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Patients with longstanding ulcerative colitis (UC) and Crohn's disease have an increased risk of developing colorectal cancer. Dysplasia can be defined as neoplastic intraepithelial change, paralleling the location of neoplasia, arising from chronic inflammation, divided in different grades from low to high grade. Different types of dysplasia have been described in UC such as "flat dysplasia", DALM or ALM. The management of dysplasia and cancer associated with UC has been strongly influenced by the considerable progress in the surgical treatment of the disease that has taken place in the last decades. The presence of dysplasia modifies the surgical attitude in sphincter-saving procedures such as ileorectal and ileoanal anastomosis where colonic mucosa is left in situ. With the stapled-anastomosis few centimeters of colonic mucosa (1-2 cm) are left in site below ileo-anal anastomosis with a risk of malignant degeneration. The hand-sewn IPAA with mucosectomy reduces the risk of retained colonic mucosa below the anastomosis, but does not allow complete removal of columnar epithelium with its potential evolution to a malignant state. Conclusions: in case of preoperative diagnosis of dysplasia we strongly recommend an oncologic resection of the specimen with TME, ligation at the origin of all the vascular pedicles and a extended lymphadenectomy.

KEY WORDS: Anastomosis, Colonoscopy surveillance, Colorectal cancer, Dysplasia, Ileal-anal pouch restorative proctocolectomy, Ulcerative colitis.

Patients with longstanding ulcerative colitis (UC) and Crohn's disease have an increased risk of developing colorectal cancer. The development of colorectal cancer in UC is well known and it is due to a chronic inflammation-dysplasia-carcinoma pathway. This risk increases exponentially with the duration of the disease: it could be considered 2.5% at 20 years, 7.6% at 30 years and 10.8% at 40 years [1]. If colorectal cancer has developed in patients with IBD, the mortality rate is higher than in patients with sporadic colorectal cancer.

Dysplasia can be defined as neoplastic intraepithelial change, paralleling the location of neoplasia, arising from chronic inflammation, divided in different grades from low to high grade [2]. Different types of dysplasia have been described in UC such as "flat dysplasia", DALM or ALM (as described elsewhere in this review). The term of DALM (*dysplasia-associated lesional mass*) has been adopted in order to describe the group of "endoscopically visible" lesions. It is a heterogeneous group of lesions that may appear as plaque–like, mass, stricture, sessile or peduncolate morphologies that have an associated flat dysplasia in the surrounding mucosa [3]. ALM (*adenoma-like mass*) is described as an adenoma like dysplastic lesion that could be either within or out-side a colitis zone, in the absence of adjacent flat dysplasia [4].

The management of dysplasia and cancer associated with UC has been strongly influenced by the considerable progress in the surgical treatment of the disease that has taken place in the last decades. In patients with longstanding disease colonoscopy is recommended for dysplasia survey. The American Society of Gastrointestinal

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Endoscopy guidelines advocate annual surveillance colonoscopy beginning eight years since disease onset.
There are two main problems which determine the operative strategy in the presence of dysplasia in UC:
– is the presence of dysplasia an absolute indication for surgery?
– should the dysplasia modify the surgical strategy and technique?

Dysplasia and indication for surgery

The term dysplasia is a complicated concept and not always accepted in the same way. In fact it has been calculated that, even among expert pathologists agreement could reach only 42% to 65%. in the evaluation of dysplasia. Different studies have shown that in clinical practice, the concept of dysplasia is not fully understood, therefore the guidelines for dysplasia in IBD are not always followed. Data obtained by a gastroenterologist interview, conducted in USA in 1995 and in New Zealand in 2004, have underlined as only 19-20% of physician correctly identify the definition of dysplasia [5]. Dysplasia associated with UC is microscopically classified as either low or high grade depending upon the degree of cytological and architectural disturbance. In patients with IBD dysplasia is often presented in flat or depressed lesions so surveillance colonoscopies should be performed in combination with an extensive biopsy protocol. The management of the different forms of dysplasia varies from no management, to intensifying the screening program, to immediate colectomy [6].
High grade dysplasia in flat mucosa or DALM, confirmed by a second experienced pathologist, is currently an indication for proctocolectomy due to the high risk (>40%) of synchronous colon cancer localized in the DALM or remote to the focal lesion [7]. (i.e. Fig. 1 and Fig. 2) There is no consensus in cases of unifocal or multifocal low grade dysplasia in flat mucosa. One problem is that biopsies taken from regenerative mucosa following an exacerbation of UC may be misunderstood for low grade dysplasia. However some studies have demonstrated a 20% risk of occult malignancy in case of low grade dysplasia [6]. Some Authors suggest a conservative approach which consists of intensified surveillance with colonoscopy at 6-month intervals even in cases of multifocal flat low grade dysplasia [8]. According to most Authors, including ourselves, the presence of dysplasia in a single colonscopic biopsy, diagnosed by a skillful pathology, is nearly always an indication for surgical intervention. Emerging data would suggest that ALM can be removed endoscopically with overall colorectal cancer incidence rate comparable to the non-colitic sporadic population. Endoscopist must provide multiple biopsy specimens from the adjacent mucosa to ensure that local flat dysplasia does not exist. A polypectomy of these lesions also requires frequent repeated endoscopic surveillance. A failure to follow up can have serious consequences [9-10].

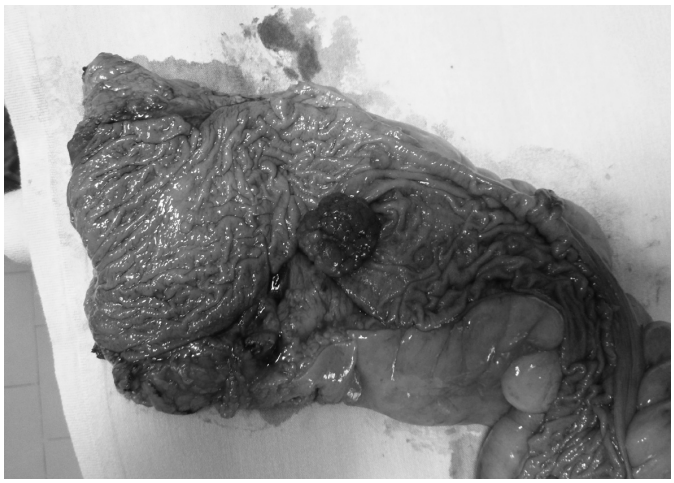

Fig. 2: Colon resected for adenocarcinoma in UC concomitant with multiple DALM.

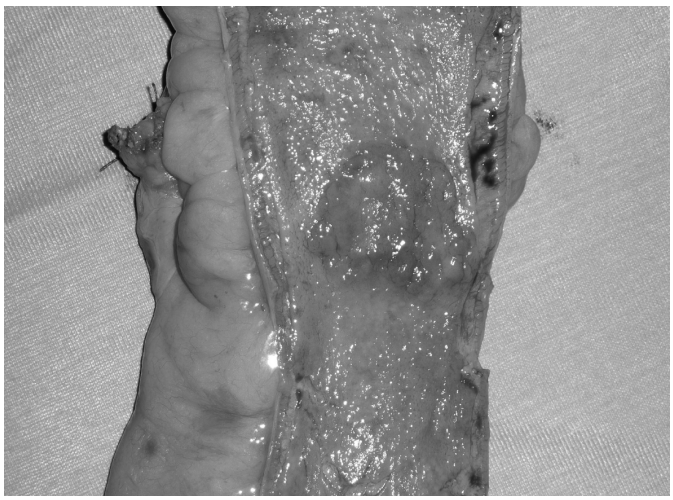

Fig. 1: Specimen of a resected colon for DALM in UC. Definitive pathologic examination gave evidence to an invasive adenocarcinoma associated with foci of mild to severe dysplasia.

Dysplasia and surgical strategies

Different surgical strategies are commonly applied for the definitive treatment of UC patients. Proctocolectomy and Brooke ileostomy removes all diseased mucosa at the expense of a permanent stoma. This option could be considered in patients with poor sphincter function or for patients who do not wish to consider a pouch. Subtotal colectomy and ileorectal anastomosis (IRA) is a "compromise procedure" in which diseased rectum is retained. Finally ileal pouch-anal anastomosis (IPAA) has become the gold standard of care for patients with UC who require surgery.

The presence of dysplasia modifies the surgical attitude towards sphinter-saving procedures such as ileorectal and ileoanal anastomosis where colonic mucosa is left in situ. In patients already operated on who have dysplasia in the colonic specimen, a surveillance program should be considered even for few centimeters of residual glandular epithelium such as in IPAA. The degree of surveillance will be established according to the length of colonic mucosa that has been left. For this reason, while patients previously submitted to IRA should undergo frequent and careful surveillance, theoretically a less strict surveillance is needed for patients with IPAA.

The presence of dysplasia or potentially curable cancer either within the colon or high in the rectum does not preclude IPAA [11]. This procedure, developed by Parks and Nicholls [12] during the 70's, has been modified during years. Initially mucosectomy, followed by hand-sewn anastomosis, was started about 1 cm above the dentate line in order to preserve normal anal sensation. Later the introduction of circular staplers with detachable heads made the technique of IPAA simpler and with a low complication rate. The anastomosis can be performed at about 1,5 to 2,5 cm from the dentate line; stapled-anastomosis performed lower than this measure leads to the risk of internal sphincter damage.

In a relatively short period of time this technique had become the preferred surgical option for treatment of UC. The advent of staplers greatly simplified IPAA surgery but also introduced a complex issue: with the stapled-anastomosis few centimeters of colonic mucosa (1-2 cm) are left in site below ileo-anal anastomosis with a risk of malignant degeneration.

The real risk of developing dysplasia in the anal transition zone (ATZ) after stapled IPAA is not known. There is a significantly higher probability of developing dysplasia in the ATZ of those patients where dysplasia or cancer had previously been found at colectomy.

The hand-sewn IPAA with mucosectomy reduces the risk of retained colonic mucosa below the anastomosis, but does not allow complete removal of columnar epithelium with its potential evolution to a malignant state. Only 13 adenocarcinoma after restorative proctocolectomy have been reported in the literature; 4 cases after stapled procedures and 6 in patients who underwent hand-sewn anastomosis (no anastomosis' informations are avaible in the remaining 3 cases) [13]. These data confirm that the risk of malignancy after ileoanal anastomosis with mucosectomy, although small, is real despite the surgeon taking care with this particular step of the procedure. Careful surveillance is needed in patients with surgical treatment for long-term ulcerative colitis or dysplasia [14].

After stapled IPAA the risk of developing dysplasia is low and it is technically possible to transform a stapled into a hand-sewn IPAA with mucosectomy. Dysplasia in the ATZ in stapled procedures is significantly linked to the presence of dysplasia or cancer in the rest of the colon. In case of preoperative diagnosis of dysplasia or evidence of dysplasia in the specimen at the time of subtotal colectomy, we strongly recommend total proctocolectomy with mucosectomy starting from the dentate line and hand-sewn IPAA [15-16].

However, today, the oncologic risk of stapled anastomosis vs mucosectomy with hand-sewn anastomosis is debate. A retrospective analysis of the clinical database of Mount Sinai Hospital of Toronto demostrates that stapled ileal anal anstomosis does not appear to be inferior to mucosectomy and handsewn anastomosis in oncologic outcome and it could be appropriate in patients with UC associated with coexisting dysplasia or cancer [17]. Nevertheless, even if most cases of adenocarcinoma below pouch-anal anastomosis have been described in hand-sewn anastomoses, our experience leads to the conclusion of performing mucosectomy and hand-sewn anastomosis in patients with all grades of dysplasia.

Differences in surgical technique

There are only two technical differences in patients with dysplasia complicating UC in comparison with uncomplicated UC and they concern the proctectomy and mesocolon excision for extended lymphadenectomy [18].

Proctectomy. Some Authors have emphasized the importance in benign disease of carrying out the proctectomy within the mesorectum to reduce the incidence of urinary and sexual dysfunction. Most surgeons, including ourselves, do not currently agree with this attitude. In fact, this goal could also be reached performing the proctectomy along the presacral avascular plain. However, both these techniques in expert hands bear the same low morbidity rate. The dissection along the parietal pelvic fascia has other advantages: it can also be used in malignant disease because it allows Total Mesorectal Excision (TME) [19], thus guaranteing the oncologically correct excision of the rectum [20].

Mesocolon excision. This is the major difference with regard to technique in case of colitis associated with dysplasia-carcinoma. In fact, the colectomy must be performed according to the principles of segmental colonic resection for malignant disease. In this view, the ligation at the origin of all the vascular pedicles and a radical lymphadenectomy should be performed [21].

Conclusions

The diagnosis of dysplasia made by an expert pathologist, also in case of low grade dysplasia, could be considered an indication to surgery.

In case of preoperative diagnosis of dysplasia we strongly recommend an oncologic resection of the specimen with TME, ligation at the origin of all the vascular pedicles and a extended lymphadenectomy.

Finally, even if the role of hand-sewn anastomosis in case

of colonic dysplasia is still debated, we strongly suggest to perform this procedure in presence of any type of dysplasia.

Riassunto

I pazienti affetti da lungo tempo da colite ulcerativa (UC) e malattia di Crohn presentano un aumentato rischio di andare incontro ad un cancro del retto. La displasia può essere definita come una alterazione neoplastica intraepiteliale, in parallelo con la localizzazione del tumore, che si origina da un'infiammazione cronica suddivisa in gradi differenti, che vanno dal basso all'elevato.
Nella colite ulcerativa sono stati descritti diversi tipi di displasia, come la "displasia piatta", DALM (*dysplasia-associated lesional mass)* o ALM. Il trattamento della displasia e del cancro associato con la UC è stato profondamente influenzato dal considerevole progresso nel trattamento chirurgico della malattia che è andato realizzandosi nell'ultima decade. La presenza della displasia modifica la tendenza della chirurgia verso le procedure intese a risparmiare lo sfintere anale, come le anastomosi ileo-rettali ed ileo-anali nelle quali della mucosa colica viene lasciata in sito. Con le anastomosi meccaniche pochi centimetri di mucosa colica (1-2 cm) rimangono al di sotto dell'anastomosi ileo-anale con il rischio di degenerazione neoplastica. Con l'anastomosi tra pouch ileale ed ano realizzata manualmente, associata a mucosectomia, si riduce il rischio rappresentato da un residuo di mucosa colica al di sotto dell'anastomosi, ma non consente l'asportazione completa dell'epitelio colonnare con la sua potenziale evoluzione verso una condizione di malignità.
In conclusione, in caso di diagnosi preoperatoria di displasia noi raccomandiamo con decisione una resezione di tipo oncologico del retto, con l'escissione totale del mesoretto, legatura all'origine di tutti i peduncoli vascolari ed una linfoadenectomia allargata

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