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Surgical Management of Early Colorectal Cancer

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Abstract. An early colorectal carcinoma is TNM stage T1NxMx. Most early carcinomas of the colon and rectum can be treated by adequate local excision, such as colonoscopic polypectomy and per-anal excision. If there are adverse risk factors, especially poorly differentiated carcinoma, lymphovascular invasion, or incomplete excision, a radical resection is indicated if there is no contraindication. In the case of a low rectal carcinoma, adjuvant chemoradiation should be considered. Recently a new classification has been developed: sm1 is invasion to the upper one-third of the submucosa, sm2 is invasion to the middle one-third, and sm3 is invasion to the lower one-third. Lesions of sm1 and sm2 have a low risk of local recurrence and lymph node metastasis; local excision is adequate. The sm3 lesions and sm2 flat and depressed types have a high risk of local recurrence and lymph node metastasis; further treatment is indicated.

Early colorectal carcinoma is defined as "invasive carcinoma that has not spread in the direction continuity beyond the submucous layer, regardless of the presence of blood-borne or lymphatic metastasis" [1]. For the TNM classification, these lesions are T1NxMx. The term superficial carcinoma or carcinoma in situ, in which the carcinoma cells infiltrate the lamina propria above the muscularis mucosa, should be avoided to prevent unnecessary misunderstanding of a malignant lesion [2]. These lesions are in the preinvasive stage [1] and do not metastasize [3, 4]. The term severe dysplasia has now been used by most knowledgeable pathologists and clinicians.

Incidence of Early Colorectal Carcinoma

In colonoscopic polypectomy series, early carcinomas are found in 2% to 12% of the adenomas removed [2, 5–8]. In a series of 2003 patients with rectal carcinoma from St. Mark's Hospital who underwent resection or excision, 3.3% of the lesions were early carcinoma [1]. Huddy et al. [9] found 6% early carcinomas in a series of 454 patients with carcinoma of the rectum who underwent low anterior resection or abdominoperineal resection. Sitzler et al. reported an incidence of 4.3% [10].

On January 1, 1998, the U.S. government recommended routine screening for people with average risk of colorectal carcinoma age over 50 years with colonoscopy. This extensive mass screening has just begun, and one can expect to find a higher incidence of early colorectal carcinoma than has been reported at the present time.

Clinical Cases of Early Colorectal Carcinoma

Most early colorectal carcinomas are polyps with invasive carcinomas. The size may range from 5 mm to as large as the circumference of the colon or rectum. They may produce bleeding or mucous discharge but do not cause obstructive symptoms. Although some skillful colonoscopists, particularly from Japan, can tell by the gross appearance if it is an invasive carcinoma [11], the ultimate diagnosis must be made by histology. Because early colorectal carcinoma may involve only focal areas of a lesion, it is essential to remove the entire lesion for the diagnosis.

Classification of Early Colorectal Carcinoma

Most clinicians are now familiar with Haggitt's classification of early colorectal carcinoma in which the invasion is divided into four levels depending on whether it is pedunculated or sessile [12] (Fig. 1). A new classification for T1 lesions has been developed in Japan [13, 14] that has more detail, is more practical, and is an important guide for management. This classification is essentially for a sessile lesion in which the submucosal invasion is divided into sm1 (invasion in upper one-third of the submucosa), sm2 (invasion in the middle one-third), and Sm3 (invasion in the lower one-third) (Fig. 2). In fact, this classification can also be applied to Haggitt's pedunculated lesion in that Haggitt levels 1, 2, and 3 are comparable to Sm1. Haggitt level 4 can be sm1, sm2, or sm3 depending on the depth of submucosal invasion.

Risk of Lymph Node Metastasis in T1

Once the malignant cells have invaded through the muscularis mucosa, they are capable of metastasizing to the regional lymph nodes or even distally to the liver or other organs. Pedunculated adenomas with invasion to Haggitt level 1, 2, or 3 have a low risk of metastasis provided there are no other risk factors. On the other hand, a pedunculated lesion with invasion to its base, or Haggitt level 4, and a sessile polyp with invasive carcinoma (Haggitt level 4) have a risk of lymph node metastasis about 10% of the time [5, 15]. Recently, the series from Japan showed that Haggitt level 4 lesions (both pedunculated and sessile) in which the invasion is limited to sm1 and sm2 have a low risk of lymph node metastasis, whereas sm3 has a high risk [13, 14]. Huddy et al. [9]

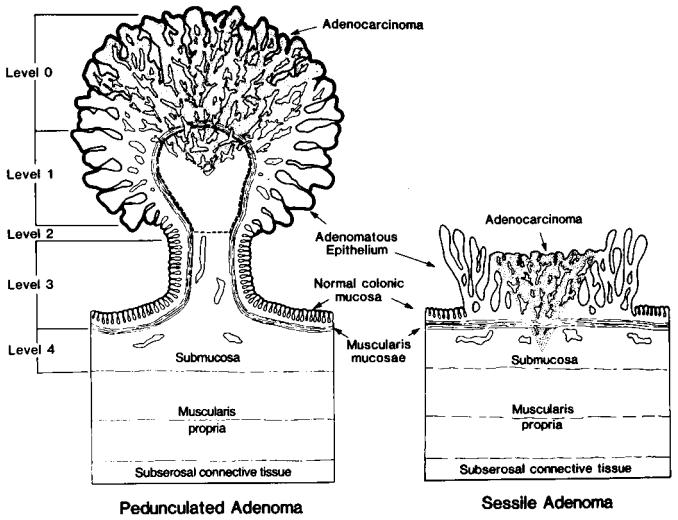

Fig. 1. Haggitt's classification. Level 0: not invasive carcinoma; level 1: invasion to the head of the pedunculated polyp; level 2: invasion to the neck of the pedunculated polyp; level 3: invasion to the stalk of the pedunculated polyp; level 4: invasion to the base of the pedunculated polyp. All sessile lesions are level 4. (From Haggitt [12], with permission)

studied specimens of carcinoma of the rectum removed by low anterior resection with wide mesorectal clearance or by abdominoperineal resection. There were 27 T1 specimens, of which 3 had lymph node metastasis (11%), whereas in 81 T2 lesions 19 had positive lymph nodes (23.5%). Although the difference was not statistically significant, it is highly suggestive that as the invasion deepens the risk of lymph node metastasis is higher. The risk of lymph node metastasis and residual carcinoma with sm3 invasion is 27% to 69% [2, 14]. These lesions should undergo further treatment.

Adverse Risk Factors

About 85% to 90% of T1 lesions do not metastasize. Although it is impossible to independently identify the 10% to 15% that do, particularly to the regional lymph nodes, many factors can reveal those patients with a high risk of metastasis. Most information is obtained from the resected T1 lesion. Finding information about T1 colorectal carcinoma in the literature is often confusing and difficult. Many authors include carcinoma in situ; similarly, many reports of "early carcinoma" of colon and rectum include both T1 and T2.

Poorly Differentiated Carcinoma

In a series of early carcinoma that underwent bowel resection, Morson reported that the only five cases with lymph node metastasis were undifferentiated carcinoma [15]. Hase et al. [16] found that undifferentiated carcinoma cells in the main body of the lesion did not have a high rate of lymph node involvement. The risk was for lesions with moderate or poorly differentiated cells in the submucosa ahead of the invasive front. On the other hand, Kikuchi et al. [14] found that the extent of the submucosal invasion (sm3), not the degree of differentiation or other parameters, determined the risk of lymph node metastasis. It is possible that

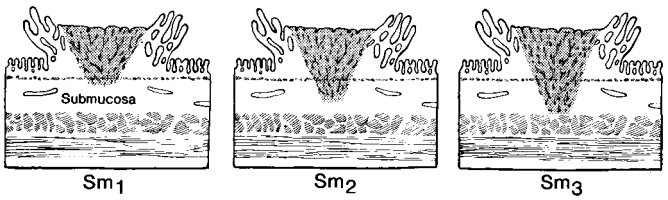

Fig. 2. Depth of invasion into submucosa. Sm1: invasion into upper third of submucosa; Sm2: invasion into middle third of submucosa; Sm3: invasion into lower third of submucosa.

the poorly differentiated carcinoma spreads to the submucosa quickly and more extensively. In general, poorly differentiated carcinoma of the colon and rectum has a high risk of lymph node as well as distant metastasis.

Lymphatic and Vascular Invasion

Lymphatic and vascular invasion adjacent to the lesion are also noted extensively in the literature to be adverse factors. The group from St. Mark's Hospital [17] reviewed 81 malignant colorectal polyps in 80 patients treated by endoscopic polypectomy and assessed the importance of carcinomatous invasion of veins in the submucosa. Venous invasion was present in 37% and lymphatic invasion in 20%. The authors suggested that lymphatic invasion not be included because the tissue retraction around the lesion may simulate the appearance of lymphatic invasion and is considered a major potential source of error. Endothelium-lined channels containing malignant cells without luminal red blood cells or muscle in their walls are considered to be examples of lymphatic invasion [17].

In the St. Mark's series [17], 72 of the lesions were pedunculated and 9 were sessile; in other words, 90% of the lesions were sm1 or sm2. This indicates that venous and lymphatic invasion with early carcinoma of colon and rectum is common if one looks for it. The series of Moriera et al. [18] showed that 8 of 16 T1 lesions had lymphovascular infiltration (five sm3 and three sm1 sm2); all five sm3 lesions had lymphovascular infiltration. Brodsky et al. [19] showed that with T1 tumors without lymphovascular invasion the risk of lymph node metastasis was 0 in 15 patients, whereas those with T1 lesions and positive lymphovascular invasion had lymph node metastasis in three of nine patients (33%). The extent of submucosal infiltration was not reported in those with positive lymphovascular invasion. Cooper [20] observed that lymphatic invasion with malignant colorectal polyps is not consistent, and that most lymphatic invasions have undifferentiated carcinoma. However, based on his personal experience and the evidence in the literature, he generally agreed that lymphatic invasion is associated with an increased risk of lymph node metastasis.

Inadequate Excision

Many early carcinomas of the colon and rectum are diagnosed by per-anal excision of the lesion in the low rectum and colonoscopic polypectomy of the lesion in the mid or high rectum and colon. The adequacy of local excision is reported as "complete," "doubtfully complete," or "incomplete" [21]. For "complete" excision, the histologic sections show normal microanatomic orientation of

the lesion and the surrounding mucosa with the submucosal layer and muscularis propria, if present [21]. "Doubtfully complete" is used when carcinoma is present within the tissues of the electrocautery burn at the margin of the excision. It is also possible that some carcinoma cells have been destroyed by the cautery [22]. "Incomplete" is used when there is histologic evidence that carcinoma has not been completely removed.

In a collective series from Japan, of 58 patients with the lesion snared via endoscopy followed by bowel resection because of invasive carcinoma near or at the cut margin, 22% had residual tumor and 5% had lymph node metastasis [2]. A study by Cunningham et al. [23] on polyps with invasive carcinoma removed by colonoscopy included 12 patients in whom the distance between the carcinoma cells and cautery mark was < 1 mm; 2 of the 12 (17%) had residual carcinoma, including one with metastatic carcinoma. It is reasonable to use 2 to 3 mm of clear margin between the carcinoma cells and cautery line as a criterion for an adequate excision margin [2]. Those with an "incomplete" or a "doubtfully complete" excision should have further treatment.

Piecemeal excision of a polyp with invasive carcinoma usually is done on large sessile polyps. Even for benign adenomas, piecemeal excision has a local recurrence rate of 19% [24]. This procedure is considered inadequate for an invasive carcinoma. Small sessile polyps, such as those of ≤ 2 cm, can be adequately snared in one piece, particularly using the technique of submucosal injection of saline before the snaring [13].

Depth of Submucosal Infiltration

New to the Western world is using the depth of submucosal invasion as one of the strongest indicators of lymph node metastasis. This evidence has been shown by many series, mainly from Japan. Kikuchi et al. [14] evaluated 182 patients with T1 adenocarcinoma removed via colonoscopy. The lesion was sm1 in 64 patients, sm2 in 82, and sm3 in 36. They showed that among 13 patients who underwent bowel resection and were found to have lymph node metastasis, 9 of the lesions (69%) were sm3 and all were of the sessile type. In addition, five patients had distant metastases (four to the liver, one to the lung), although only two of these patients had positive lymph nodes. All five patients had sm3 and lymphovascular invasion; all five lesions were sessile and were located in the rectum. There was no evidence of lymph node metastasis or local recurrence of sm1 lesions. Lymphovascular invasion alone was not an independent risk factor. It was found with 30% of sm1 lesions, but none showed lymph node metastasis or local recurrence. For sm2 invasion, the risk is significant only in those with flat and depressed-type lesions, most likely because of inadequate local excision.

In a collective series from Japan, among 58 patients with massive invasive carcinoma (sm3) who underwent bowel resection, 13 (22%) had residual carcinoma and 3 (5%) had regional lymph node metastasis [2]. The depth of invasion to sm3 has also been shown to have a high risk of lymphovascular invasion [18]. Therefore, sm1 and sm2 invasions have a low risk of lymph node metastasis. The sm3 and the flat and depressed-type sm2 lesions have a high risk of both local recurrence and lymph node metastasis.

Treatment

Colon and Upper Rectum

Pedunculated lesions with invasive carcinoma to Haggitt levels 1, 2, and 3 (sm1) can be treated with colonoscopic polypectomy provided there are no adverse factors, as described above. Otherwise, a standard bowel resection is indicated [14, 25]. The same approach is applied to pedunculated Haggitt level 4 (sessile sm1 and sm2) lesions. Patients with sm3 lesions or flat and depressed-type Sm2 lesions should undergo bowel resection [14, 25].

Mid Rectum

The T1 carcinoma of the mid rectum (7–10 cm from the anal verge) is a challenge. It is too far up for a per-anal excision. However, it can be removed by colonoscopic excision, a transsacral approach, and transrectal endoscopic microsurgery [26]. The same criteria for the colon and upper rectum can be applied. A radical resection in this area is a low anterior resection including a J-pouch coloanal anastomosis, which has less problem with urgency bowel movements especially during the first year [27, 28].

Low Rectum

The T1 carcinoma of the low rectum (up to 7 cm from the anal verge) is unique in that one can easily see and palpate it. Basically, all T1 lesions that are not larger than 3 cm in diameter can be treated with a full-thickness local excision. Further treatment with an abdominoperineal resection is indicated for lesions with adverse factors and sm3 lesions [29]. In most cases, a low anterior resection (LAR) even with coloanal anastomosis is impossible after a wide full-thickness local excision at this level. Although there have been no controlled studies to evaluate the postoperative chemoradiation in T1 lesions with adverse factors, the adjuvant chemoradiation for T2 lesions after local excision showed good benefit [29–31]. It is reasonable to use postoperative chemoradiation for T1 lesions with adverse factors as an alternative to abdominoperineal resection (APR).

Conclusions

Most T1 lesions without adverse factors can be locally excised, as the risk of local recurrence and lymph node metastasis is low. A T1 lesion with adverse factors, including sm3, has at significantly high risk of local recurrence and lymph node metastasis. Further treatment is indicated. The golden opportunity to cure these patients is *now*, not later. The series from Baron et al. [32] showed that an immediate LAR/APR after initial local excision for lesions with adverse pathologic features has a disease-free 5-year survival rate of 94.1% compared with 55.5% ($p < 0.05$) for those who undergo LAR/APR after local recurrence or lymph node metastasis has occurred.

Résumé

Un cancer du côlon au début est classé T1NxMx selon la classification TNM. La plupart de ces cancers peuvent être traités par un geste local, comme par exemple, une polypectomie colonoscopique ou une excision locale par voie basse. Cependant,

s'il existe des facteurs de risque de mauvais pronostic, comme un cancer peu différencié, un envahissement des ganglions et des vaisseaux lymphatiques, ou une résection incomplète, il faut procéder à une résection radicale, sauf contraindication chirurgicale. Pour les cancers du bas rectum, il faut envisager une chimioradiothérapie. Récemment on a développé une nouvelle classification dans laquelle Sm1 signifie l'invasion du tiers supérieur (superficiel) de la sous-muqueuse, Sm2, l'invasion du tiers moyen, et Sm3 l'invasion du tiers inférieur (profond). Les lésions des classes Sm1 et Sm2 ont un potentiel réduit de récidive locale et de métastases ganglionnaires : une excision locale est suffisante. Les lésions Sm3, Sm2 «plate» et «déprimées» sont à haut risque de récidive et de métastases ganglionnaire : un traitement complémentaire est indiqué.

Resumen

El carcinoma colorrectal precoz se define, siguiendo la clasificación TNM, como un estadio T1NxMx. Muchos de los carcinomas precoces de colon y recto pueden tratarse, adecuadamente, con una excisión local mediante una polipectomía colonoscópica o una excisión "per anal". Sin embargo, cuando existen factores de riesgo: carcinomas poco diferenciados, invasión linfo-vascular o excisión incompleta, la resección quirúrgica radical constituye el tratamiento de elección, siempre que no exista contraindicación operatoria alguna. En el cáncer rectal bajo puede estar indicada la quimio y radioterapia adyuvante. Recientemente, se ha propuesto una nueva clasificación de estos cánceres precoces. Así, Sm1 indica que la neoplasia sólo invade el tercio superior de la submucosa; en el SM2 la invasión alcanza al tercio medio y en el SM3 al tercio inferior. Lesiones Sm1 y SM2 rara vez recidivan localmente o metastatizan en los ganglios lifáticos; la excisión local constituye la técnica quirúrgica de elección. Lesiones SM3 y SM2 de tipo plano o deprimido, presentan un gran riesgo, por lo que a la recidiva local y metastatización ganglionar se refiere; la excisión local es insuficiente.

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