Colorectal villous tumors
Accuracy of the preoperative biopsies

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Abstract

This study was undertaken to assess the reliability of the endoscopic biopsies in the evaluation of colorectal villous tumors (CRVT). In 163 consecutive patients referred for surgical treatment of CRVT, preoperative evaluation had been routinely done by colonoscopy and multiple biopsies. Tumors were classified in 3 groups : low grade tumors, high grade tumors and adenocarcinomas. Infiltration in depth was staged on the postoperative specimens according to the Dukes-Astler-Coller's classification. All the tumors were completely resected by surgery and definitive pathological diagnosis was established. An exact correlation between the pre- and postoperative staging was observed in 48% of the cases. Accuracy averaged 54% in the group-by-group comparison, with an overstaging rate of 6.7%, and an understaging rate of 39%. The incidence of adenocarcinomas was 22% in the group with clearly benign preoperative biopsies and 50% in the other cases. There were significantly more B2 and C tumors among the patients referred after 3 or more endoscopic attempts (33%) than after one or two sessions (10%) ($p < 0.0003$). We confirm that in spite of multiple endoscopic biopsies, only a complete resection permits an exact staging and an appropriate therapeutic choice. (Acta gastroenterol. belg., 1999, 62, 9-12).

Key words : colon, rectum, villous adenoma, villous tumor, preoperative biopsy, adenocarcinoma.

Introduction

Colorectal villous tumors (CRVT) are benign tumors having a high potential of malignancy. Malignant transformation is reported to occur in 8 to 76 percent of the tumors (1,2,3). Accurate diagnosis is required to choose the best treatment. Conventional diagnostic methods include digital rectal examination and proctocolonoscopy with multiple biopsies. Ultrasonography provides some additional information in selected rectal tumors, with a sensitivity of 50 percent in detecting malignancy (4,5). Nevertheless, an exact diagnosis remains difficult on endoscopic biopsies due to the heterogenicity of the tumors, the rather superficial character of many biopsies, several pitfalls in sampling and the sometimes difficult evaluation of "dysplasia". The aim of our study was to assess the reliability of of the preoperative biopsies in the diagnosis of CRVT by comparing in our experience the results of such biopsies with the final histological data.

Patients and methods

Over a 15-year period of time, 163 patients (mean age, 66 years ; range, 28-91 ; sex ratio : 1) were admitted in our department for surgical treatment of CRVT. All the tumors were sessile and two thirds (65.7%) were rectal. The distribution along the colon and rectum is reported in Table I. All patients had undergone one or more colonoscopies with multiple biopsies, as large as possible. The number of sessions before referral varied from 1 to 5 per patient (Table II).

Table I. — **Location of the villous tumors**

	n	%
Right colon	21	12.9%
Left colon	35	21.5%
Upper rectum	15	9.2%
Mid rectum	35	21.5%
Low rectum	57	35.0%

Table II. — **Number of preoperative endoscopic sessions**

n patients	number of endoscopies
114	1
31	2
11	3
5	4
2	5

Preoperatively, villous tumors were classified in 3 groups : low grade tumors (with low or moderate dysplasia), high grade tumors (with severe dysplasia, or carcinoma *in situ* in which malignant transformation was intra-epithelial and limited by the basal membrane) and adenocarcinomas, infiltrating the lamina propria or the submucosa (stages "A1" and "A2", respectively ; personal classification). Deeper infiltration into the intestinal wall was defined according to the Dukes-Astler-Coller classification on the postoperative specimens (6).

All the tumors were surgically resected "in toto". The type of procedure was determined by the size and location of the tumors. A colorectal resection was carried out in 78 cases (48%) and a local excision in 85 cases (52%) (Table III). All the surgical specimens were analysed by the serial technique. Strict criteria of dysplasia were applied by the same pathologist (GL).

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Table III. — **Type of surgical treatment**

	n	%
Colorectal resection		
Segmental colectomy	35	21.5%
AR[1] resection	32	19.6%
AP[2] excision	5	3.1%
Rectal resection + coloanal	4	2.5%
Proctocolectomy	2	1.2%
Local excision		
Endorectal	75	46.0%
Colotomy	9	5.5%
Rectotomy	1	0.6%

[1] AR anterior rectal resection
[2] AP abdominoperineal excision

Pre- and postoperative pathological conclusions were compared. Accuracy, positive predictive value (PPV) and negative predictive value (NPV) were evaluated. Qualitative data were compared using the Chi-square test.

Results

The pre- and postoperative data are detailed in Table IV. Preoperatively, the tumors were classified as low grade, high grade and adenocarcinomas in 99, 48 and 16 cases respectively. On histological examination of the resected tumors, there were 66 low grade villous adenomas, 34 high grade villous adenomas and 63 adenocarcinomas (Table V). Among this last group, there were 9 "A1", 20 "A2", 27 "B" and 7 "C" cancers.

An exact stage-by-stage correlation between the pre- and postoperative results was observed in 78 cases (47.8%) (Table IV). An exact group-by-group correlation was observed in 88 cases (53.9%) (Table V). Among the 99 adenomas preoperatively staged as "low grade", 15 were high grade adenomas and 28 (28,2%) were adenocarcinomas. Of the 48 preoperative "high grade" tumors, 9 were low grade, 18 were high grade and 21 (43.7%) were adenocarcinomas. Among the 16 "preoperative" carcinomas, there were 1 low grade lesion, 1 high grade, and 14 adenocarcinomas. Tumors were "group-overstaged" in 11 cases (6.7%) and understaged in 64 (39.2%).

Table V. — **Group by group correlation**

Postop	low grade	high grade	infiltrating
Preop			
low grade (99)	56	15	28
high grade (48)	9	18	21
adenocarcinoma (16)	1	1	14

low grade : slight, moderate dysplasia.
high grade : severe dysplasia, cancer in situ.
carcinoma : lamina propria (A1) and deeper.

When the preoperative biopsies were classified in 2 groups, clearly benign (low grade) on one hand, and dubious on the other hand (high grade and malignant), the overall correlation rate was 67.5%, with a PPV of 84% and a NPV of 56.5% (Table VI).

Table VI. — **Correlation for tumors preoperatively classified as clearly benign or dubious**

postop.	benign	high grade/ carcinoma
preop.		
clearly benign	56	43
dubious	10	54
accuracy	0.67	
ppv	0.84	
npv	0.56	

If one considers the boundary between A1 and A2 as the limit between superficial and infiltrating cancers (7), 54 tumors of the whole series were infiltrating cancers (Table IV). This incidence of 33.1% is considered as our "a priori" incidence of invasive tumors. When the preoperative biopsies were clearly benign, the rate falls to 22 % (22/99) and rises to 50% (32/64) in patients with high grade lesions (19/48 ; 39.5%) or carcinomas (13/16 ; 81%) in the preoperative biopsies.

There were 10 tumors "B2 or C" (8.7%) in the group of patients referred after the first endoscopic session, 5 (16%) after the second session, and 6 (33%) after the third or later. Difference between the first and the last groups was highly significant ($p < 0.0003$).

Table IV. — **Comparison of pre- and postoperative results of the pathological findings. Detailed data**

Preoperative	Postoperative							
	Low grade	High grade	A1	A2	B1	B2	C1	C2
Low grade (99)	56	15	6	10	6	2	2	2
High grade (48)	9	18	2	7	5	6	0	1
A1 (11)	1	1	1	0	1	5	1	1
A2 (5)	0	0	0	3	1	1	0	0
Total	66	34	9	20	13	14	3	4

A1 : adenocarcinoma extending into the lamina propria.
A2 : adenocarcinoma extending into the submucosa.

Discussion

The majority of adenocarcinomas of the large bowel are considered to arise from adenomatous polyps (8,9). The *size* of the adenoma and the extent of the *villous component* are major independent risk factors associated with high grade dysplasia, which is an anatomic condition correlating with the transformation of a benign adenoma to a malignant tumor (3,7,10). A greater incidence of focal malignant changes is indeed observed in larger adenomas (46% in adenomas over 2 cm in diameter), although 9.5% of the adenomas between 1 and 2 cm in diameter contain invasive adenocarcinoma (11). Malignant changes are found in 40% of villous adenomas (11). Furthermore, it has been confirmed by Atkin *et al.* in a large *clinical* survey that risk of subsequent colorectal cancer after endoscopic excision of rectosigmoid adenomas was significantly greater in patients with tubulo-villous, villous, or large (1 cm or more) rectosigmoid adenomas (12).

Accurate diagnosis and staging are required to select the best treatment : local destruction (laser, diathermocoagulation, ...) of benign tumors, local destruction or excision of superficial cancers, radical resection of invasive cancers. Tumor transgression should be avoided during excision biopsy in any case with suspicion of malignancy (9).

Comparing the assessment of malignancy in the initial biopsy specimens with that of the final histological diagnosis, Taylor *et al.* observed a 34% rate of false negative and a 10% rate of false positive reports (13). Our series reports rates of 43% and 16%, respectively and thereby confirms the low reliability of preoperative diagnosis based on biopsies taken at random. The overall accuracy between pre and postoperative evaluation averages a mere 50%. More significant, a group by group comparison offers a 53.9% rate of accuracy. This rate falls to 49% if the "A1" tumors are classified with the "high grade tumors, according to the definition of cancer by Morson (14). 28% (28/99) of the low grade lesions were adenocarcinomas (among which B2 and C tumors), whereas "only" 44% of the high grade adenomas were adenocarcinomas.

Factors that are possibly responsible for this rather low performance include the size and sessile pattern of the tumor, its heterogenicity, bad sampling and subjective evaluation of dysplasia, even among experts (15). The degree of dysplasia varies from area to area within the same lesion and malignant foci may border a benign tissue (fig. 1). On the other hand, preoperative biopsies "at random" may harvest the sole islet of carcinoma of the tumor and lead to overdiagnosis of malignancy (9). Malignancy has been observed deeply hidden within a benign adenoma and, in spite of all endeavour, biopsies remained superficial with regard to the deeply located cancer. Moreover, to trace malignancy in a biopsy requires an adequate sample and good orientation. For example, misplaced epithelium, within the muscularis mucosae or the submucosa, that mimicks invasion ("pseudo-invasion"), is observed in up to 3% of benign adenomas, especially in polypectomy specimens (16). Finally, the limit between benignity and malignancy is not clearcut. Dysplasia, defined as an unequivocal neoplastic transformation confined within the boundaries of the basement membrane, is characterized by the presence of atypical architectural and cytological tissular features similar to those observed in carcinogenesis. Although criteria have become clearer (17,18), evaluation remains difficult in some cases. High grade dysplasia is considered as a high cancer risk, while low grade dysplasia, which can regress or progress slowly, represents a low cancer risk. When the basal membrane has been penetrated, the tumors are infiltrating adenocarcinomas (third group). With respect to the prognosis, invasion of the submucosa that includes the risk of venous or lymphatic invasion is a crucial step. In spite of strict criteria of dysplasia, applied by the same pathologist, only an accuracy rate of less than 67% was observed in our series (Table VI).

Diagnosis of malignancy remains largely uncertain. Especially in the larger tumors, repeated benign biopsies lead to false security and delay the adequate treatment for as many as 2 years as observed in 1 case of our series. It could however be argued that the tumor was not malignant from the very beginning. It is however noteworthy that the rate of B2 and C tumors was significantly higher in patients referred after 3 endoscopic sessions or more. Large, sessile villous lesions are difficult to remove by snaring, but must not be biopsied piecemeal, as they frequently contain focal invasive carcinoma. Not only may this result in incomplete excision, but orientation for microscopic examination will then be impossible. A surgical approach *ab initio* is frequently more satisfactory (9).

If one admits that only the Dukes "A" tumors are eligible for a local destruction, if feasible, as many as 12% of the low grade lesions (12/99) should be treated by radical resection. Conversely, 75% of the high grade tumors (36/48, Table IV) could be treated by local

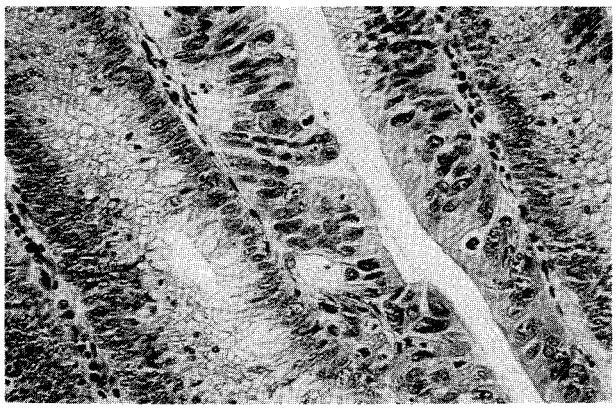

Fig. 1. — A gland showing obvious high grade dysplasia is located between two clearly benign appearing adenomatous glands (Hematoxylin and Eosin, × 320).

destruction while 25% of the others require resection with curage. Since 62% (10/16) of the tumors described as invasive preoperatively (A1 and A2) extended into the muscularis propria, a radical resection should be indicated in the "clearly benign" and "dubious" lesions in 12,5% and 34,3% respectively.

In *conclusion*, our data underline that endocopic biopsies are poorly reliable to accurately determine the degree of malignant transformation in CRVT, with an understaging rate of 39%. One or more benign biopsies are not a reassuring argument. 22% of the tumors considered as clearly benign on endoscopic biopsies were cancers infiltrating the muscularis mucosae or beyond, and so were 50% of the high grade-dubious tumors. Making decision on endoscopic biopsies remains hazardeous. 12% of the low grade CRVT and 33% of the high grade-dubious lesions should be treated by a radical resection. Even if ultrasonography offers some additional information in selected rectal tumors, long-term surveys with repeated multiple biopsies of incompletely excised CRVT are not justified, and danger of tumor transgression in cancer must be kept in mind. Complete resection is required as soon as possible. After initial incomplete endoscopic resection, operable patients with CRVT left in situ should be considered as candidates for diagnostic and therapeutic surgery to be given the best chance of cure.

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