Histopathological types of colonic adenomas incidence of dysplastic changes in Riyadh, Saudi Arabia

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Abstract

One hundred thirty seven adenomas of the colon from 112 patients were identified by histological examination of surgically or colonoscopically removed adenomas All lesions had a radial diameter of 1.0 cm or less .Fifty six of 137 adenomas (41%) contained high-grade epithelial dysplasia, twenty five patients had multiple adenomas, Colonoscopically and grossly, the lesions were described as sessile , tubular, villous or tubulo vilous growth. These lesions may be precursors of small, flat, ulcerated colonic carcinomas. Our study encompasses the histology and differential diagnosis of screen detected polyps, focusing on features which discriminate lesions at highest risk of malignant transformation.

Key words: Dysplasia, colon, lesions, carcinoma

Introduction

The majority of published clinical, histologic, and genetic data on colonic neoplasia indicate that colonic adenomas are precursors to most or all of colonic carcinomas, and that the risk of development of carcinoma within an adenoma increases with the size and histologic grade of the lesion **(1-5).** Since the majority of colonic adenomas have an exophytic, polypoid configuration which are a circumscribed lesions projecting in the bowel lumen, colonoscopic identification and removal of polyps has been widely used as an effective prophylactic against the development of colonic carcinoma **(6-7)**. Nevertheless, many advanced carcinomas and a small percentage of early carcinomas fail to contain a residual precursor adenoma **(8-13)**. While it is very probable that large advanced carcinomas progressively destroy adjacent non-carcinomatous dysplastic epithelium (9-12), the identification of small, superficially invasive carcinomas without an identifiable contiguous polypoid adenoma has led to the reemergence of the concept of "de novo" development of colonic carcinoma **(14-15)**. An alternate explanation for the existence of small, invasive carcinomas without a precursor polypoid adenoma is that these lesions may arise from very small, highly dysplastic adenomas which are rapidly re-placed by the expanding malignancy. The sporadic identification of similar lesions at our institution has prompted us to undertake a systematic analysis of colonoscopically and surgically excised adenomas in order to determine the relative frequency and clinicopathologic changes of adenomas.

Materials and methods

The surgical pathology files from different hospitals in Riyadh, Saudi Arabia were searched for all cases coded during previous 2 years period (2009-2010) as containing colonic adenoma. One hundred thirty seven adenomas were obtained from colonoscopically and surgically excised specimens from 112 patients, following exclusion of specimens from patients with familial polyposis or long-standing ulcerative colitis. Multiple level hematoxylin-eosin-(H&E) stained sections from lesions were independently examined by

two observers. Patient demographic data lesion location (ascending, transverse,descending or rectosigmoid colon) lesion size (< 1cm, 1-2cm, or > 2cm).Histologic picture as (tubular, tubulovillous, villous,or flat), and grade of epithelial dysplasia (low or high grade) were determined for all lesions. Adenomas were classified as flat when they lacke the exophypoid configuration. The dysplastic mucosa was never greater than two times the thickness of the adjacent non dysplastic mucosal segment. The histologic grade of the epithelial dysplasia in each adenoma was determined by the following criteria: high-grade lesions showed stratification of nuclei and numerous mitotic figures through the full thickness of crypt epithelium, with loss of nuclear polarity, marked nuclear atypia, and complete absence of cytoplasmic mucinous differentiation. These cytologic features had to involve at least three tubules or crypts The presence of marked crypt architectural complexity or nuclear karyorrhexis was not used as an independent criterion for determination of dysplasia grade. Clinical records, including colonoscopy reports, were reviewed for all patients in whom adenomas were identified.

Data analysis

Fisher's exact test was used for analysis of data. A P value of < 0.05 was accepted as statistically significant.

Results

Of the 137 adenomas. These were found in patients. The demographic, gross, and histo-logic features are presented in Table (1). The mean age of the patients was 43 years (range, 14 - 78) and 83% were Male. However, a non-polyosis cancer family syndrome had not been documented in any of these patients. Multiple adenomas were identified in 25 patients of the 137 patients (18% of total adenomas). Tubular adenomas were classified as tubular, tubulovillous or villous adenoma. They are also classified as low grade and high grade according to the degree of dysplasia. High grade dysplasia considered to be more sensitive marker of malignant potential. Low grade dysplasia includes mild to moderate loss of normal epithelial maturation, nuclear stratification and mucin depletion accompanied by variable degrees of simple glandular crowding. Tubular adenomas were 10 cases (7.3 %), tubulovillous 17 (12.4 %) and purly villous 6 (4.4 %). One hundred thirty of the adenomas were excised colonscpically by snare and electrocautery or, in two lesions, by pincer biopsy. Seven adenomas were removed as part of a segmental colectomy for a separate invasive carcimoma. In these specimens, the adenomas were identified incidentally during the gross pathologic examination and sectioning. Both of these carcinomas had a grossly sessile, ulcerated appearance without exophytic polypoid component. As sessile flat, plaque-like, or an "abnormal mucosal fold " .Ten flat edenomas were located in the ascending colon , four in the transverse colon, five in the descending colon , and 10 in the rectosignoid colon.

Analysis of histologic sections of the flat adenomas supported the colonoscopic impression that all (104) had a purely tubular morphology. The low-magnification configuration was of a slightly raised plaque, regardless of whether the lesion was located within flat mucosa or on the tip of a mucosal fold (Figure 1).

The characteristic architecture of a crowded collection of dysplastic crypts located at the superficial lumenal surface of the mucosa, with underlying, well-spaced, nondysplastic crypts, was identified in serial sections in all cases (Figure 2). In some lesions, focal full thickness mucosal dysplasia was present, often with mucosal invagination and thinning, and always in the center of an adenoma which showed only superficial mucosal dysplasia at the periphery of the lesion (Figure 3).

High –grade dysplasia , based upon the identification of full thickness crypt epithelial nuclear stratification and loss of cytoplasmic mucinous differentiation ,was found in (97) of (137) adenomas in total (Figure 4). Concomitant crypt budding and excessive nuclear debris were present in (9) lesions, respectively (Figure 5).

In at least (42) cases, the degree of nuclear complexity was such that a diagnosis of intramucosal carcinoma was considered

In comparisom, histologic grading was also performed upon the polypoid tubular adenomas. The rectosignmoid colon, 67 cases were specified. Histologic grading revealed (3) of the (10) polyp-

oid tubular adenomas (30 %) to be high grade. A tubular had a ten-fold greater frequency of containing high-grade dysplasia than an analogous polypoid adenoma with an equivalent spherical diameter ($p < 0.05$).

Both of the colonic surgical resection specimens in which flat adenomas were identified contained simultaneous, non contiguous, flat and ulcerated carcinomas without a residual polypoid adenoma at the periphery of the lesion. These cancers were located in the ascending and rectosigmoid colon Cularis propria, and the larger lesion extended into pericolic adipose tissue. The edge of both lesions showed an abrupt transition from benign colonic mucosa to ulcercinoma (Fig6), with focal extension of highly dysplastic crypts along the surface of rolled benign mucosa in one of these lesions. A single regional lymph node metastasis was found in one of these patients, Villous structures form at least 80% of villous adenomas and more than 20% of tubulovillous adenomas. Villi may be long slender, finger like palmate villi, leaf like, broad branched processes or foreshortened villi , isolated slender overgrowths. The presence of at least one identifiable villous in polyp biopsies or fragments deserves to report as predominantly tubular histology.

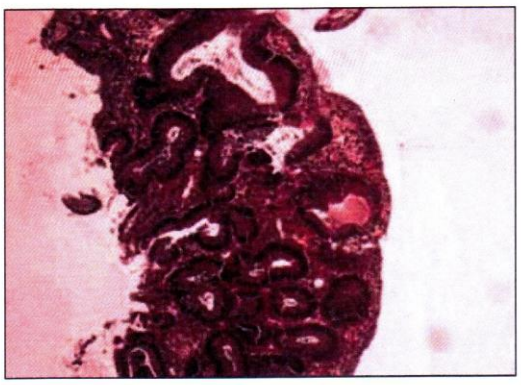

Figure 1. Flat colonic adenomas from involving (top) flat and (bottom)folded mucosa .(H&E stain: magnification x 15).

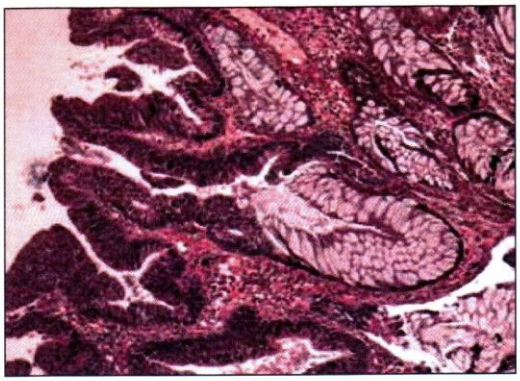

Figure 2. Colonic adenoma from patient dysplastic crypts clustered at the superficial lumens surface of the mucosa with underlying non- dysplastic crypt epithelium.(H&E stain: magnification x 48)

Table 1. Shows the age of the patients

Years	10-19	20-29	30-39	40-49	50-59	60-69	70-80	Total
Male	4	12	14	20	32	4	5	91
Female	3	3	3	2	5	2	1	19

Table 2. Shows the Percentage of Dysplastic changes

	Flat	Tubular	Tubular villous	Villous	Total
High grade	73	3	15	6	97
Low grade	31	7	2	0	40

Table 3. Shows the Histological types according to the site affected

Site	Total	Flat	Tubular	Tubular villous	Villous
Rectosigmoid	**67**	**50**	**6**	**8**	**3**
Transverse	**32**	**29**	**1**	**2**	**0**
Descending	**26**	**18**	**2**	**5**	**1**
Ascending	**12**	**7**	**1**	**2**	**2**
	137	**104**	**10**	**17**	**6**

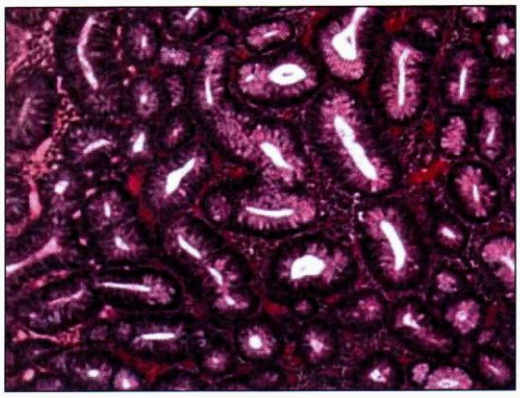

Figure 3. Colonic adenoma ,showing full thickness mucosal dysplasia in the central ,invaginated portion of the lesion. (H&E stain; magnification x 25).

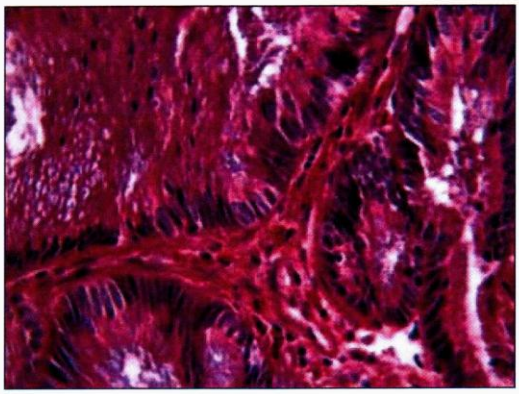

Figure 4. High grade flat colonic adenomas from full thickness epithelial nuclear stratification, loss of cytoplasmic mucin production, and marked nuclear atypia. (H&E stain; magnification x 120)

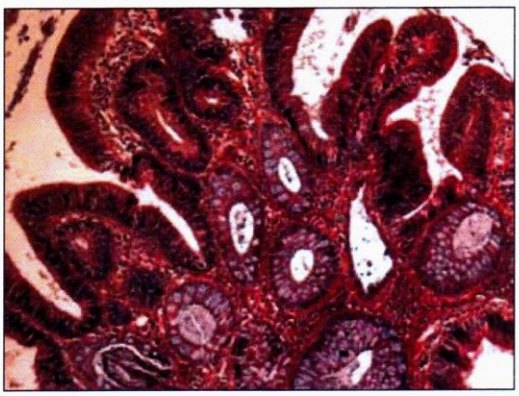

Figure 5. Excessive nuclear debris and crypts complexity in flat colonic adenoma (H&E; stain; magnification x 240).

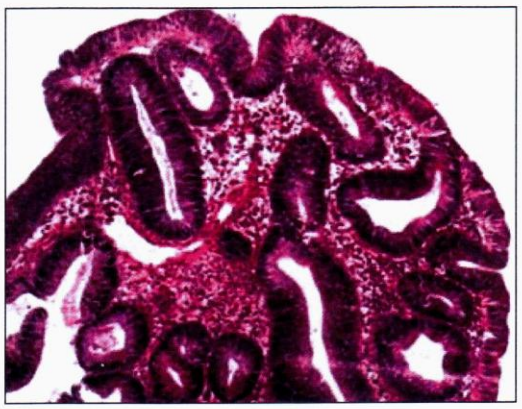

Figure 6. Flat, ulcerating carcinoma, showing abrupt transition from benign to carcinomatious epithelium. (H&E stain: magnification x15.)

Discussion

The most widely accepted morphologic classification of dysplastic colonic polyps includes tubular, tubulovillous, and villous adenomas (**1-2**), Adenoma type, size, and grade of epithelial dysplasia have been emphasized as factors associated with those lesions containing carcinoma. The gross configuration of exophytic colonic polyps (pedunculated and sessile) has also been shown to correlate with these parameters (**16**). Sessile adenomas tend to be larger and more often have a prominent villous histologic component. Polyp configuration also dictates, in large part, the mechanical feasibility of complete colonoscopic removal.

Characteristically, they consisted of slightly elevated, erythematous mucosal plaques, often with a central invagination or depression. These authors focused on the histologic architecture of the lesions, consisting of dysplastic tubules clustered at the lumenal surface of the mucosa, with sparing of the deeper crypt compartment . Apart from these reports, the clinical and pathologic features of adenomas have remained largely unrecoginzed, and a systematic analysis of colonic adenomas in order to determine the relative frequency of these lesions has not been performed. The results of the present study indicate that colonic adenomas are not exceedingly uncommon lesions. Of the patients who underwent surgical or colonoscopic excision of adenomas at our institution during the period included in the study. However, this may

be an underestimate of the relative frequency of these lesions due to their inconspicuous endoscopic configuration, particularly in a poorly cleansed bowel. Histologic recognition of flat adenomas is not difficult, especially if the approiate colonoscopic description is available. Most striking is the dominant radial growth phase of dysplastic crypt epithelium at the mucosal surface with absent, or only focal, central vertical extension of dysplastic epithelium to the base of the mucosa, a feature which allows the recognition of flat adenomas even in folded or distorted mucosal specimens.

Flat colonic adenomas appear to be a striking exception to the observation, applicable to polypoid adenomas, that small lesions less than 1 cm in diameter are very unlikely to exhibit high-grade dysplasia and, by implication, represent a low cancer risk. The frequency of high – grade dysplasia observed in flat adenomas in the present study (75 %) and previous studies (**12**) indicates that colonoscopic recognition and removal of these lesions is likely to be of importance to any colon cancer surveillance program. Recognition of these lesions by the histologist and communication of their potential significance to the clinician may also be of importance, since 25 patients of the 112 patients in this study had multiple adenomas. Identification of one of these adenomas, particularly if it exhibits high –grade dysplasia, may warrant heightened colonscopic surveillance with particular attention to small, lesions.

Although invasive carcinoma was not observed to arise within any of the flat adenomas described in this study, an increased risk for the development of carcinoma within these lesions is implied by the high frequency of high grade dysplasia found within them (73). Furthermore, at least (32) of the lesions in this study showed a high degree of architectural complexity and nuclear atypia and may have classified as "intramucosal carcinoma" by some observers (**10**).

It is also interesting to note that adenomas were found in two surgical resection specimens in this study, both of which contained flat, ulcerating invasive carcinomas without a residual polypoid adenoma at the cancer margin. Carcinomas of this type, particularly small lesions, have been described in several.

Case reports and larger series (**3-9**) and have been stated to represent " denovo" colon carcinoma, has spontaneous concept, particularly in light of recent data obtained form DNA hybridization analysis indicating a progressive accumulation of genetic allelic deletions and point mutations in advancing stages of colonic neoplasms (**4**).

A more likely possibility is that small, ulcerating carcinomas arise from small adenomas , which are rapidly destroyed by the expanding carcinomatous epithelium The small, flat, highly dysplastic adenomas described in this study are likely candidates for these precursor lesions .

Conclusion

The results of this study indicate that small, flat adenomas represent a limited, but significant, percentage of sporadic colonic adenomas encountered at our institution, and are much more likely to exhibit high –grade epithelial dysplasia than similarly sized polypoid tubular adenomas. They may occur simultaneously at multiple sites within an individual colon. Therefore colonoscopic and histologic recognition of these lesions may play an important role in prophylactic colon cancer surveillance programs. Histologically, these lesions consist of a plaque-like proliferation of dysplastic tubules, particularly along the superficial luminal mucosal surface, often with architectural complexity and prominent intracellular nuclear debris. Non dysplastic flat polyps were considered to have no malignant potential. There is increasing evidence that all lesions in the flat adenomas spectrum represent potential precursors in an alternative pathway to adeno carcinoma .Colonic adenomas may be precursors to small, ulcerating carcinomas which lack an associated residual polypoid adenoma. Prospective analyses of patients in whom flat adenomas have been identified will be required in order to precisely define the natural history and carcinoma risk associated with these lesions. Our study has highlighted that the management of patients with colorectal polyps is highly dependent on the quality of pathological evaluation.

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