RESEARCH

The endoscopically normal colon: when is mapping biopsy histopathologically justifiable?

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Abstract

Objective Mapping biopsy of endoscopically normal colon is a contentious area and generates considerable work for histopathology services. Managing demand for pathological testing is a current healthcare priority. In this retrospective audit, the authors aimed to establish diagnostic yield of mapping biopsy in this specific subgroup and identify situations where practice could be safely streamlined.

Design Cases were retrieved over a 10-month period. Histopathology results were correlated with relevant endoscopy reports. The data were anonymised and analysed.

Setting Department of Cellular Pathology, Southampton General Hospital, UK.

Results 717 cases were retrieved. 308 (43%) cases were reported as endoscopically normal. 278 (90%) cases with endoscopically normal/near normal mucosa showed normal/near normal histology. 30/308 (9.7%) endoscopically normal cases showed pathological abnormalities. 9/308 (2.9%) cases of microscopic colitis were detected. Of the 30 cases with pathological abnormalities, 20 (66.7%) presented with change in bowel habit and 6 (20%) had a pre-existing diagnosis of inflammatory bowel disease.

Conclusions Pathological abnormalities in endoscopically normal colon are found most frequently in those who present with change in bowel habit or a known history of inflammatory bowel disease. The authors support biopsy in these individuals and believe that mapping biopsy of endoscopically normal colon in patients referred for other reasons (eg, bright red rectal bleeding or iron deficiency anaemia) should not be performed routinely as diagnostic yields are very low. Guidelines on appropriate use of mapping biopsy in this setting are limited. Streamlining patients based on reason for referral or presenting symptoms may be a useful step towards more effective management of histopathological demand.

Introduction

Endoscopic colonic mapping biopsies are widely used as a diagnostic tool in the investigation of inflammatory bowel pathology and represent a significant proportion of the workload of any gastrointestinal histopathology service. Mapping biopsy of the colon involves a series of multiple mucosal biopsies taken sequentially from proximal to distal. In a full colonoscopy this may include biopsies from terminal ileum, caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid and rectum. In sigmoidoscopy, the biopsies are limited to the left side of the colon. The role of biopsy in the endoscopically normal colorectum is an area of contention.[1–3] Although it is firmly established that certain pathology, for example, microscopic colitis (lymphocytic colitis and collagenous colitis)[4 5] and Crohn's disease[6–8] may occur in endoscopically normal mucosa, the reported rates of histological diagnoses made from seemingly normal mucosa vary widely, between 3% and 32.1% in previously published studies.[1 6 9–16]

Exclusion of microscopic colitis is a common reason for mapping biopsies to be taken during an endoscopically normal sigmoidoscopy or colonoscopy. The Royal College of Pathologists commented in their document 'Histopathology and cytopathology of limited or no clinical value' that endoscopic biopsy of the normal colon should only be performed in patients in the correct clinical setting with a history of persistent watery diarrhoea without blood.[17] The British Society of Gastroenterology in association with the Joint Advisory Group in Gastrointestinal Endoscopy state in their document 'Quality and Safety Indicators for Endoscopy' that

biopsies should be performed in 100% of individuals with persistent diarrhoea.[18]

Objective

The aim of this study was to audit mapping biopsy practice for normal colonoscopies in our hospital and to assess whether biopsy taking was being specifically targeted at those with persistent watery diarrhoea or, as we suspected, mapping biopsies were being submitted to our department from a much wider range of patients. We then wanted to identify groups where biopsy taking could be reliably streamlined, without a detrimental impact on patient care. Furthermore, reducing inappropriate colonic biopsy taking would minimise the additional risks of the procedure for patients.[19]

Design and setting

This retrospective study was carried out in the cellular pathology department at Southampton General Hospital, UK. The department operates a specialist reporting service within a large teaching hospital. Using the laboratory computer database (Masterlab), a search was performed using the specimen entry coding system to retrieve cases logged as 'colonic mapping biopsies' (coded COXM) between January and October 2007. Information reported by the endoscopy unit was correlated with the relevant pathology report for each case. The data were anonymised and entered onto an excel spreadsheet for further analysis. No formal slide review was carried out as the initial histological assessments had all been performed by specialist gastrointestinal pathologists. No alterations to individual case management were made as a result of this work.

Results

Seven hundred and seventeen colonic mapping biopsy cases were retrieved from the Masterlab database. The cases retrieved included mapping biopsy series of the whole colon from terminal ileum to rectum, left-sided mapping biopsy from splenic flexure to rectum and mapping biopsy series taken together with targeted biopsies of specific mucosal lesions. These data are displayed in table 1. During the same time period, 2146 full endoscopies and 927 flexible sigmoidoscopies were recorded as having been performed on the endoscopy department database.

In 308 (43%) of the mapping biopsies assessed, the mucosal surfaces were considered endoscopically normal or near normal (in the near normal cases observations were primarily recorded as normal but additional detail was given, for example, technical difficulties such as tortuous colon or poor bowel preparation, altered anatomy and skin tags).

Of the endoscopically normal/near normal cases, 30/308 (9.7%) showed significant pathological abnormalities. These were reported as three cases of inflammatory bowel disease (type unspecified), two cases of inflammatory bowel disease (ulcerative colitis type), three cases of colitis (aetiology not specified), eight cases of lymphocytic colitis, one case of collagenous colitis, two cases of proctitis (aetiology not specified), seven cases of melanosis coli, one case showing features of atrophy, two cases showing a hyperplastic polyp and one case of drug associated inflammation.

Of the remaining cases, 258/308 (83.8%) showed entirely normal histology and a further 20/308 (6.5%) showed near normal histology (reported as minor changes of uncertain clinical significance). Overall therefore, 278/308 (90.3%) of the cases with endoscopically normal/near normal mucosa showed normal/near normal histological findings.

Of the 30/308 (9.7%) cases where pathological changes were identified, 20/30 (66.7%) patients presented with change in bowel habit, either as an isolated symptom or together with other abdominal symptoms, and 6/30 (20%) were patients with an existing diagnosis of inflammatory bowel disease who were under surveillance (table 1).

Only four of the cases with pathological findings arose from other referral/symptom groups. Cohorts with zero yields were patients presenting solely with bright red rectal bleeding or those under investigation for iron deficiency anaemia alone (table 1).

In our cohort of 308 endoscopically normal/near normal cases (irrespective of presenting symptoms) we reported 9 cases of microscopic colitis (2.9%) consisting of 8 cases of lymphocytic colitis and 1 case of collagenous colitis.

Conclusion

This study confirms the established view that pathological changes can be detected microscopically in the setting of endoscopically normal mucosa. However, the diagnostic yield in our cohort is small (9.7%) and is lower than that reported in much of the literature.[1 5 8–14] The biopsies from 278/308 (90.3%) of the endoscopically normal/near normal cases we studied also showed normal/near normal histological appearances. Of note, 9 cases of microscopic colitis were detected in the group of 308 cases, a rate of 2.9%. A recent study from North America documents the incidence rate of microscopic colitis as 8.6 cases/100,000 person-years (rate of collagenous colitis 5.5/100 000 person-years; rate of lymphocytic colitis 3.1/100 000 person-years).[20] In Marshall's study of 111 patients with chronic diarrhoea and normal colonoscopies there were no definitive cases of either collagenous or lymphocytic colitis; however, 13 (11.7%) cases with some features of lymphocytic colitis and 1 case (0.9%) of possible collagenous colitis were recorded.[1] There is variable guidance on the best approach to examination and sampling in patients with chronic diarrhoea and a normal colonoscopy; however, full colonoscopy shows an increased diagnostic yield over flexible sigmoidoscopy because in some conditions, for example, collagenous colitis, pathological changes may be patchy or confined solely to the proximal colon.[21] Recommendations on the

Table 1 Indications for endoscopy and histopathological findings

Indication for endoscopy	Number of cases out of total	Number of cases with endoscopically normal/near normal mucosa	Number of cases with completely normal histology	Number of cases with near normal histology (minor changes)	Number of cases with abnormal histology	Pathological abnormalities reported in endoscopically normal mucosa
Change in bowel habit	260 (36.3%)	145/260 (55.8%)	129/145 (89%)	3/145 (2%)	13/145 (9%)	Three melanosis coli
						One atrophy
						One drug related inflammation
						One inflammatory bowel disease (type unspecified)
						Five lymphocytic colitis
						One hyperplastic polyp
						One colitis (aetiology not specified)
Change in bowel habit with bright red rectal bleeding	95 (13.2%)	38/95 (40%)	35/38 (92.1%)	0/38 (0%)	3/38 (7.9%)	Two melanosis coli
						One proctitis (aetiology not specified)
Change in bowel habit with other abdominal symptoms	85 (11.9%)	43/85 (50.6%)	31/43 (72.1%)	8/43 (18.6%)	4/43 (9.3%)	One colitis (aetiology not specified)
						Two lymphocytic colitis
						One hyperplastic polyp
Inflammatory bowel disease (existing diagnosis under surveillance)	110 (15.3%)	17/110 (15.5%)	7/17 (41.2%)	4/17 (23.5%)	6/17 (35.3%)	Two inflammatory bowel disease (ulcerative colitis)
						One colitis (aetiology not specified)
						Two inflammatory bowel disease (type unspecified)
						One proctitis (aetiology not specified)
Bright red rectal bleeding only	53 (7.4%)	12/53 (22.6%)	11/12 (91.7%)	1/12 (8.3%)	0/12 (0%)	
Iron deficiency anaemia only	31 (4.3%)	18/31 (58.1%)	18/18 (100%)	0/18 (0%)	0/18 (0%)	
Abdominal pain only	20 (2.8%)	11/20 (55%)	8/11 (72.7%)	2/11 (18.2%)	1/11 (9.1%)	One lymphocytic colitis
Miscellaneous (eg, family history, cancer surveillance, dark red rectal bleeding, polyps)	16 (2.2%)	7/16 (43.8%)	6/7 (85.7%)	0/7 (0%)	0/7 (0%)	One melanosis coli
Ill-defined abnormality	15 (2.1%)	5/15 (33.3%)	5/5 (100%)	0/5 (0%)	0/5 (0%)	
Abdominal pain with other abdominal symptoms	14 (2%)	8/14 (57.1%)	6/8 (75%)	1/8 (12.5%)	1/8 (12.5%)	One collagenous colitis
Abnormal radiology	10 (1.4%)	3/10 (30%)	2/3 (66.7%)	1/3 (33.3%)	1/3 (33.3%)	
Inflammatory bowel disease (new presentation)	4 (0.56%)	0/4 (0%)	0/4 (0%)	0/4 (0%)	0/4 (0%)	
Iron deficiency anaemia with other symptoms	4 (0.56%)	1/4 (25%)	0/1 (0%)	0/1 (0%)	0/1 (0%)	One melanosis coli
Total	717	308/717 (43%)	258/308 (83.8%)	20/308 (6.5%)	30/308 (9.7%)	

numbers of biopsies to be taken are limited, Marshall *et al* suggest six biopsies from throughout the colon in patients with chronic diarrhoea should be sufficient.[1]

Our study has also shown that in certain clearly defined clinical situations, the likelihood of identifying significant pathological changes from a series of mapping biopsies of endoscopically normal colonic mucosa is very low. For example, biopsies taken from patients presenting with isolated bright red rectal bleeding, those being investigated solely for iron deficiency anaemia, those referred for abnormal radiology or ill-defined abnormalities yielded no pathological

abnormalities when the colonoscopic appearances were recorded as normal.

Although there have been other, more clinician orientated, papers calling for greater uniformity in this area of practice,[1 22] pathologists continue to report considerable numbers of histologically normal colonic mapping biopsy series from patients with endoscopically normal colonic mucosa and a wide range of non-specific symptoms (frequently not in keeping with the typical history of microscopic colitis). Preparing and examining these sections is labour intensive and time consuming for both laboratory staff and pathologists. After histopathological processing, a colonic mapping biopsy series of six to eight mucosal samples optimally produces slides with between 36 and 48 individual pieces of tissue for microscopic examination. It is also costly; a colonic mapping biopsy series currently costs approximately £60 for histological processing in our laboratory. This figure does not include the additional costs of equipment to perform the biopsy during the colonoscopy.

In this study, we found that the majority (86.7%) of the biopsies with pathological abnormalities came from patients who presented with change in bowel habit or were from patients with an existing diagnosis of inflammatory bowel disease who were referred as part of colonoscopic surveillance programmes.

If, in this study cohort, we had only received biopsies from patients with normal colonoscopies who had presented with change in bowel habit (as an isolated symptom or in conjunction with other symptoms) or who already had an established diagnosis of inflammatory bowel disease, we would have reduced the biopsy rate from 308 to 243 (a 21% reduction). Even with this reduction in biopsy rate we would still have identified 26/30 (87.7%) of those with pathological abnormalities successfully. Of the four diagnoses which would not have been detected if this streamlining had been implemented, two (50%) were melanosis coli.

This reduction of 21% is considered to be a conservative estimate. We believe that with more stringent criteria for selecting patients referred with change in bowel habit (ie, restricting biopsy to those with persistent watery diarrhoea), biopsy rates could be reduced still further. Currently, no quantitative parameters on the frequency or circumstances of any change in bowel habit are defined in the small amount of existing guidance on biopsy of the endoscopically normal colon,[17 18] despite this being a difficult and often very subjective area on which an accurate clinical history could be obtained. Specific criteria would help to clarify patient symptoms and would further aid endoscopists in more effective selection of the most appropriate patients for biopsy.

In summary, we have confirmed in this study that microscopic pathological abnormalities in biopsies from endoscopically normal colon are detected most frequently in patients presenting with change in bowel habit or those with known inflammatory bowel disease and we support continued biopsy taking in patients carefully selected from this cohort. We believe that more stringent criteria could be applied to select the most appropriate patients presenting with change in bowel habit to try to focus mapping biopsy procedures on those with persistent watery diarrhoea. Mapping biopsy series from endoscopically normal colonic mucosa in patients presenting with other symptoms (eg, bright red rectal bleeding alone and those being investigated solely for iron deficiency anaemia) should not be taken in routine practice as diagnostic yields are extremely low.

At a time when increasing efficiency and managing demand for pathological testing are key priorities in healthcare, streamlining patients for colonic mapping biopsy on the basis of presenting symptoms and clinical history may be a useful first step in the development of straightforward guidelines on when mapping biopsies of the endoscopically normal colon are justifiable. Distribution of simple protocols supported by histopathological data would allow more effective management of demand in this very specific, but clinically contentious, area of endoscopic practice.

What is already know on this subject

- Pathological changes do occur in endoscopically normal colonic mucosa but are uncommon outside the context of persistent watery diarrhoea or an existing history of colonic disease.
- There is only limited clinical guidance available on when biopsy of the endoscopically normal colon is appropriate.
- Pathologists receive significant numbers of histologically normal biopsies from endoscopic studies of the lower gastrointestinal tract.
- Demand management is becoming an increasingly important tool in the restructuring of future pathology services.

What this study adds

- 90% of biopsies from endoscopically normal/near normal mucosa showed normal/near normal histology.
- In the few cases (10%) where pathological changes were found, the majority of patients presented with either change in bowel habit or had an existing diagnosis of colonic disease.
- The two most common pathological diagnoses made in this study of mucosal biopsies from the endoscopically normal colon were melanosis coli and microscopic colitis.

How might it impact on clinical practice in the future

- Concentrating biopsy taking on those with either persistent watery diarrhoea or an existing diagnosis of colonic disease would significantly reduce numbers of histologically normal biopsies taken form this cohort of endoscopy patients.
- Our findings support the need for additional clinical guidelines in this area.

Contributors BG had the idea for this study. VJE retrieved, analysed the data with some early assistance from CV and JH, and drafted the manuscript. SB commented on an early draft. BG and ACB

commented and helped revise later drafts of the manuscript. VJE revised and submitted the paper. Following suggestions for revision, SP and VJE collected further data. VJE analysed this data and made the appropriate changes to the manuscript. BG commented on the new manuscript. VJE resubmitted the paper with minor revisions.

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