The Evaluation Of Histopathological Findings For Patients With Normal Colonoscopy

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قيميت نتائج الفحص النسجي للمريضي الذين شخوا طبيعيا بناظور القولون

خلاصة البحث: أن ناظور القولون هو أحد الطرق المستخدمة لغرض التشخيص والعلاج وكذلك يستخدم للبحث عن أسباب التغيير في حركة الأمعاء (القفص أو الإسهال) وكذلك الأعراض الأخرى كالآلام البطن والنزف المعوي أو فقدان الوزن وفقر الدم مجهول البداية.

غرض الدراسة: تهدف هذه الدراسة في تقييم أهمية الفحص النسجي لعينات القولون للمرضى الطبيعيين باستخدام ناظور القولون والذين يعانون من أعراض مختلفة كالإسهال المزمن وغيرها.

المرضى وطرق العمل: بين الفترة من الأول من حزيران 2008 ولغاية الأول من حزيران 2009 أجريت الدراسة على 100 مريض الذين أدخلوا إلى مركز الجهاز الهضمي في السليمانية لإجراء ناظور القولون.

إن كل المرضى الذين كانت نتائجهم بالناظر طبيعية قد شملوا بهذه الدراسة والمرين الذين تم اخذ خزعات القولون منهم لغرض فحصها نسبيا.

النتائج: إن معظم المرضى كانوا في العقد الرابع من عمرهم ولم يوجد فارقا كبيرا بين كلا الجنسين.

كذلك وجد أن 40% من المرضى كانت نتائج الفحص النسجي لديهم غير طبيعية بينما كانت النتائج طبيعية في 57%. إن الإسهال المزمن كان أكثر الأعراض السريرية شيوعا حيث شكل نسبة 40% وكانت نتائج الفحص النسجي لهم هو التهاب القولون المجهي (lymphocytic colitis) وبنسبة 60%.
Abstract

Background: Colonoscopy is a method of endoscope that has had a major role in diagnosis and treatment. Colonoscopy also is used to look for causes of unexplained changes in bowel habits (diarrhea or constipation) and to evaluate symptoms like abdominal pain, rectal bleeding, weight loss and unexplained anemia.

Objective: The aim of this study is to evaluate the benefits of histopathological examination of colonic biopsy in patients who had normal colonoscopy result and presented with different symptoms (chronic diarrhea and others).

Method: During a period between 1st of August 2008 to 1st of August 2009, a prospective and retrospective study was done on 100 patients who presented with different symptoms and admitted to gastrointestinal tract center in Al-Sulaimania teaching hospital for colonoscopic examination. All the patients who were found to have a normal colonoscopic result and biopsies were taking from them were included.

Results: Most frequent patients were in the 4th decade of life and nearly equal male to female ratio. It was found that 43% of all patients with normal colonoscopy had abnormal colonic histopathology (microscopic colitis 28%, non specific colitis 15%), and normal histopathology in 57% for different presenting symptoms. Most common presenting symptom was chronic diarrhea found in 40% and their histopathological diagnosis were mainly lymphocytic colitis found in 16 patients (40%).

Conclusion: It was found that there was abnormal colonic histopathology in 31 patients (77.5%) of 40 patients with chronic diarrhea and in 9 patients only (22.5%) were normal. So according to this study, a diagnostic investigation for chronic diarrhea and other symptoms using a flexible colonoscopy is highly efficient and cost effective.

Introduction

Colonoscopy is a method of endoscope that has had a major role in diagnosis and treatment, it allows observation of mucosal surface of large bowel with a biopsy of identified lesions which sent for histopathological examination, also, it is used for therapeutic purposes including snare polypectomy and endoscopic mucosectomy to remove colorectal neoplasm especially adenoma or carcinoma with minimal submucosal invasion. (1, 2)

Colonoscopy also is used to look for causes of unexplained changes in bowel habits (diarrhea, constipation) and to evaluate symptoms like (abdominal pain, rectal bleeding, weight loss and unexplained anemia) and is used as routine scanning test for people of 50 years and older. (3).

The results of colonoscopy are said to be normal if the lining of the colon is a pale reddish-pink, with normal vascularity and there are no abnormal looking masses in its lining. (3)

Microscopic colitis:- is inflammation of the colon in which the patient presented as abdominal pain, watery diarrhea and sometimes rectal bleeding, and the colonoscopy
usually shows no signs of inflammation on the visible surface of the colon (i.e. the result of examination is normal colonoscopic result). Histopathologically there are 2 types of microscopic colitis (collagenous and lymphocytic), both types presented with 3-20 times non bloody-watery bowel movements per day accompanied by cramping abdominal pain.

Patients are almost always more than 30 years old (mean age 55y). Collagenous colitis mainly affects middle and old age women while lymphocytic colitis affects males and females equally. Both diseases are benign in nature, with neither debilitating weight loss nor malignancy as potential outcomes. Some scientists think that collagenous colitis and lymphocytic colitis are the same disease in different stages.

A diagnosis of collagenous colitis or lymphocytic colitis is made after tissue samples taken during a colonoscopy or flexible sigmoidoscopy are examined with a microscope.

Microscopically:- in lymphocytic colitis the surface epithelium is somewhat flattened with loss of mucin and cytoplasmic vacuolization, and intraepithelial lymphocytes more than one lymphocyte per five epithelial cells with neutrophils, eosinophils, and occasional crypt abscesses. Normally the lymphocytes and occasional eosinophils may be present between the surface epithelial cells, which rest on a continuous thin basement membrane; the number of lymphocytes is one lymphocyte per five epithelial cells of colon. However collagenous colitis is moderately active colitis in the mucosa including cryptitis or crypt abscess and lymphocytic infiltration, the characteristic feature is the presence of discontinuous zone or band of collagen beneath the superficial lining cells. The thickness of this band is (12-30 microns). The thickness of the band varies so several tissue samples from different areas of colon may need to be examined.

No definite cause has been found for microscopic colitis although the possible causes are bacteria and their toxins, viruses or non-steroidal anti-inflammatory drugs. Some researchers have suggested that microscopic colitis results from an autoimmune response which means that the body's immune system is destroying cells for no known reason. Lymphocytic colitis shows a strong association with other autoimmune diseases including celiac sprue, thyroiditis, arthritis and autoimmune gastritis. The collagenous colitis may be associated with chronic wasting diseases and chronic autoimmune diseases like chronic hepatitis, rheumatic fever, vasculitis, etc.

The aim of this study is to evaluate the benefits of Histopathological examination of colonic biopsy in patients who had normal colonoscopy result and presented with different symptoms (chronic diarrhea and others).

**Patients and Method**

During a period between 1st of August 2008 to 1st of August 2009, a prospective and retrospective study was done on 100 patients who presented with different symptoms (abdominal pain, chronic diarrhea, and chronic constipation, bleeding per rectum and unexplained anemia and admitted to gastrointestinal tract center in Al-Sulamania teaching hospital for colonoscopic examination. All the patients who were found to have a normal colonoscopic result were included, the examination was done by Olympus type (Evis, LUCERA CLV-260) flexible colonoscopy, biopsies from terminal ileum and cecum were received in separate containers (test tubes) containing 10% neutral buffered formalin and then sent for histopathology lab, a gross description of tissue was performed, including the number of tissue fragments and dimension of each
tissue fragment. Then the specimen was put in filter paper then in cassette, processed in Auto processor (Sakura type) and embedded in paraffin, sectioning in 4 micrometers thickness by microtome (Sakura, Accu-cut), then stained by Haematoxylin and Eosin stain.

**Results**

The number of the patients in this study were 100, 51 females, and 49 males. Their age ranged between 20-70 years with the mean age of 41.4 years and most of them were in forth decade of life as shown in table-1 and Fig.-1.

Figure -2 shows the frequency of main presenting symptoms of (100) patients with normal colonoscopy.

Most of patients presented with chronic diarrhea (40%), followed by chronic constipation (21%), bleeding per rectum (18%), abdominal pain (7%), discomfort in anus (6%), unexplained iron deficiency anemia (4%), and mucous in stool 4% only.

Table -2 shows the histopathological results of (100) patients with normal colonoscopy examination. The results were (57%) normal histopathological findings, (28%) microscopic colitis, (25% lymphocytic, and 3% collagenous), and 15% were non specific colitis.

Table -3, Fig -3: show the histopathological diagnoses in 40 patients with chronic diarrhea in different age groups.

Table -4 and Fig.-4 show the presenting symptoms in patients diagnosed histopathologically as a microscopic colitis.

This means that about 67% of patients with microscopic colitis presented with chronic diarrhea, and about 11% with chronic constipation, 7% with abdominal pain, 7% with pain in anus, 4% with bleeding per rectum, and other 4% with unexplained iron deficiency anemia.

Figure- 5: shows lymphocytic colitis with increase in intraepithelial lymphocytes.

Figure-6 shows collagenous colitis with thick collagenous band below the basal lamina.

**Table- 1: Age and sex distribution of (100) patients with normal Colonoscopy.**

<table>
<thead>
<tr>
<th>Age\y</th>
<th>male</th>
<th>female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-</td>
<td>11-20</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2-</td>
<td>21-30</td>
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<td>3-</td>
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<td>41-50</td>
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<td>11</td>
</tr>
<tr>
<td>5-</td>
<td>51-60</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>6-</td>
<td>61-70</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>51</td>
<td>100</td>
</tr>
</tbody>
</table>
Fig -1: Age and sex distribution of (100) patients with normal colonoscopy:

FIG.-2 Frequency of presenting symptoms of (100) patients with
Table-2 Histopathological diagnoses of 100 patients in relation to sex.

<table>
<thead>
<tr>
<th>Histopathology findings</th>
<th>Female no</th>
<th>Male no.</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Normal results</td>
<td>30</td>
<td>27</td>
<td>57%</td>
</tr>
<tr>
<td>2 Lymphocytic colitis</td>
<td>10</td>
<td>15</td>
<td>25%</td>
</tr>
<tr>
<td>3 Collagenous colitis</td>
<td>3</td>
<td>0</td>
<td>3%</td>
</tr>
<tr>
<td>4 Nonspecific colitis</td>
<td>8</td>
<td>7</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>51</strong></td>
<td><strong>49</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table 3: histopathological diagnoses in 40 patients with chronic diarrhea in different age groups:

<table>
<thead>
<tr>
<th>age in years</th>
<th>Normal</th>
<th>Non specific colitis</th>
<th>lymphocitic colitis</th>
<th>collagenous colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>21-30</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>31-40</td>
<td>3</td>
<td>2</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>41-50</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>1</td>
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<tr>
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<td>61-70</td>
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<tr>
<td><strong>total</strong></td>
<td><strong>9</strong></td>
<td><strong>12</strong></td>
<td><strong>16</strong></td>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>
Fig. 3: histopathological diagnoses in 40 patients with chronic diarrhea

Table -4 presentation of microscopic colitis:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Total</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Chronic diarrhea</td>
<td>19</td>
<td>67.86%</td>
</tr>
<tr>
<td>chronic constipation</td>
<td>3</td>
<td>10.71%</td>
</tr>
<tr>
<td>abdominal pain</td>
<td>2</td>
<td>7.14%</td>
</tr>
<tr>
<td>Pain in anus</td>
<td>2</td>
<td>7.14%</td>
</tr>
<tr>
<td>Bleeding per rectum</td>
<td>1</td>
<td>3.57%</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>1</td>
<td>3.57%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>28</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>
Fig -5 Lymphocytic colitis. H&E x400

Fig -6 Collagenous colitis. H&E x400
Discussion

Most frequent patients in the current study were in the 4th decade of life and nearly equal male to female ratio. Most common presenting symptom was chronic diarrhea found in 40% and their histopathological diagnoses were mainly lymphocytic colitis in 16 patients(40%), followed by non specific colitis (30%), normal histopathology (22.5%), and collagenous colitis(7.5%).

In this study, microscopic colitis (lymphocytic and collagenous) was found in 47.5% of patients with chronic diarrhea and normal colonoscopy, which is near to 42% reported in France by Gineston et.al (11). While higher than those reported by Prior et al in England 4 % (12), Lee et al in Korea 18% (13), and 14% which was found by Marshall et al. (14).

Non specific colitis was diagnosed in 30% in patients with chronic diarrhea which is higher than those reported by Yusoff et al (15), which was reported only in 0.4%.

This great difference can be explained by small size of sample in current study or the histopathologists were over diagnosed the cecal biopsy as a microscopic or non specific colitis especially when there is clinical suspicion of those diseases.

The collagenous colitis which was found in 3% of normal colonoscopy female patients, and all presented with chronic diarrhea, and affect middle age group, which agree with other reported studies (16).

Normal Histopathological results were found in 57% of cases in this study and 22.5% in patients with chronic diarrhea, which is disagree with that mentioned by other study ,which was 84.9% (17).

Conclusion

The colonic biopsy from patients with normal colonoscopic findings especially those with chronic diarrhea are mandatory to reach or exclude diagnosis especially of microscopic colitis.

References
2. Geobesk Ectors N,DHaugenG,Rutgeerts P.Is ileoscopy biopsy worthwhile