Gut-associated Lymphoid Tissue (GALT) Carcinoma or Dome Carcinoma?

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Abstract. *Background/Aim:* The vast majority of colorectal carcinomas (CRCs) evolve from mucosa not associated to lymphoid tissues aggregates via the adenoma-carcinoma sequence or via the serrated pathway. Rarely CRCs evolve from gut mucosa associated to lymphoid tissue (GALT). *Materials and Methods:* Based on the presence of a circumscribed elevation in the colorectal mucosa, GALT carcinomas are also referred to as dome carcinomas (DC). *Descriptions of the surface mucosa covering 21 GALT-CRCs appearing in pathological reports were reviewed. Results:* Three of the 21 GALT-CRCs fulfilled the criteria of dome carcinoma. Of the remaining 18 GALT-CRCs, nine were described as polypoid lesions, five as plaque-like lesions, two as sessile elevated lesions or mass, one as ulcerated and one as histological finding. *Hence, only 14.3% (n=3) of the 21 GALT-CRCs displayed a dome configuration, whereas the majority, 85.7% (n=18), exhibited structures other than dome shapes at gross or at histologic examination. Conclusion:* It becomes apparent that by using “dome” in addressing carcinomas in the colorectal mucosa, many cases of GALT carcinomas might be overlooked. Another drawback of using the “dome” nomenclature is that dome-like outlines may be detected in small metastatic tumors in the submucosa or in small colorectal carcinomas not arising from GALT mucosa. Instead, by using “GALT carcinoma”, that is the histologic diagnosis in addressing these neoplasias, all cases of GALT-CRCs will be included.

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The colorectal mucosa may be divided into two quantitatively, structurally and functionally different mucosal fractions. One fraction, associated with microscopically tiny lymphoid tissue aggregates, is called gut-associated lymphoid tissue (GALT) mucosa (1). The GALT mucosa is covered with a single layer of cells with few or no goblet cells. This single layer of cells display broad invaginations (microfolds) that amplify the cell surface forming intraepithelial pockets. Electron microscopy shows clear-cut micro-folds or micro-ridges that give the cell its name, namely M cells. The function of the M cells is to absorb luminal antigens, macromolecules and microorganisms via clathrin-mediated endocytosis (1) and haul them into the underlying collection of gut-indigenous, thymus-independent lymphoid tissue for immediate immunological processing. The constellation M cells-lymphoid tissue builds a lympho-epithelial immunological cross-talk unit, a relay complex for antigen-gut recognition. The frequency of the lymphoglandular complexes (that is GALT mucosa) increases from the proximal to the distal colon, being highest in the rectum (2). In colons with inflammatory bowel disease, the frequency of GALT complexes was significantly higher (mean 0.32/mm *muscularis mucosae*) (2). Nasciembeni *et al.* also studied the lymphoid aggregate density in the colon. They found a mean of 0.3 lymphoid aggregates/cm² in 77 consecutive colectomies from patients with Crohn's disease and a mean of 2.7 lymphoid aggregates/cm² in the mucosa of patients with colorectal cancer (3). Multiple lymphoid aggregates are newly formed in the submucosa and deeper layers in Crohn's colitis (4).

The other mucosal fraction, comprehending the vast majority of the colorectal mucosa, is not associated to lymphoid tissue aggregates. This GALT-free mucosa is built with mucus-producing goblet cells and columnar cells furnished with regular microvilli roofed by the extracellular glycoprotein glycocalix. The function of this huge mucosal fraction is to protect underlying structures and absorb fluids, vitamins and some nutrients.

It is generally accepted that the overwhelming majority of colorectal carcinomas (CRCs), the third most frequent cancer

Table I. Descriptions of the luminal configuration covering 21 gut-associated lymphoid tissue (GALT) carcinomas appearing in published reports in the literature.

Authors (reference)	Year	No. cases	No. GALT-CRCs	Description of surface mucosa
Rubio (8)	1984	One	One	Irregular plaque-like lesion
De Petris <i>et al.</i> (9)	1999	One	Two	One dome, one ulcerated
Jass <i>et al.</i> (10)	2000	One	One	Dome
Clouston, Clouston, Jass (11)	2002	Two	One (Case 1) One (Case 2)	Polypoid lesion Polypoid lesion
Rubio and Talbot (12)	2002	One	One	Polypoid lesion
Stewart <i>et al.</i> (13)	2008	Two	One (Case 1) One (Case 2)	Polypoid lesion Plaque-like lesion
Asmussen, Pachler, Holck (14)	2008	Two	One (Case 1) One (Case 2)	Flat polypoid lesion Plaque-like lesion
Rubio <i>et al.</i> (15)	2010	One	Three	One dome, one plaque-like lesion, one, an histological finding
Coyne (16)	2012	One	One	Irregular sessile polyp
Puppa, Molaro (17)	2012	One	One	Raised plaque
Yamada, <i>et al.</i> (18)	2012	One	One	Polypoid lesion
Rubio, Befrits, Ericsson (19)	2013	One	One	Polypoid lesion
Yamada, Sekine, Matsuda (20)	2013	One	One	Sessile elevated lesion
Kannuna, Rubio <i>et al.</i> (21)	2015	One	One	Sessile mass
Rubio, Schmidt (cfr. Figure 1)	2016	One	One	Sessile villous polyp

worldwide, evolve from the GALT-free mucosa through adenoma-carcinoma sequence (5) and the serrated pathway (6). In contrast, CRCs arising in GALT mucosa are very rare. In 1954, Cuthbert Dukes described in patients with ulcerative colitis a lesion in the submucosa characterized by “misplaced” colonic epithelium surrounded by nodular lymphoid tissue (7). Dukes’ description corresponds to that of GALT mucosa. He believed that the “misplaced” epithelium was the result of mucosal repair following regeneration of a mucosal ulcer and that the epithelium detached and buried in the submucosal would encourage cancer development (7). Searching for a confirmation of Dukes’ hypothesis we reported the first case of GALT carcinoma in the colon in 1984 (8).

Based on the presence of a circumscribed elevation in the colorectal mucosa, GALT carcinomas have been also referred to as dome carcinomas (DCs).

The purpose of this communication was to review the descriptions of the mucosa covering GALT-CRCs.

Materials and Methods

The narratives of the architecture of the luminal mucosa given in the pathological reports in 21 GALT-CRCs were reviewed.

Results

Results of the review of the pathological reports in 20 GALT-CRCs reported in the literature, as well as in a recent case of GALT-CRC found in a colectomy specimen (Figure 1), are given in Table I. The results revealed that three of the 21

Figure 1. GALT carcinoma covered by a villous adenoma. a. GALT carcinoma showing adenocarcinoma islands in the submucosal (at arrows) surrounded by lymphoid tissue. On top, sessile villous adenoma (H&E staining, magnification $\times 2$). b. Detail from the sessile villous adenoma with high-grade dysplasia (H&E staining, magnification $\times 20$). c. Detail from one adenocarcinoma island in the submucosa surrounded by lymphoid tissue. Muscularis mucosae at arrows (H&E staining, magnification $\times 10$).

GALT-CRCs fulfilled the criteria of dome carcinoma. Of the remaining 18 GALT-CRCs, nine were described as polypoid lesions, five as plaque-like lesions, two as sessile lesions or mass, one as ulcerated and one as histological finding.

Discussion

This study revealed that only 14.3% (n=3) of the 21 GALT carcinomas showed dome configurations. The remaining 85.7% (n=18) exhibited, at gross examination, structures other than dome shapes ranging from polypoid lesions, plaque-like lesions, sessile polyps or lesions, sessile masses or ulcerated lesions to normal histology (Table I). Based on these results, it becomes apparent that by using “dome” in addressing carcinomas in the colorectal mucosa, many cases of GALT carcinomas will be overlooked. Superficial pinch biopsies may contain only dysplastic epithelium from an adenoma concealing a GALT-CRC in the submucosa. Another drawback of using the “dome” nomenclature is that dome-like configurations may be detected in small metastatic tumors in the submucosa or in small carcinomas not arising in GALT mucosa.

Conversely, by using “GALT carcinoma” in addressing these neoplasias, all cases of GALT-CRCs will be included in that diagnosis.

Conflicts of Interest

None.

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