Value of Colon Mucosal Biopsy in the Patients with Chronic Diarrhea and Normal Appearing Colonoscopy

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Abstract

Patients who are suffering from chronic diarrhea frequently undergo endoscopic evaluation. There are controversial reports regarding to the role of taking biopsy from the patients with chronic diarrhea and normal colonoscopy. This study was conducted to determine the frequency of clinically important histologic abnormalities in such patients. We selected 150 cases suffering from chronic diarrhea (with more than four weeks of duration).

At least five biopsies from different parts of colorectal mucosa were taken. One pathologist reviewed each biopsy specimen. Finally clinically significant abnormalities were seen in 28 patients (18.6%) composed of 14 collagenous, 11 lymphocytic and 2 eosinophilic colitis and 1 case of melanosisis coli.

Histologic lesions do exist in nearly one fifth of the patients with chronic diarrhea and normal colonoscopy. Since these disorders (lymphocytic, collagenous and eosinophilic colitis) show good response to anti-inflammatory drugs, we suggest performing routine mucosal biopsies in such patients.

Key words: Normal colonoscopy, colon mucosal biopsy

Introduction

Colonoscopic examination combined with colorectal biopsy plays an important role in the diagnosis and treatment of suspected colonic disease. It has been suggested that taking biopsies from normal appearing colorectal mucosa in patients with diarrhea is valuable and can show abnormalities.

Regarding to this, in the recent years more attention has been directed to two conditions that were reported to cause diarrhea when colonoscopic examination is normal: collagenous and lymphocytic colitis, but there are other conditions that can cause chronic diarrhea with normal colonoscopic presentation like laxative abuse, food allergy, irritable bowel syndrome, secretory diarrhea, CMV colitis, ischemic bowel disease, amyloidosis, melanosisis coli, radiation injury, infectious colitis, eosinophilic colitis and NSAID-induced colitis. One of the most important ways to diagnose some of these entities is performing colon mucosal biopsy.

Some reports suggest that colon biopsies should be routinely abstained during endoscopy in patients with normal-appearing mucosa who had chronic diarrhea but the exact frequency of collagenous and lymphocytic colitis and other clinically important entities are unclear. The purpose of this study is to determine the frequency of histologic abnormalities in patients with chronic diarrhea and normal endoscopies to ascertain the
clinical significance of these findings for the therapeutic decision-making.

Materials and Methods:
In this prospective study, 150 patients with chronic diarrhea (more than four weeks of duration) underwent colonoscopy and colorectal mucosal biopsy examination. In all of these cases colonoscopic findings were quite normal and from all of the patients at least five biopsies were taken from proximal and distal parts of the colon (cecum, ascending, transverse, descending colon and rectum).

Diarrhea was defined as frequent or loose stool, generally representing a change in a patient’s usual stool pattern.

Complete clinical data including age, sex, gastrointestinal symptoms and absence of coexistence disease obtained.

All 150 patients were cases of chronic diarrhea, normal colonoscopy and no evidence of any other accompanying diseases. It is worthy to note that none of these 150 patients had history of any medication (cases with the history of any drug consumption were omitted).

Specimens obtained from colon mucosal biopsies of these patients were fixed in 10% buffered formalin and stained with H&E. Masson-trichrome staining was done for all 18 patients who were suspected histologically to have collagenous colitis. Iron staining for the diagnosis of melanosis coli was done for one patient with some macrophages in the lamina propria, which were laden with brown granules (to rule out hemosiderin pigment).

All the biopsies were reviewed by only one pathologist for the establishment of the diagnosis of any pathologic change.

Results
Among the 150 patients having chronic diarrhea and macroscopically normal-appearing mucosa in endoscopic examination, there were 86 females and 64 males, their age ranging from 18 to 76 year (Mean age #38). Table-1 shows the histologic findings of colorectal biopsies in this group of patients.

According to table-1, 28 cases (19.6%) had specific diagnosis (9.3% and 7.3% of the patients, with histologic criteria compatible with collagenous and lymphocytic colitis respectively).

There are some other data regarding age and sex of the studied patients:

- The range of age in lymphocytic colitis in our study was from 18 to 51 years (mean age #37), and female to male ratio of 7/4 (1.7).
- Range of age in collagenous colitis was from 23 to 57 years (mean age #43) and female to male ratio of 10/4 (2.5).
- Two cases classified as eosinophilic colitis including one 64 year old male, and one 26 year old female.
- Only one 54 year old female had melanosis coli.

<p>| Table 1: Histologic Findings in 150 Patients Having Chronic Diarrhea and Normal Mucosa |
|-----------------------------------------------|---------------------|------------------|</p>
<table>
<thead>
<tr>
<th>Histologic Findings</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collagenous colitis</td>
<td>14</td>
<td>9.3%</td>
</tr>
<tr>
<td>Lymphocytic colitis</td>
<td>11</td>
<td>7.3%</td>
</tr>
<tr>
<td>Eosinophilic colitis</td>
<td>2</td>
<td>1.3%</td>
</tr>
<tr>
<td>Melanosis colii</td>
<td>1</td>
<td>0.7%</td>
</tr>
<tr>
<td>Focal active colitis</td>
<td>4</td>
<td>2.7%</td>
</tr>
<tr>
<td>Non-specific colitis</td>
<td>50</td>
<td>33.3%</td>
</tr>
<tr>
<td>Normal mucosa</td>
<td>68</td>
<td>45.5%</td>
</tr>
</tbody>
</table>

Discussion
Patients having chronic diarrhea often present some problems in diagnosis. Colonoscopy with biopsy is useful in the investigation of patients with chronic diarrhea and is a very important part of the examination in most of such patients, providing histologic diagnosis in 31% of patients.5, 10

Some causes of unexplained chronic diarrhea including lymphocytic and collagenous colitis, eosinophilic colitis and melanosis coli can be identified by colonic mucosal biopsy.5, 11 But there are some controversial reports about taking mucosal biopsies when gross colonoscopic findings are normal.2, 3

Some reports have suggested that colorectal biopsies have to be routinely obtained during the endoscopy in patients with normal-appearing mucosa.2 In this regard collagenous and lymphocytic colitis are two entities that have attracted special consideration in the recent years as causes of chronic diarrhea. The colonic mucosa appears macroscopically normal and the diagnosis can be established by biopsy.7, 8

The incidence of collagenous and lymphocytic colitis remains a matter of uncertainty but one
review estimated the former to be the cause of 0.3 to 5% of cases with chronic diarrhea. In one large
review in the literature there were six cases of
collagenous and six lymphocytic colitis in 1469
patients during one year. It is worthy to mention
that these 1469 patients were all colonoscopy cases
presented with all types of symptoms and different
colonoscopic findings. There are other studies
reporting frequency of collagenous colitis as 3/1000
and 22/6491 colon biopsies.8,12

In studies more similar to ours i.e. (chronic
diarrhea and normal colonoscopy) there are some
controversial results. In one study over 111 patients
with chronic diarrhea and normal colonoscopy in a
period of 2.5 years in Missouri there were no
definite cases of collagenous and lymphocytic colitis,
so they concluded that only in patients with
severe or debilitating symptoms biopsy is
mandatory.8

In another study over 89 patients only rectal
biopsies, was performed and no histologically
important finding was identified, so they suggested
that rectal biopsy is unnecessary.9 There are other
reports with the opposite findings as follow:

1) In a study over 100 patients in Missouri, 13
cases of melanosis coli, seven intestinal
spirochetosis and two cases of collagenous
colitis were seen, that means 22% of significant
histologic abnormality.13

2) In another study on 118 patients with chronic
diarrhea and normal colonoscopy 10 cases of
collagenous colitis, nine cases of lymphocytic
colitis and four cases of melanosis coli were
identified, which means 21.1% of significant
histologic abnormality.13

3) In one study on 132 patients with chronic
diarrhea and normal colonoscopy, 7 cases of
collagenous colitis, 21 lymphocytic colitis and 8
melanosis coli were seen which means 27.2% of
significant histologic abnormality.4

In our study on 150 selected patients with chronic
diarrhea and normal colorectal mucosa, there were
18.6% (28 cases) specific diagnosis. It means that
about One-fifth of the patients with chronic diarrhea
and normal colonoscopy show histologic changes
that are useful for treatment and decision-making for
the clinician. It seems that there are some differences
in our country comparing to other parts of the world.
e.g. melanosis coli is less common in Iran but
collagenous and lymphocytic colitis are more common.
According to our study, routine mucosal biopsy of the rectum and colon in patients with
chronic diarrhea and normal colonoscopy is justified
and it is recommended to take multiple biopsies from
different segments of the colon in order to gather
more data.

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