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ARTICLE

Histological Evaluation of Preoperative Biopsies from Ampulla Vateri

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Frequency of the lesions of the papilla Vateri is increasing in Hungary because of epidemiological reasons. Over two years nearly 300 ampullary endoscopic biopsies were taken in our hospital. In 36 percent of the patients the papillary specimens demonstrated acute or chronic inflammation, in 44 percent adenoma, including 5 percent with severe dysplasia, in 5 percent adenomatous hyperplasia and in 7 percent adenomyosis or other benign tumors (2%) were found. Around 7 percent of the ampullary samples proved to be malignant, but only in 2.6 percent were the malignancy of intraampullary origin. Nearly 25 percent of biopsies were repeated once and 10 percent twice or more. Concordance of endoscopic and pathologic diagnoses was 69 percent on average but it increased to 83 percent after including repeated biopsies. In the adenoma-carcinoma group the concordance was 90 percent. The sensitivity of the pathological diagnosis with forceps biopsy was only 77 percent, but it became at least 86 percent following papillectomy. In order to improve diagnostic reliability more extensive use of papillectomy is proposed with close cooperation between the endoscopist and pathologist. (Pathology Oncology Research Vol 9, No 1, 32–41, 2003)

Keywords: papilla Vateri, preoperative diagnosis, sampling error, papillectomy, biopsy of Vater's papilla, pathohistology, forceps biopsy

Introduction

Papillary lesions are frequent in Hungary because of spicy and fatty diet, high alcohol consumption and smoking. The contribution of duodenoscopy, endoscopic retrograde choledocho-pancreatography (ERCP) and endoscopic biopsy is essential in the differential diagnosis of Vater's papilla obstruction.[15] Although recent data emphasize necessity of routine biopsies of such lesions,[21] a single ampulla biopsy has been reported to miss the right diagnosis in 30-40% of cases.[3,8,11,21,35] The aim of this study was to examine the divergence between the endoscopic and morphologic diagnoses established with endoscopy followed by routine Vater papilla biopsies during a 2 year period.

Materials and methods

Number, mean age and pathological classification of patients with Vater's papilla biopsies are given in *Table 1.* Formalin fixed samples were embedded in paraffin. Serial sections were stained with HE and PAS. Adenoma and carcinoma samples were immunostained with monoclonal DAKO anti p53 serum according to the indirect method using 5-aminoethylcarbasol as chromogen. The extent of the reaction was determined as percentage of positively stained tumor cell nuclei. When immunoreactivity was observed in 10% or more of the epithelial nuclei in the high power fields, the lesion was classified owerexpressing p53.[26,36] Inflammed duodenal tissue was used as a negative control.[18]

Diagnoses of the endoscopic and pathological reports were compared and the differences registered. If these diagnoses were identical already at the first examination thus the disease was accurately diagnosed „at the first look", the case was called unequivocal. If the patient had more biopsies and endoscopies and the diagnoses were identical at least once - the case was ranged into the congruent group. If pathological and endoscopic reports remained different, the alteration was called histologically and/or endoscopically equivocal (not definitively diagnosed). Numbers of congruent cases are shown in the tables as the difference between the number of all patients and the sum of unequivocal and equivocal (not definitively diagnosed) cases for each disease. Papillectomies, brush cytologies+intraductal biopsies were collected from

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Table 1. **Pathological classification and divergent endoscopic diagnoses of Vater's papilla biopsies**

Histological diagnosis		Number of		Number of reports		Definitively not diagnosed		Women		Men	
		patients	%	first*	all	n	%	n	Mean age	n	Mean age
Inflammation		83	36	53	90	23	***28***	46	64.5 ± 16.2	37	62.7 ± 15.4
Adenomatous hyperplasia		11	5	6	12	3	***27***	6	63.4 ± 11.5	5	58.4 ± 14.0
Adenomyosis		16	7	4	20	9	***56***	8	69.2 ± 12.7	8	66.0 ± 11.5
Adenoma with dysplasia	mild	45	20	36	56	1	2.2	29	65.2 ± 15.6	16	60.8 ± 14.9
	medium	42	19	34	68	1	2.4	24	67.9 ± 12.8	18	64.7 ± 14.2
	severe	10	4.5	9	20	0	0	3	66.7 ± 15.1	7	63.7 ± 13.1
Carcinoma		17	7.6	15	24	1	5.8	7	75.4 ± 14.6	10	65.0 ± 10.5
Carcinoid, etc		2	1	0	4	1	***50***	0		2	54.0 ± 8.0
Sum		226	100	157	294	39		123		103	
Average				69%			***17.2***		65.9 ± 11.2		64.7 ± 15.4

Mean age of all patients is 65.14 year. *Diagnosed at the first look (unequivocal cases)

the endoscopic reports and their numbers are indicated in T*ables 2, 3.* In *Table 2* autopsy data of patients died from carcinoma were used too.

Results

Number and mean age of women was higher in each group than that of men except carcinoma, where more men were affected *(Table 1)*. The greatest number of equivocal cases were in the groups of inflammation, adenomatous hyperplasia and adenomyosis – 28%, 27% and 56% respectively.

By histology around 36% of the biopsies demonstrated acute or chronic inflammations. Inflammation caused denudation of the villi, ulcers *(Figure 1a)*, epithelial hyperplasia, rarely metaplasia *(Figure 1b)*, which could be differentiated from dysplasia by the pathologist. Endoscopic diagnosis of chronic inflammation might result in hyperchromasia of nuclei *(Figure 1c)* but this reactive atypia was regularly negative with p53 staining, thus it

Table 2. **Carcinoma in papilla biopsies**

Most probable site of origin according to clinical data		Number of							p53 staining		Mean age year
		Patients	Biopsies	Brush cytology*	Not definitively	Sections	Men	Women	Degree, %	Negative, n	
Intrapapillary		6	9		*1*	3	3	3	~70	1	69.0 ± 12.0
Parapapillar	Bile duct	2	4	1		1	2		~60		72.0 ± 8.0
	Pancreas	5	6	2		1	3	2	100	1	73.1 ± 7.0
	Duodenum	1	2				1			1	61
	Undetermined	1	1	1			1		50		50
Distant metastasis**		2	2			1		2	55	1	47 ± 8
Total		17	24	4	*1****	6	10	7	~70	4	67.0 ± 13.0

*Intraductal biopsy too. **From uterus and breast cancer. ***Supposed benign at endoscopy

Table 3. **Alterations of intrapapillar origin**

Histological diagnosis	Number of patients	Number of biopsies	Number of brush cytology*	Number of papillectomies	Definitively diagnosed first**	not diagnosed n	not diagnosed %	p53 stain degree, %	p53 stain negative, n	Number of men	Number of women	Mean age year
Inflammation	58	62	1		33	21	*36*	1-2	28	19	39	63.6 ± 14.2
Adenomatous hyperplasia	10	11	3	1	4	4	*40*	1-5	8	5	5	55.6 ± 5.5
Adenomyosis	10	11	5	1	2	6	*60*	<5	5	3	7	65.5 ± 12.8
Adenoma with dysplasia mild	39	50	1	10	31	2	5	10	20	13	26	63.5 ± 15.0
Adenoma with dysplasia medium	31	52	3	10	25	1	3	20	6	12	19	66.1 ± 13.0
Adenoma with dysplasia severe	3	8		1	2	0	0	80	1	2	1	69.0 ± 10.0
Carcinoma	6	9			4	1	16	~70	1	3	3	69.0 ± 12.0
Sum	157	203	13	23	103	35			69	57	100	
Average					65%		*22*					64.0 ± 14.1

could be excluded from adenomas.[1] Laminas of the blocking valves of the ampulla should not be confused with villous adenoma by the pathologist - they have characteristic cylindrical epithelium without goblet cells *(Figure 2a).* Equivocal diagnoses were: adenomas 16, malignant tumors 5, adenomyoses 2.

In 5% of patients the smallest sign of dysplasia was not found and the morphologic diagnosis was adenomatous hyperplasia *(Figures 3a,b, 4a,b).* The endoscopic report spoke about adenoma in the case of voluminous alterations. Beyond adenomas (2) Crohn disease were the equivocal diagnoses.

Adenomyosis occurred in 7% of patients. Microscopically adenomyosis may simulate carcinoma infiltrating smooth muscle layers *(Figure 3c).* Equivocal diagnoses were: adenoma 4, sometimes „beginning adenoma" 3, carcinoma 1, and inflammatory pseudotumor 1.

Biopsies in 20%, 19% and 4.5% of patients demonstrated adenomas with low-, medium grade and severe dysplasias, respectively *(Figure 2b,c,d,e).* In deep or intraductal structures sometimes no adenoma could be verified only dysplasia of the lining epithelium *(Figure 4e)* spoke in favour of an adenoma. Inflammation was frequent in adenomas (*Figure 1d).* As considerable part of the biopsies was repeated, the number of not definitively diagnosed cases was minimal, only around 3%. Equivocal diagnoses were: lymphoma 1, adenomyosis 1.

In our series 7% of ampullary biopsies demonstrated carcinoma but only 2.6% were carcinomas of ampullary origin (*Table 2, Figures 2f, 4f).* The grade of tumor and in some biopsies the pancreatobiliary type of the carcinoma was obvious *(Figure 4f),* but in itself the pathological report could rarely add new data to the origin (and size) of the malignancy. Extrusion of mucin trough a patulous papilla made probable an intraductal papillary mucinous neoplasia of the pancreas *(Figure 4c,d).* The endoscopically not diagnosed carcinomas were only 5.8%. Equivocal diagnosis was adenoma in 2 cases.

Similar calculation – the comparison of endoscopic and histological diagnoses – was repeated in a smaller but more homogenous group of patients. In this group only intraampullary alterations were supposed *(Table 3).* Number of patients with various diseases are less than in *Table 1,* because persons whoose imaging (CT, ultrasound) or other reports (positive intraductal cytology or biopsy) indicated extraampullar alteration – were omitted. (See for example carcinoma row of *Tables 1* and *3* and the whole *Table 2.*) In this second calculation the number of equivocal cases were in the same order as previously but a bit larger than in *Table 1.* They are 5%, 3%, 0% and 16% in adenoma - carcinoma groups which are in practice the most important (*Table 3)* – that is in average 10%. Therefore this value can be the average of the endoscopically not unequivocally diagnosed cases, further including some clinically less significant groups (inflammation, etc) 17.2% *(Table 1)* or 22% *(Table 3)* can be calculated. In some percent bulging papilla may be caused by other rare tumors (carcinoid, etc., *Table 1, Figure 3d,e,f*). False endoscopic diagnosis of these uncommon cases - according to the meaning - may be more common.

The ampulla has so highly complex architecture with mucosa, glands and ducts being closely related to the mus-

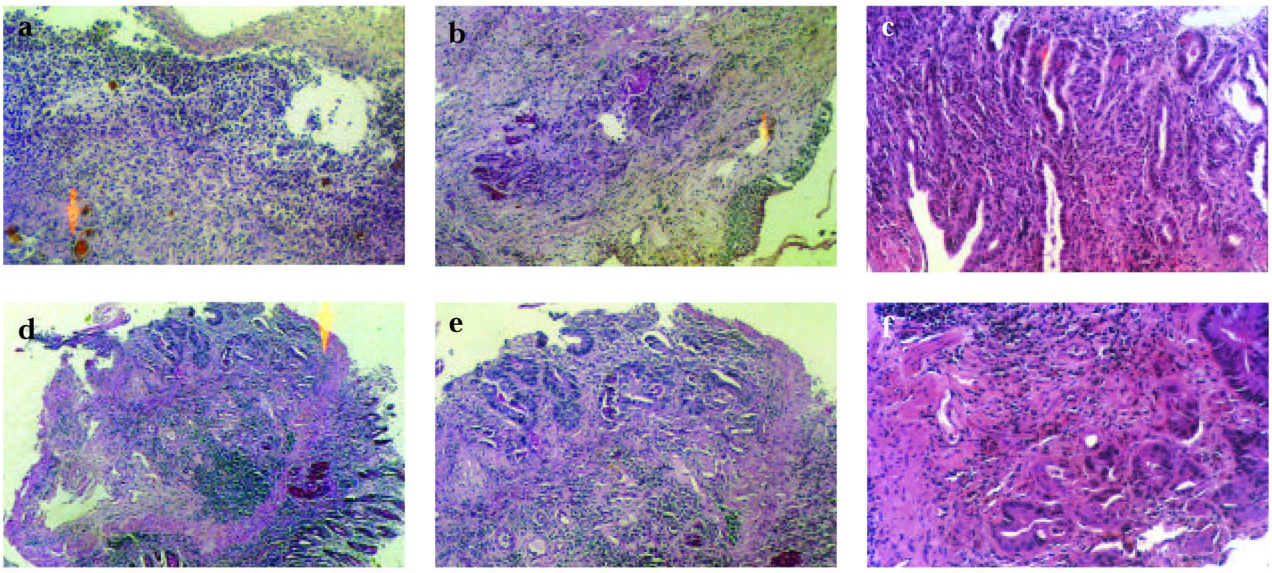

Figure 1. *Inflammation associated alterations in ampulla. (a) Acute ulcer, arrow: bile pigment among leucocytes. 1990/2000, HE, 20x. (b) Chronic papillitis, arrow: squamous epithelial metaplasia. 3654/1999, HE, 20x. (c) Reactive glandular atypia in consequence of chronic inflammation. 3229/1999, HE, 20x. (d) Concomitant chronic inflammation in tubulovillous adenoma. Arrow labelled area is magnified in e and f. 258/2000, PAS, 4x. (e) Some distorted glands are at the edge. PAS, 10x. (f) Dysplasia is seen at the border. If this part would have been missed by forceps biopsy, the diagnosis had been false negative. The right diagnosis is: severe dysplasia with stroma reaction in tubulovillous adenoma. PAS, 20x.*

cles that even if the biopsy is obtained from an adequate site *(Figure 1d,e,f)*, the histological diagnosis of a highly differentiated early carcinoma was very difficult. If its invasive part was missing from the specimen, the differential diagnosis from an adenoma or adenomyosis was possible on cellular level only *(Figure 3b,c)*. Lymphatics could be identified troughout the mucosa of small bowel and ampulla - as contrasted with the colon *(Figure 5f,g)*. The small number of dysplastic cells in the specimen could be labelled with p53 immunohistochemistry *(Figure 5d,e)*. *Table 3* shows that in inflammation and adenomatous hyperplasia p53 staining was negative, or only 1-2% of epithelial cells were labelled. In low, medium grade, severe dysplasias and carcinomas the p53 positivity was growing in the same order, but some cases remained consistently negative or not hundred percent of dysplastic cells were stained[23] (*Figure 5f,g, Table 2)*.

As diagnostic accuracy of biopsies from suspicious papilla was limited and variable – many patients had multiple endoscopic measures and biopsies. *Table 4* summarises various groups of repeated biopsies. Right at the start (A) adenomas were eradicated – most of them surgically – and monitored for a long time. 15-20% of these benign tumors was endoscopically eradicated, that is papillectomised *(Figures 2c, 5a)*. Endoscopic resection was carried out in large pieces and the patient strictly followed up by endoscopy *(Figure 5a,b,c)*. In the course of repeated biopsies the consecutive clinical and histological diagnoses could differ, moreover the tipical pattern of development indicated the succes or failure of the papillectomy. Several months sometimes years passed with monitoring and the pathologist at the time of each new biopsy knew which elements of the pattern have already appeared in the past because he had his own register about patients to be monitored.

Negative endoscopic biopsy in the presence of endoscopic evidence of adenoma or malignancy is regarded with doubt by the endoscopist.[21] This was the cause of rebiopsies in groups B and C. Until the pathologist could not make an unequivocal diagnosis on regular (forceps) biopsy specimens a radical surgical resection was not performed. Consideration was given to use jumbo duodenoscope and forceps for big particle or snare biopsy, or papillectomy to minimize sampling error.

Examination of these big particle or snare biopsies and papillectomies was wery useful for the pathologist who evaluated the previous biopsies of the same patient. The p53 staining was easier to execute and could be more reliably evaluated *(Figure 5d,e)*. *Table 5* shows that endoscopic and histological diagnoses of 23 papillectomies were identical with tree exceptions. The exceptional histological diagnoses of the 23 „adenoma" endoscopically were an adenomyosis, an inflammatory pseudotumor and in addition in one adenoma deeply situated in situ carcinoma, which possibly could not have been discovered using forceps biopsy. The concordance of the endoscopic diagnosis with histology was 86%. In 9 instances the forceps biopsy preceded the papillectomy and histological diag-

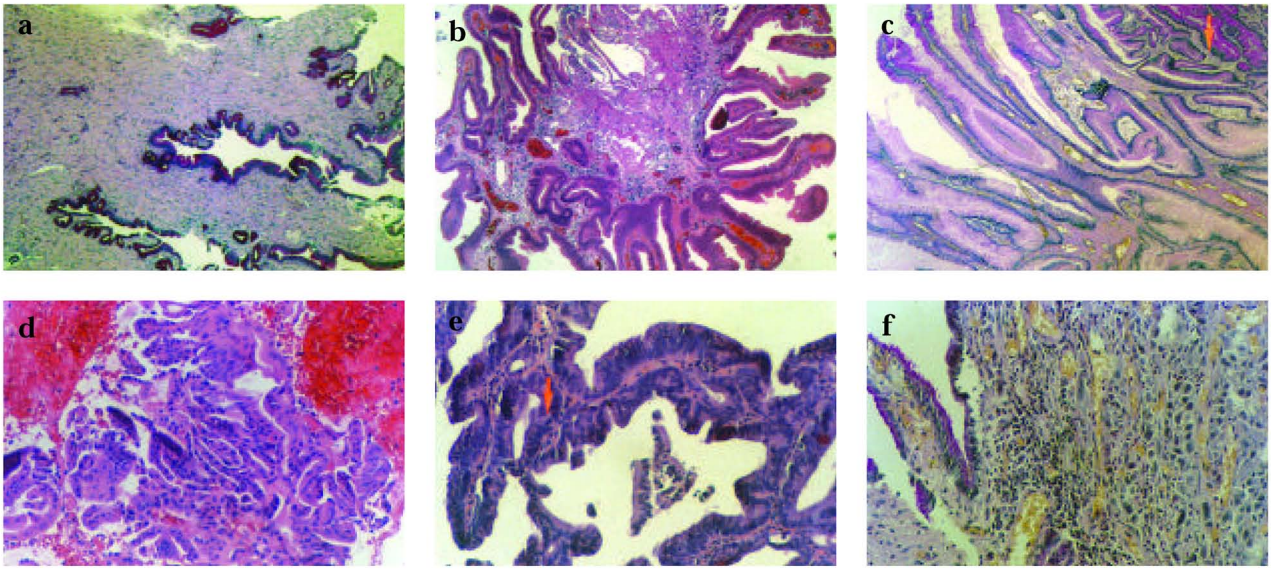

Figure 2. *Superficial proliferations on the papilla of Vater. (a) Part of normal closing valve of ampulla covered by cuboidal epithelium without goblet cells. PAS, 10x. (b) Villous adenoma of the closing valve with mild dysplasia. PAS, 10x. (c) Villous adenoma with low grade dysplasia, papillotomy specimen. Arrow: regular PAS staining. 10x. (d) Medium grade dysplasia in fragments of a villous adenoma. If the fragments are not connected with fields of obviously ampullary origin, it might be a duodenal adenoma also a parapapillar tumor. HE, 20x. (e) Severe dysplasia in villous adenoma, arrow: mitosis. PAS, 10x. (f) Infiltrating anaplastic carcinoma. Fragment of closing valve proves localisation in papilla Vateri. PAS, 20x.*

noses with forceps biopsy and papillectomy were identical only in 7 cases. Thus, the sensitivity of forceps biopsy histology is less (77%) than that of the endoscopic diagnosis in adenoma cases.

Definitive histology can be obtained only after processing of the postoperative specimens including operative endoscopy. Similar results can be obtained from autopsy reports. In our series 6 papilla biopsies were malignant *(Table 2)* aut of 10 later dissected patients with pancreas and bile duct carcinomas. In 2 autopsy cases only some dysplasia was noted in the previous papilla biopsy (suspicious cases) and in two others only inflammation was found previously. Thus the sensitivity was 60% or 80% respectively.

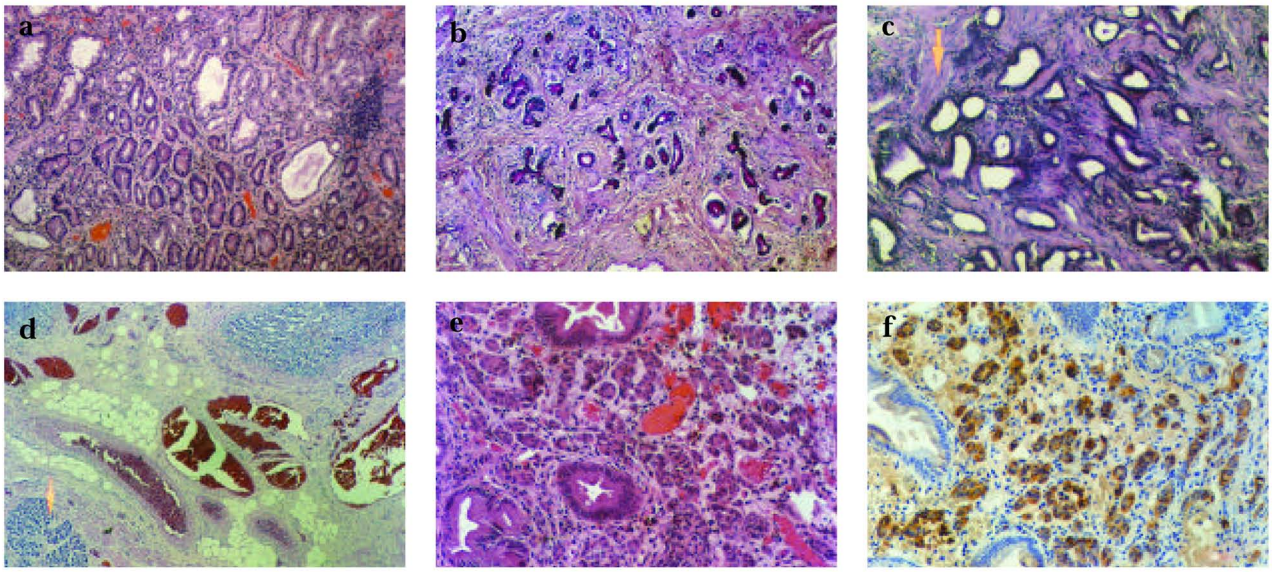

Figure 3. *Bulging papilla of Vater. (a) Adenomatous hyperplasia. HE, 10x. (b) Fibroadenoma. PAS, 10x. (c) Adenomyosis. Arrow: muscle fibres. PAS, 10x. (d) Hemangioma cavernosum. Arrow: pancreas tissue. HE, 4x. (e) Carcinoid tumor. HE, 20x. (f) Chromogranin reaction of the previous carcinoid tumor, indirect immunostaining by monoclonal DAKO serum, 20x.*

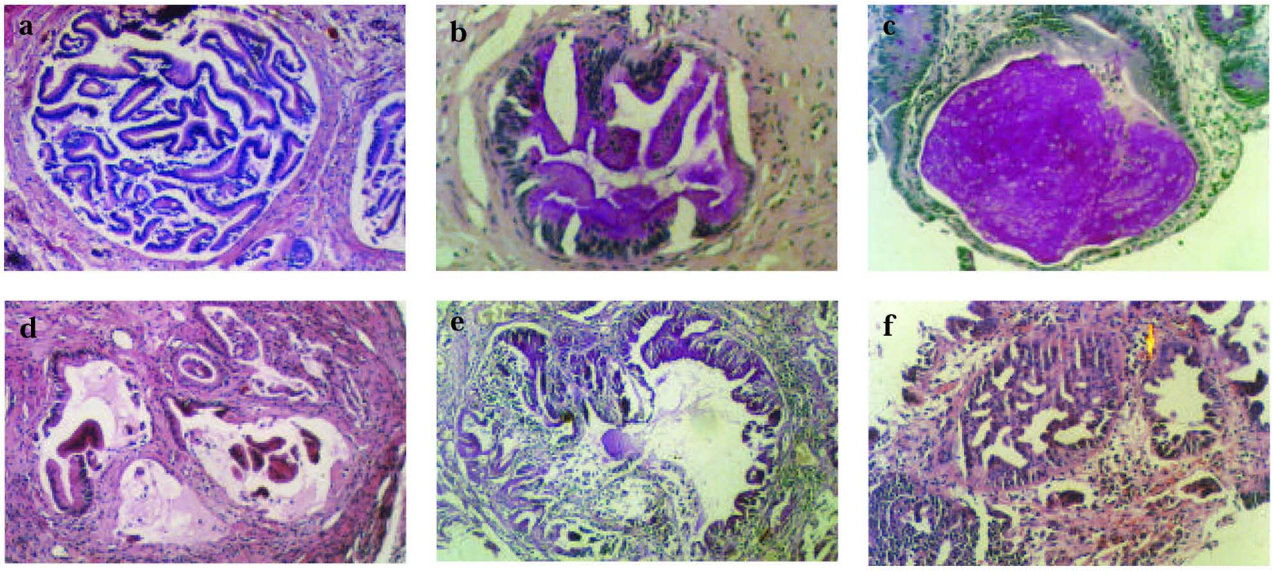

Figure 4. *Intraductal or deep glandular alterations. (a) Intraductal adenomatous hyperplasia. s47/2000, HE, 10x. (b) Intraductal papillary hyperplasia without significant dysplasia. 6589/1999, HE, 10x. (c) Pancreatobiliary duct with low grade dysplasia in a sector of lining cuboidal epithelium. The PAS-positive mucous plug is suspicious of mucinous hyperplasia or tumor of the retrograde pancreatic duct epithelium. 7641/1999, 20x. (d) Bland looking cells in ductal mucus: it might be the sign of mucous hyperplasia or carcinoma in the pancreas. Intraductal biopsy or brush cytology is needed. 3292/2000, HE, 10x. (e) low and medium grade dysplasia of the lining duct epithel. 7430/1999, PAS, 20x. (f) Pancreatobiliary type carcinoma of lining ductular epithelium, propagation in smaller lumina. Arrow: remnants of ductular muscular elements. 2721/2000, HE, 20x.*

Discussion

A well trained endoscopist might be able to esteem the type of a papillary alteration by its macroscopic appearence and consistency when taking forceps biopsy. There are series with more accurate diagnoses by endoscopic appearence than by histology from the endoscopic biopsy of the papilla.[7,15] Endoscopist and pathologist classify the alteration by its most striking macroscopic and microscopic characteristics, respectively and the failure of any (or both) type of information may result in divergence of endoscopic and pathological diagnoses.

Endoscopically spontaneous bleeding, ulceration, friable or indurated surface and unusual firmness are all endoscopic evidences of malignancy. However, inflammatory pseudotumors and adenomyomas are frequently firm at forceps biopsy, too. Valves of the ampulla may become thickened, indurated from chronic inflammation[13] reminescent of carcinoma or adenoma. Adenomyomas consist of pancreatobiliary ducts arranged in lobular configuration surrounded by fascicles of smooth muscles. Their hamartomatous or proliferative nature is unsettled yet. Mean age of this group is 66 year,[1] that is very near to the mean age of malignancies. The small volume of tissue gained by forceps biopsy often makes impossible to verify the lobular structure of the alteration and it causes deviation from the true histological diagnosis. We hope that use of ampullectomy as preopeative biopsy brings nearer to the definitive prognostic significance of adenomyosis.

The most frequent debate between pathologist and endoscopist is whether the alteration is inflammation or adenoma. If the biopsy is too small, the pathologist is prone to diagnose inflammation, because the dysplasia can not be established with certainty and a concomitant inflammation is always present in adenomas. Diagnosis of adenomas is based on the typical morphological features, but may be difficult if the specimen is fragmentary. The villous structures found in normal small bowel and adenomas as well may show only subtle differences. The papillary fronds in the adenoma exhibit greater irregularity, increased lenght, uneven surface and more darkly stained cells compared with normal villi. The proliferating adenomatous cells may line preexisting villi with a papillary pattern preserved for a variable distance. In some cases only one, or even none of these features were observed in our series and only the elevated (>5-10%) p53 positivity spoke in favour of an adenoma. For these difficulties was proposed to use only dysplasia and atypia instead the term „adenoma".[16] Diagnostic problems of high grade dysplasia versus carcinoma are similar to that at gastrobiopsy.[6] We do not diagnose a carcinoma when atypical or even anaplastic cells are found to line architecturally normal structures within the mucosa without structural distortion. However p53 positivity with high grade dysplasia is an indication of surgical therapy.[29] The adenoma-carcinoma sequence seems to be as significant in the small intestine as

in the large bowel[14,19,20,25,27,36] and the transformation rate of adenomas to carcinoma is considered up to 30%[34,35] – thus the true histological diagnosis is essential. Using the traditional forceps technique the endoscopic and histological diagnoses approached each other by repeating the biopsy. It seems that endoscopically the adenomas can be many times better recognised than by the histology of a crumbled forceps biopsy missing structural criterions of an adenoma. High sensitivity of endoscopic diagnosis of adenoma proves that the overall macroscopic (endoscopic) picture of an alteration may contain more information than the microscopic picture of its fragments with low grade dysplasia. At the same time adenomatous hyperplasia can not be well diagnosed endoscopically because at present time there are no macroscopic criteria separating adenomatous hyperplasia from adenomas. It is possible that some lesions are morphologically transitional between hyperplastic proliferations and true adenomas.[4, 6] If preoperative biopsy of adenomas were routinely carried out by papillectomy - not only histological diagnosis would be more safe but a common and persistent endeavour of pathology and endoscopy could find macroscopic criteria for separating such hyperplastic proliferations from adenomas. It is obvious from our study that employing papillectomy as diagnostic biopsy the difference between clinical and histological diagnoses will be less in both diseases without rebiopsy. Clinical practice of endoscopic eradication of adenomas by papillectomy[3,4,11,20,22,24,34,35] gained enough experience for replacement of operative papillectomy mostly in elderly cases, but long term follow up for possible relapses is necessary.

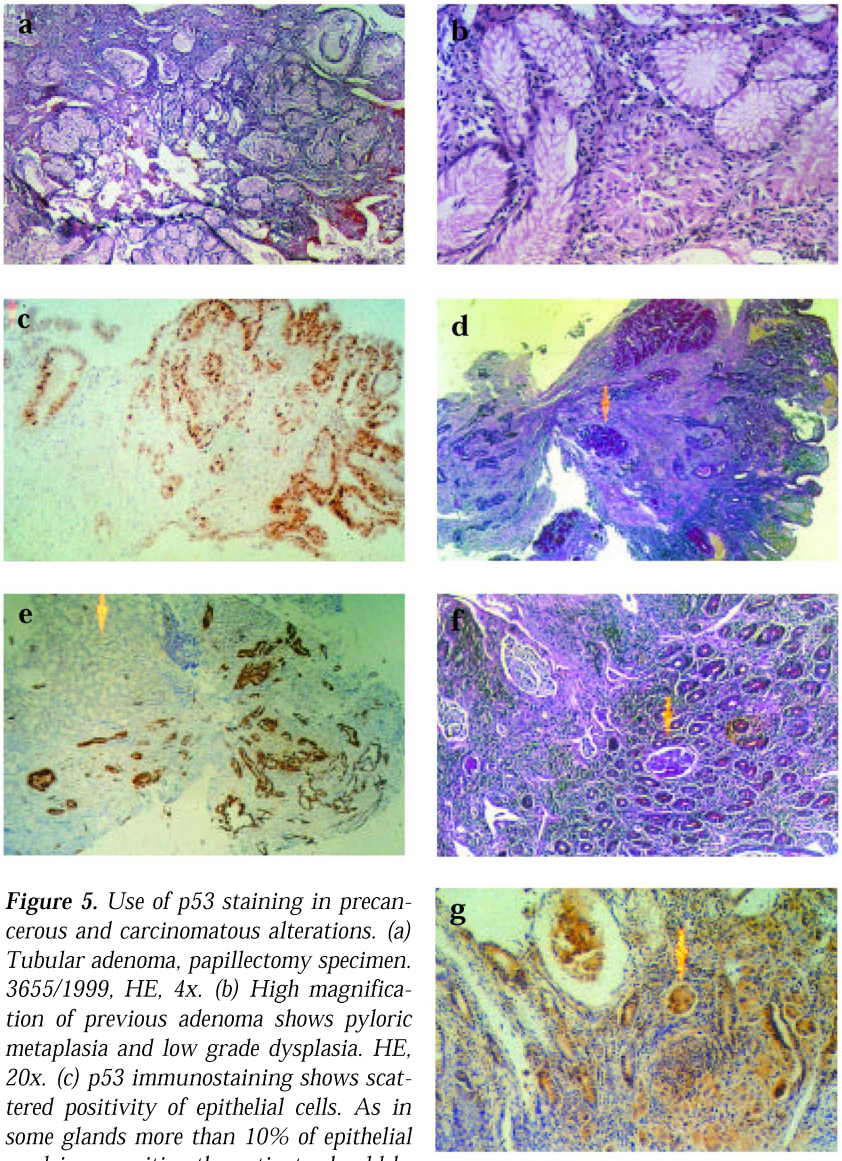

Figure 5. *Use of p53 staining in precancerous and carcinomatous alterations. (a) Tubular adenoma, papillectomy specimen. 3655/1999, HE, 4x. (b) High magnification of previous adenoma shows pyloric metaplasia and low grade dysplasia. HE, 20x. (c) p53 immunostaining shows scattered positivity of epithelial cells. As in some glands more than 10% of epithelial nuclei are positive the patients should be monitored. 4x. (d) There are dark staining suspicious glands in the stalk of the forceps biopsy specimen. Arrow: Brunners gland. 1019/2001, PAS, 4x. (e) Dark staining glands in the previous specimen are p53 positive: infiltrating parapapillar carcinoma from the head of the pancreas. (f) Lymphatics within the epithelium of the mucosa are filled with tumorous thrombi (arrow), propagation from a parapapillar carcinoma. 9140/2000, PAS, 10x. (g) On p53 stained preparation the tumorous thrombi remained negative (some percent of tumors do not stain with p53). 10x.*

Carcinoma of the ampulla Vateri accounts for 0.006-0.2% of all routine autopsy cases,[9,26,35] for 5% of operable carcinomas of the gastrointestinal tract[8,23] and for 10-36% of all pancreaticoduodenal tumors.[32] In endoscopic series its prevalence was found in 1.5-2.6%.[21] Only small tumors are confined to one of the tree ductal components of the ampulla (the common chanel, the intraduodenal portion of the common bile duct and intraduodenal pancreatic duct) from which they had probably arisen.[5,25] The similarity in presentation and the difficulty to locate the origin of the tumors often lead to put together carcinoma of the ampulla and carcinomas arising from its immediate vicinity under the term „periampullary tumor"[21]. Duodenal tumors involving the ampulla, cancers of the head of pancreas extending to the ampulla and carcinomas of the distal bile duct involving the ampulla are all periampullary

Table 4. **Types of repeated papilla biopsy series (alltogether 97 biopsies)**

Type	*Clinical (endoscopic) diagnosis*	*First histologic*	*Last diagnosis*	*Number of*		*Additional data*
				biopsy/ patients	*patients*	
A	Adenoma (with previous dysplasia or p53 positivity)	in situ cc adenoma with dysplasia adenoma	adenoma adenoma inflam	3-4	1 4 5	Decreasing p53 positivity and dysplasia
B	Unusual ampullary alteration, ulcer, adenomyosis, etc,	inflam adenoma adenomyosis	adenoma inflam adenoma	2	5 6 5	Negative intraductal biopsy and cytology, calculi
C	Parapapillar tumor with synchronous ampullar or near ampullar alteration, sometimes multilocular biopsy	adenoma inflam adenoma inflam inflam adenoma	cc cc adenoma adenoma inflam inflam	2-3	1 3 3 2 1 2	Suspicious intraductal brush cytology, biopsy and image technique modalities
D	Any diagnosis	damaged, not evaluable	any diagnosis	2	2	too small specimen
Total					40	

Cc: carcinoma, inflam: acute and chronic inflammation.

tumors.[24] Real tumors of the ampulla of Vater represent only 10% of all periampullary tumors, their prognosis is more favorable than that of the other periampullary tumors in general[10,25,28] – this is the significance of the origin of cancer. Thus the aim of papilla biopsy is mainly to exclude or verify the papillary origin of the carcinoma. Histologically periampullary carcinomas are classified into intestinal (>80%) and pancreatobiliary type tumors.[19] Although this classification alludes to the origin of tumors, as the duct system of pancreas, duodenum and biliary tract shared common embryologic start point: both histologic type may arise from every localisation.[1,2] Ampullary carcinomas are almost all intestinal.[30] Among carcinomas extending into the ampulla of Vater intraductal papillary mucinous neoplasms of the pancreas can be identified in ampulla biopsies. In this case the papilla biopsy can simulate noninvasive carcinoma of papilla Vateri.[1,14] However, intraductal biopsy or brush cytology[31] may be positive and ERCP with diffuse dilatation of the Wirsung duct and filling defects prove the extraampullar origin. The aim of the preoperative biopsy alone is therefore to assess histologically the presence or abscence of a malignancy or the presence and extent of severe dysplasia. To have an opinion about the extent and origin of the malignancy not only the histological picture but also the brush cytology and ERCP image of the surroundings should be known.

The most remarkable difference between the ampullary and regular gastrointestinal biopsies is the variable accuracy of preoperative pathologic diagnoses in the former.The uncertainty of diagnostic accuracy of preoperative ampulla biopsies is caused mainly by hidden position of relative small malignant tumors missing from forceps biopsies.[26] In many cases the tiny carcinoma is within an adenoma and the biopsy may sample only the benign lesion.[32] This is true also for malignancies of ampullary origin. Although patients with isolated ampullary alter-

Table 5. **Concordance of the endoscopic and histological diagnoses of the forceps biopsy on the evidence of the histological diagnosis of papillectomy.**

	Histological diagnosis of papillectomies		*Concordance ("sensitivity")*
	identical with	*different from*	
Endoscopic diagnosis	20	3*	0.86 (20/23)
Histological diagnosis after forceps biopsy prior to papillectomy	7	2	0.77 (7/9)

*The different histological diagnoses from the endoscopic "adenoma" were: adenomyosis, inflammation pseudotumor and intraadenomatous in situ carcinoma.

ations *(Table 3)* form a more homogenous group with a consistent increase in the mean age of patients with adenoma: 63, 66 and 69 year in order of low-, medium grade and severe dysplasia respectively, however, this is the group where ERCP and brush cytology give less aid than in cases of extraampullary alterations - in other words the duodenoscopy with histology is more important. They may yield retrospectively false negative results when processing the surgical specimens (in most cases by an other pathologist, not the same one who has evaluated the preoperative biopsy[12]). Among 14 operated adenomas 4 proved to be malignant in our previous series.[7] The sensitivity is 71%. According to the clinical course of this material out of 21 patients with periampullary carcinoma only 8 had preoperative unequivocal malignant histological diagnosis, further 7 were histologically suspicious for malignancy (dysplasia) and 6 were histologically false negative before operation.[33] Sensitivity is again 71% which agrees with other literature data.[11,21,35] A diagnostic papillectomy evidently could give better results.

A deffinitive tissue diagnosis is a prerequisite for the appropriate management but forceps biopsies in several percent of cases do not allow unambiguous determination of the lesion – this problem is characteristic for the patients with ampullary tumors and is unique in gastrointestinal endoscopy.[4,15] The gastroenterologist more dependent on the imaging and cytological techniques including endoscopic ultrasonography, etc,[17,31,34] than on the histological report compared to other gastrointestinal endoscopies. To overcome this difficulty we propose more extensive diagnostic and therapeutic use of papillectomy instead of forceps biopsy. The quality of histological specimens will be higher, the pathological diagnosis more accurate and the need for rebiopsies can be significantly reduced. To further elaborate the conditions, mode, indications and contraindicatons of the diagnostic papillectomy should be a common task for endoscopists, clinicians and pathologists as the golden rule is: ***evaluation of Vater papilla biopsies is a part of the gastrointestinal endoscopy, where the closest cooperation is necessary between pathologist and endoscopist.***

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