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Diagnostic Difficulties in Pouchitis – Experience from a Single Institution

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The aim of the study was to analyze the clinical, endoscopic and histological signs of pouchitis in patients operated on because of ulcerative colitis (UC) and familial adenomatous polyposis (FAP). Between 1984 and 2002, the Department of Surgery carried out 218 restorative proctocolectomies in patients with UC and 120 in FAP patients. The follow-up to assess the intensity of inflammatory changes included 110 patients: 72 UC and 38 FAP. During the endoscopic examination, samples were taken for routine histological examinations. The histological assessment was based on the so-called Moskwitz's Histological System. Acute pouchitis is diagnosed if the score is ≥4, and chronic condition - if the score is ≥4. We used a modified PDAI scale to analyze the symptoms, taking into account the microscopically detectable histological features of chronic pouchitis. The clinical symptoms of pouchitis were revealed in 28 patients (25.5%), endoscopic symptoms in 36 patients (32.7%), and histological parameters in 48 patients (28 - 58.3% with ≥4 score of acute pouchitis and 20 - 41.7% with ≥4 score of chronic pouchitis). The signs of acute and chronic pouchitis were evident in endoscopy and histology, with no clinical features observed in many cases. Patients with symptoms of chronic pouchitis require a continuous follow-up.

Introduction

In 1978, Parks and Nicholls presented the first results achieved after forming the pouch during the so-called "restorative proctocolectomy". In the eighties, subsequent modifications were introduced, among others by Fonkalsrud and Utsunomiya [8, ac. 12]. This relatively new method still requires postoperative follow-up. In patients after restorative proctocolectomies, apart from general surgical complications, we can also observe complications, which are typical for restorative surgery, such as fistulas, abscesses, strictures of the anastomosis and pouchitis [4].

In 1999, Schumpelick argued that after the acceptance of pouches in restorative surgery of the gastrointestinal tract, we should still attempt to answer the question of what pouchitis was and whether the changes observed in the mucosa of the pouch constituted risk factors for a patient [25].

Investigating the changes in the mucosa of the created pouch, we can observe their high dynamics - an atrophy of the villi (the so-called "colonic metaplasia"), inflammatory lesions, changes in the mucin profile and dysplasia [1, 3, 14, 18, 19, 27]. Inflammatory changes are frequently secondary to adaptative changes, and the observed symptoms of chronic inflammation and colonic metaplasia are markers, which allow for the assessment of the inflammation grade [6, 20].

"Pouchitis" is a term introduced in 1977 by N.G. Kock to describe inflammatory changes in the pouch created from the lower part of the ileum [ac. 9]. It is a set of clinical symptoms of a diverse intensity without a standard definition. The patients suffer from high body temperature, stomachaches and watery stools with small amounts of mucus and blood, soiling, cachexia and arthralgia, dermal changes and episcleritis [10, 11, 13, 20, 24]. Symptoms of pouchitis were observed in 10 - 75% of patients who had undergone surgery because of ulcerative colitis, and rarely only in patients operated on because of familial adenomatous polyposis (0 - 6%) [2, 6, 8, 20, 26].

The etiology of pouchitis is still unknown. Currently, we can distinguish the so-called "hypothetical primary factors" and "secondary surgical factors". The hypothetical primary factors of pouchitis are as follows: caecostasis, an increase of pathogenic intestinal flora, abnormal metabolism of bile acids and deficiency of short-chain fatty acids [9, 13, 16, 20]. Also, oxygen free radicals and the overproduction of nitrogen monoxide play an underestimated role in initiation of the inflammation cascade [15]. Other theories should be also mentioned, according to which pouchitis is a re-manifestation of ulcerative colitis, idiopathic indeterminated colitis or Leśniowski-Crohn's colitis [1, 13, 26].

The secondary factors include surgical complications, such as anemia, stricture of the anastomosis, fistulas, elongated loop at the end of the pouch, an inflammatory reaction

TABLE 1
Moskowitz's Classification

Acute pouchitis rate		Chronic pouchitis rate	
acute inflammatory infiltration		chronic inflammatory infiltration	
insignificant	1	insignificant	1
average + abscesses in crypts	2	average	2
significant + abscesses in crypts	3	significant	3
ulceration		colonic metaplasia	
examined area	1	partial	1
25 - 50%	2	almost complete	2
>50%	3	complete	3

of the tissues surrounding the pouch, and a large cuff of the pathologically changed rectal mucosa [4].

The aim of the study was an analysis of clinical, endoscopic and histological symptoms of pouchitis in patients operated on due to ulcerative colitis and familial polyposis (FAP).

Material and Methods

Between 1984 and 2002, in the Department of the General, Gastroenterological and Endocrinological Surgery, 218 restorative proctocolectomies were performed in patients with ulcerative colitis and in 120 individuals with FAP. The follow-up to assess the intensity of inflammatory changes included 110 patients: 72 ulcerative colitis cases and 38 FAP cases. The patients were followed-up within 3 - 84 months (mean, 21.58±18.86) from the closure of the decompressing ileostomy. During the endoscopic examination, samples from two different fragments of pouch lining were taken using tiny forceps, to later undergo a routine histological examination. The specimens were examined by two especially skilled pathologists.

The histological assessment was based on the so-called Moskwitz's Histological System. The histological classification of pouchitis proposed by Moskowitz makes the microscopic assessment of the acute and chronic pouchitis objective by ascribing scores to individual features. The score points are then summarized (Table 1) [24]. Acute pouchitis is diagnosed if the score is ≥4, and chronic if the score is ≥4.

For the complete analysis of the results we used the PDAI scale (Pouchitis Disease Activity Index), which was presented by the Mayo Clinic Team in 1994 [24]. This scale analyzes and summarizes different criteria: clinical, endoscopic and histological. Among clinical symptoms, an important factor is the number of stools exceeding the post-operative average, bleeding, reoccurring tenesmus and stomachaches, as well as body temperature above 37.8˚C. Endoscopic features include contact bleeding, secretion, swelling, erosion, deficiency of the vascular net and granulation tissue. In the original scale, only the features characteristic for acute inflammation are evaluated, but in our material we modified the tool, also assessing the histological signs of chronic inflammation. When all the symptoms were evaluated, the maximal score was 18; pouchitis was diagnosed when the score was ≥7 points.

The statistical analysis was based on the non-parametric Mann-Whitney's test.

Our study received an approval of the Bioethical Commission of Poznań University of Medical Sciences. The investigation was based on routine, follow-up examinations and was not experimental in character.

TABLE 2
Clinical symptoms of pouchitis (in a 3-day follow-up)

Clinical symptoms	Patients
stomach aches	15
≥2 stools per day or more	13
temp. ≥37.8˚C	12
bleeding	6

TABLE 3
Number of clinical symptoms of pouchitis per one patient

Number of clinical features	Patients
4	1
3	4
2	7
1	16

TABLE 4
Endoscopic symptoms of pouchitis in 36 patients

Endoscopic symptoms	Patients
contact bleeding	28
secretion	16
swelling	15
erosion	14
deficiency of the vascular net	8
granulation tissue	8

Results

Clinical symptoms of pouchitis within the maximum of a 3-day follow-up were revealed in 28 patients (25.5%). Table 2 presents the frequency of clinical symptoms occurrence.

TABLE 5

Number of endoscopic symptoms of pouchitis per patient

Numer of endoscopic symptoms	Patients
5	4
4	8
3	3
2	7
1	14

TABLE 6

Pouchitis - cumulative data

	Ulcerative colitis	FAP	Total	%
clinical	20	8	28	25.5
endoscopic	30	6	36	32.7
histologic ≥4	38	10	48	43.6
modified PDAI ≥7	19	2	21	19.1

For the purpose of clinical symptoms assessment, also the number of clinical signs per patient was taken into account (Table 3). Endoscopic symptoms of pouchitis, noted in 36 patients (32.7%), are presented in Table 4. Also in the case of endoscopic symptom assessment, we analyzed the number of endoscopic symptoms being the evidence of pouchitis per one patient. The results of the analysis are presented in Table 5.

Histological indicators of pouchitis were observed in 48 patients, including 28 patients (58.3%) with ≥4 score of acute pouchitis and 20(41.7%) with ≥4 score of chronic pouchitis (Figs. 1 and 2).

The general breakdown of the results is presented in Table 6. The table comprises also the results of the study using the PDAI score as modified by the authors.

When the modified PDAI score was employed, the pouchitis symptoms with the score of ≥7 were detected in 19 patients operated on due to ulcerative colitis and in 2 individuals subjected FAP procedures. There was a substantial difference between the time lapse between the closure of an ileostomy and the pouchitis occurrence - 13.15±5.7 months and 39.8±24.8, respectively, for $p<0.0001$.

Discussion

For objective pouchitis assessment, it is necessary to take into account its clinical, endoscopic and histological features. The most comprehensive assessment of the changes is currently ensured by three scores:

- The pouchitis triad - the Hospital of St. Mark's;
- The Pouchitis Disease Activity Index (PDAI) - the Mayo Clinic;
- The Heidelberg Pouchitis Activity Score (PAS) [5, 6, 24].

The pouchitis rate differs significantly in the clinical, endoscopic and histological assessment. The clinical image of the pouchitis is not equivalent to the endoscopic image and certainly not equivalent to the microscopic one. In the material described by Ettorre, the clinical features in patients who had undergone restorative proctocolectomies due to ulcerative colitis were observed in 28% of the cases, and the histological indicators - in as many as 90% of the cases [2]. The most common clinical features were recurrent stomachache and an increased number of stools, exceeding the post-operational average. Also during endoscopic examinations, contact bleeding was noticed very often.

In our investigations, the symptoms of pouchitis were most often detected histologically, and rather seldom in the macroscopic assessment during endoscopy. The clinical features of pouchitis occurred most rarely. It is disputable whether the occurrence of one or even two clinical symptoms confirms the occurrence of fully symptomatic pouchitis (4.6% - 3 and 4 clinical features, up to 25.5% - each, even single clinical symptom). We should also bear in mind that individual symptoms do not have to denote this particular disease only. It seems that also in the endoscopic image pouchitis is confirmed only if at least 3 symptoms are detected (13.6% in the present study vs. 32.7%).

In spite of these differences in the incidence of individual symptoms, it is worth to cite Simchuk, who claimed that pouchitis does not only manifest itself in the histological, but also clinical symptoms, e.g. an increased number of stools and a change in their consistency, as well as fever [26].

Consecutive authors presented their scores as the systems aiming at maximum objectivization of the observed changes [5, 24]. The above-cited Heuschen claims that the paS score can be characterized by a higher sensitivity and lower specificity than the PDAI. In the multifactor analysis, endoscopic and histological findings exhibited a higher correlation with pouchitis in comparison to the clinical ones [5]. An absence of clinical symptoms does not rule out pouchitis. It has to be bear in mind that the assessment of the clinical changes facilitates the differentiation. Whether to include or exclude clinical symptoms is a subject to be discussed between scientists and practicing doctors.

The authors of papers assessing the risk of pouchitis emphasize the need for long-term follow-up. Some of them refer to the so-called cumulated risk of pouchitis occurrence, which can increase over time, and it is ranging from 8 to 11 years of observation in patients operated on due to ulcerative colitis from 28 to 50% [4, 6, 11, 22]. Increasingly more often attention is paid to chronic pouchitis. In 1995, Veress reported that 37% of patients with symptoms of chronic inflammation were diagnosed with "low grade" dysplasia [28]. It gave rise to questions such as: "Is chronic pouchitis a risk

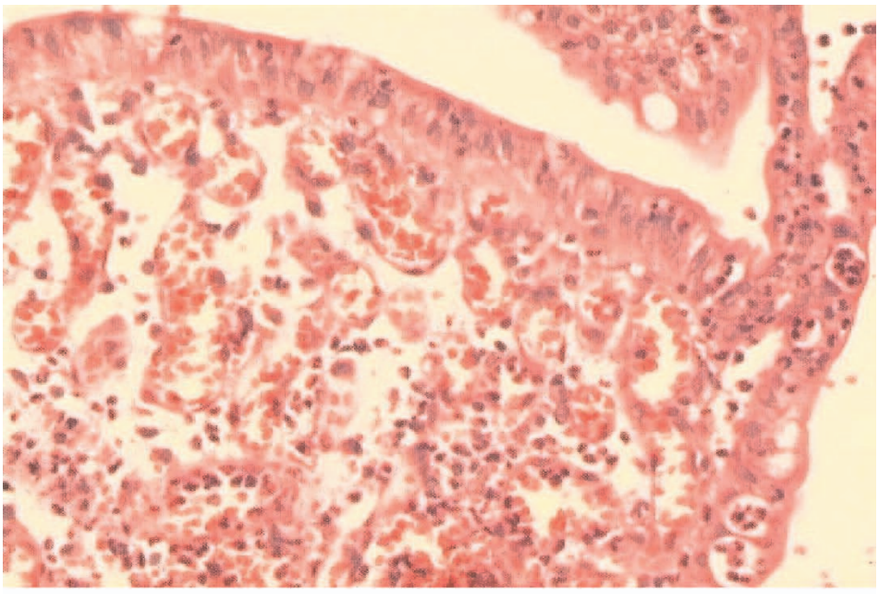

Fig. 1. Small intestine mucosa of the J-pouch. Acute pouchitis. 14 months after proctocolectomy. HE. Magn. 250x.

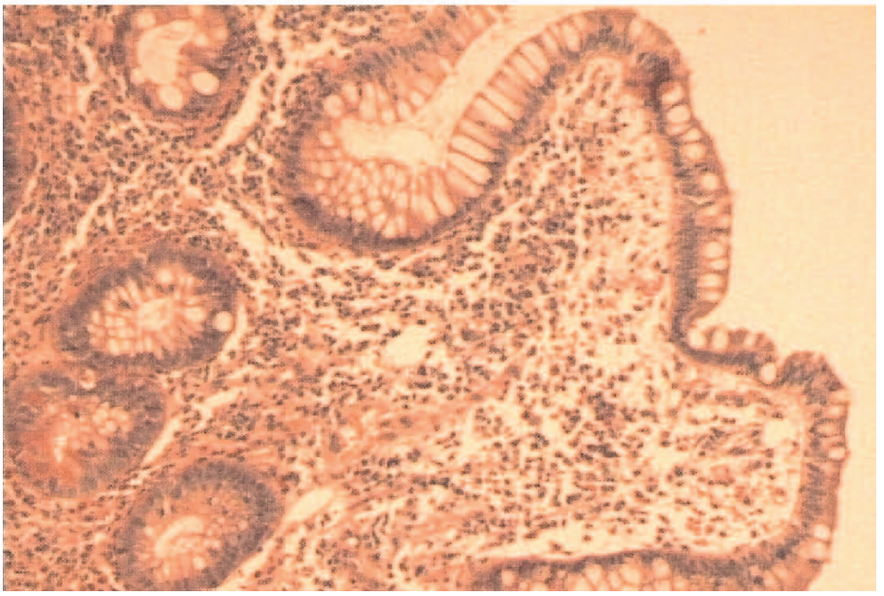

Fig. 2. Small intestine mucosa of the J-pouch. Chronic pouchitis. 24 months after proctocolectomy. HE. Magn. 130x .

factor?" and "Is the hypothesis of pouchitis transforming into dysplasia and subsequently to cancer correct?" These issues confirm the need for continuous endoscopic and histological control, especially in view of the fact that in 2001, Heuschen described an adenocarcinoma, which developed in the pouch 3 years after a restorative proctocolectomy [7]. A probable neoplasia in the pouch should be considered separately from the reports about cancer (adenocarcinoma) in the cuff of the rectal mucosa [21, 23]. This problem became a subject of our interest many years ago; in order to assess inflammatory changes in the pouch, we introduced a modified Mayo Clinic score, by which we were able to evaluate not only the acute pouchitis score, but also the chronic pouchitis score from the Moskowitz's classification. It appeared that the symptoms of chronic histological pouchitis occurred in as many as 41.7% cases vs. 58.3% of cases with the symptoms of acute pouchitis. The patients with low-grade dysplasia are under continuous follow-up.

The review of the literature indicates numerous difficulties in the assessment of treatment efficiency. The difficulties often have their source in different, individual definitions of pouchitis, with various classification of symptoms, a lack of uniform monitoring rules, and first of all in results achieved in small groups of patients presented in individual reports. All these factors in combination clearly indicate the necessity to popularize the best scores, which allow for objectivization of treatment effects.

One of the most significant reports was presented in 2001 by Heuschen and al. [6] The follow-up included the group of 210 patients operated on due to ulcerative colitis and 98 individuals with FAP. The research focused on patients with symptoms of grade II and III pouchitis. The pouchitis symptoms occurred only in two patients with FAP. Also in our study, according to the assessment based on the PDAI score, the symptoms of pouchitis scored as ≥7 occurred in 19 patients operated on due to ulcerative colitis and in two with FAP, with a noticeable difference in the time lapse between the closure of ileostomy and pouchitis development.

It is important always to try to differentiate between primary and secondary pouchitis, as this differentiation determines the decision on the selection of efficient treatment [4, 6]. In case of pharmacological treatment of pouchitis, in 54 - 80% of the patients metronidazole is prescribed and used in a form of intravenous infusion, and also for rinsing of the pouch. Other prescribed antibacterial drugs are ciprofloxacin and amoxicillin. Sometimes such drugs as corticosteroids, infusions of 5-aminosalicylic acid, butyric acid suppositories and glutamines, cyclosporine A, azathioprine, allopurinol and probiotic bacterial preparations are also used [13, 20]. In case of the secondary pouchitis triggered by surgical complications, which in the majority of cases is manifested as a stricture of the anastomosis, mechanical dilation is advised. As it follows from the present study, caecostasis within the created pouch and secondary pouch infection before ileostomy closure are the most common causes of pouchitis. Therefore, it is advisable to introduce preventive treatment, which is lavage of the pouch with saline with metronidazole, starting from the second postoperative day and periodical dilation of the stricture in the pouch that has not yet been connected to the anus.

Regular follow-up visits should take place every 3, 6 and 12 months [6]. An individual decision depends on the clinical presentation and the results of histological tests. However, we have to remember that regular follow-up visits are in fact unrealistic. In the majority of cases patients come to us after they notice some disturbing and persistent ailments. The complaints reported by the patients are a signal for a check-up, during which an endoscopic examination, including specimen collection for histological examination, is carried out.

We use the Moskowitz's score to assess the inflammatory changes; in order to evaluate the colonic metaplasia we employ the score of Laumonier and al., which was presented in our previous reports [17 - 19]. Inflammatory changes are assessed according to the modified PDAI score, taking into consideration histological features of chronic pouchitis. Histological assessment is always conducted by two skilled pathologists. Symptoms of acute and chronic pouchitis may be clearly evident in the endoscopic and histological examination, with no clinical features observed in many cases.

In the histological examination it is indicated to pay attention not only to features of acute, but also of chronic inflammation. It seems that the group of patients with symptoms of chronic inflammation needs to be subjected to constant and regular control.

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