of Vater alone is almost impossible.

Many reports include oral protrusion in the major papilla form as a longitudinal fold\(^18\), and we formerly classified this protuberance into 4 types remarkable, moderate, mild, extremely or none by the grade of protuberance. However, this classification is subjective.

Since a clear border cannot be drawn between these classes, we investigated only the presence of protrusion. An oral protrusion was noted in all cases of the flat and irregular types. The oral protrusion is an elevation of the bile duct into the duodenal cavity by penetration of the wall of the duodenum. The oral protrusion reflects the state of the bile or pancreatic duct and is closely related to the angle of incidence of the common bile duct.
and to the expansion and histologic change of the terminal part of the common bile duct.

The muscle of Oddi, the wall of the bile duct, fibrous hypertrophy in the surrounding tissue, and functional factors are believed to be related to the origin of the oral protrusion.

The frenulum is considered to have little clinical significance, and only its presence was investigated in this study. Ishikawa\textsuperscript{6}) reported that the frenulum develops in about 80\% of persons, while Kasugai \textit{et al.}\textsuperscript{14}) reported that the frenulum develops in 26.3\% of persons, and that its relationship with the form of the papilla is unclear. In our study, 100\% of the flat type and 66.7\% of irregular type cases had a frenulum.

Anomalous connections of the pancreaticobiliary duct and abnormal adherence of the cystic duct are abnormal clinical conditions in which bile and pancreatic juice are mixed in the bile duct. These conditions often cause cholangitis and are thought to be related to cancer of the pancreas and the biliary tract. We did not find a relationship between the form of the papilla and anomalous connections of the pancreaticobiliary duct or abnormal adherence of the cystic duct. However, the number of our cases was small, and a larger study is needed.

Since Del Valle\textsuperscript{19}) reported on postcholecystectomy syndrome and suggested that benign stricture of the papilla is the cause of biliary dyskinesia, many reports concerning papillary findings at operation or autopsy have been published. If no obvious cause, such as past history of calculus or operation, pancreatitis, or other conditions, is noted, the origin of papillary fibrosis is usually difficult to explain. Even chronic spasm is believed to cause papillary fibrosis. The inflammation and stimulation in the area of the papilla are different from those in the region of the duodenal mucosa, pancreas, and bile duct. An unusual form of papillitis, or rebuilding develops in the area of the papilla\textsuperscript{6}).

This form of papillary change occurs with aging and with exposure to bile, pancreatic juice, and bowel contents, which readily cause inflammatory changes. Occlusion has been suggested to develop in the pancreaticobiliary duct and would influence the cholangio-pancreatic system. The papilla, the pancreas, and the biliary tract are closely related. When a change in one of these three is outside the physiologic range, it may cause morbid changes in the others\textsuperscript{4}). For example, sclerotic change occurred in the papilla and sphincter of Oddi, the pressure with the cholangiopancreatic duct increased, and biliary stasis developed. For these reasons, cholecystolithiasis, pancreatitis, and pancreatic cancer might develop. In our study, many flat type and irregular type cases were associated with cancer of the pancreas. We performed papillary biopsies in some cases; malignant cells were present, other in some cases but not in others. Therefore, we believe that the form of the papilla might be related to both benign and malignant diseases, for example, direct invasion, in the pancreaticobiliary duct.

As the most important means of classification, the form of the papilla can suggest both abnormal function and the relationship to disease. The relationship to diseases of the pancreaticobiliary tract should be considered in cases of flat and irregular type protuberance, and in villous type cases, and in cases with a separate opening as an epithelial form. Our findings suggest that attention should be paid to the form of the papilla at endoscopy of the upper digestive tract. If an unusual form of papilla is confirmed, it may be necessary to perform tests on the pancreaticobiliary tract such as computed tomography and magnetic resonance cholangiopancreatography.
References


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