Dysplasia in Chronic Ulcerative Colitis; more problems and few solutions

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Dysplasia in ulcerative colitis was defined as an unequivocal neoplastic change that is intraepithelial and within the confines of the glandular basement membrane. Although that definition has stood the test of time and the classification is still the golden standard, the recommendations of treatment and follow up has significantly debated and changed.

The purpose of this lecture is to outline the difficulties and controversies associated with dysplasia.

Key words: dysplasia, ulcerative colitis

INTRODUCTION

Dysplasia in ulcerative colitis was defined as an unequivocal neoplastic change that is intraepithelial and within the confines of the glandular basement membrane. Although that definition has stood the test of time and the classification is still the golden standard, the recommendations of treatment and follow up has significantly debated and changed.

The purpose of this lecture is to outline the difficulties and controversies associated with dysplasia.

The association of ulcerative colitis, dysplasia and carcinoma has been described in four different stages. The first stage was the paper associating colonic carcinoma with ulcerative colitis, was published by Crohn and Rosenberg in 1925. The second phase is the paper of Warren and Sommers who were the first to suggest that ulcerative colitis associated dysplasia was a precursor of cancer in patients with ulcerative colitis. The third phase is the publication from Morson and Pang where they have reported the coexistence of cancer colectomy specimens and five out of nine cases of ulcerative colitis who had high grade dysplasia diagnosed pre-operatively by rectal biopsies. The fourth phase was the report by Blackstone et al describing DALM and suggesting radical treatment.

All the above suggest that dysplasia is a precursor but can also be a marker for co-existence colorectal cancer in areas away from the tumour.

CONTROVERSIES AND PROBLEMS

1. Incidence versus prevalence

The prevalence of dysplasia suggest the diagnosis at the initial endoscopy which could be present for an undetermined period of time and is likely to be advancing while the incidence of dysplasia means dysplasias which are detected after the patient has undergone a surveillance. Until authors start differentiating between incidents and prevalence, it will be very difficult to have a clear global picture about these elements as in most studies if not all the two elements are grouped in one.

2. The second major problem is the number of biopsies required. Ruben et al. have shown to have 90% confidence of diagnosing dysplasia there is a need of at least 33 biopsies and for 95% of not missing dysplasia there is a need of 64 biopsies. In most departments this practice is not used, as it requires huge manpower in pathology. This means that there will be a significant number of patients that will be missed out using the routine traditional random biopsies. Fortunately however, there is tremendous advancement in visualising the colon like chromo and magnified colonoscopies.

These new techniques have shown a significant improvement in detecting dysplasia than in comparative traditional techniques and also there are fewer biopsies needed.

3. Once the biopsy is taken the problem is the significant inter and intra-observer variation. This variation is to such an extent that it was recommended to make such a diagnosis of dysplasia there is a need for the biopsy to be seen by two different people, one of them should have a special interest in gastrointestinal pathology. The main problem still lies between differentiation of low grade dysplasia from indeterminate dysplasia rather than high
grade dysplasia in which there is a much better concordance. This however may minimise the errors but will not totally eliminate having negative colectomies for patients with particular low grade dysplasias. The other problem is the differentiation between understanding what the term "indefinite for dysplasia" means. This term is usually given to the following circumstances:

The specimen is inadequate in size or orientation.

When there is inflammation. Inflammatory epithelial changes can mimic dysplasia. Furthermore, certain epithelial changes can be seen after intravenous cyclosporin in patients with ulcerative colitis thus complicating the picture even further.

We have seen in our referral practice that less experienced pathologists tend to use the term "indefinite for dysplasia" more than experienced pathologists.

4. The fourth difficulty of controversy in dysplasia is the classification and the recommendation for follow ups/treatment. The initial Riddell classification has produced a recommendation, which has somehow changed, we would like to propose a modified classification and follow up.

a) Negative for dysplasia.
   Discharge.

b) Indefinite for dysplasia.
   If this is due to inflammation, re-treat the colitis for the inflammation to subside and target biopsies. If there is still a nuclear abnormality then this warrants changing the diagnosis into flat low-grade dysplasia.

c) Flat low-grade dysplasia.
   The literature is divided between the majority who suggest that there is substantial risk of progression of these lesions into advanced disease like high-grade dysplasia, DALM or invasive cancer and therefore the proposed treatment is proctocolectomy. There is however the other group who quite legitimately feel that this is an overtreatment in many patients and hence the negative proctocolectomies after such operations. Our feeling is that these cases should be discussed in the MDT and a combined decision should be taken in which patients would be informed about the possibility/probability of negative colectomy versus advanced disease, morbidity and complications associated with surgical treatment.

d) Flat high-grade dysplasia.
   There is no controversy about this disease due to the fact that there is significant risk associated with or progressing into cancer that the best treatment is total proctocolectomy. There is currently an opinion that even for flat high-grade dysplasia local/segmental/limited operation is suggested.

e) DALM (Dysplasia Associated Lesion/Mass).
   It has been suggested by most, not all authors, that there is a high risk of progressing into cancer in patients with DALM and therefore the treatment is proctocolectomy.

f) ALM (Adenoma Like Mass).
   Adenoma-like mass is a pedunculated tumour that is indistinguishable from an adenoma. Although classically and traditionally this has been grouped with DALM, there are enough reasons for separating it. There is recent evidence to suggest that if ALM is present in an area of colitis there is a significant chance of progressing to advanced disease and therefore radical surgery, if on the other hand ALM is situated outside the colitic mucosa then the treatment is a polypectomy as suggested by Torre [12]. The difficulty is to sometimes to differentiate ALM from a sporadic adenoma. It is suggested that histologically if there is no flat dysplasia in the adjacent surrounding tissue and if there is no regular typical or atypical dysplasia in the pedicle then this is more likely to be a sporadic adenoma rather than ALM. It is interesting to see that even the ALM in an area of colitis has been treated like a normal polyp by some.

5. The final area of difficulty is the efficacy and type of surveillance needed. Since the paper of Morson and Pang there was a dominant school of thought that to lower the incidence and prevalence of cancer in patients with ulcerative colitis is through surveillance. Subsequent literature however showed that surveillance is less effective in colon cancer and indeed to save one life you need to colonoscopy anything between 690 – 1000 patients and therefore the group who are pro-surveillance are outnumbered by the group who are a larger group like the American Gastrological Association who stated that surveillance for dysplasia and patients with ulcerative colitis is not efficient.

SUMMARY

DISPLAZIJA KOD HRONIČNOG ULCEROZNOG KOLITISA, JOŠ PROBLEMA I NEKOLIKO REŠENJA

REFERENCES


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