Medicine

DIFFERENTIAL DIAGNOSIS BETWEEN COLONIC CROHN`S DISEASE AND ULCERATIVE PANCOLITIS: ENDOSCOPIC AND HISTOLOGIC CRITERIA

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ABSTRACT
THE PURPOSE OF THIS PAPER IS TO CLARIFY THE PARAMETERS USED FOR A DIFFERENTIAL DIAGNOSIS BETWEEN CROHN`S COLITIS AND ULCERATIVE PANCOLITIS AND TO IDENTIFY THOSE WITH THE HIGHEST DIAGNOSTIC VALUE. THE IMPORTANCE OF THE STUDY WILL BE REFLECTED IN LOWER RATES OF DIAGNOSIS DELAY, LOWER RATE OF LONGTERM COMPLICATIONS AND INTO A BETTER THERAPEUTIC APPROACH.
THIS IS A RETROSPECTIVE STUDY, WHICH WAS PERFORMED ON 54 PATIENTS DIAGNOSED WITH CROHN`S COLITIS OR ULCERATIVE PANCOLITIS, WHO WERE ANALYZED EPIDEMIOLOGICALLY AND PHENOTYPICALLY. THEY WERE DIVIDED IN 2 GROUPS AND COMPARED BASED ON THE ENDOSCOPICAL AND HISTOLOGICAL CHARACTERISTICS.
THE ENDOSCOPIC LESIONS WITH THE HIGHEST DIAGNOSTIC VALUE FOR CROHN`S WERE FOUND TO BE THE LONGITUDINAL AND DEEP ULCERS, AND ALSO, HIGHER SEVERITY OF LESIONS THE ON THE RIGHT COLON. AS FOR ULCERATIVE PANCOLITIS HISTOPATHOLOGICAL CHARACTERISTICS WITH THE HIGHEST DIAGNOSTIC VALUE WERE FOUND TO BE THE ASSIMTERICAL AN DIFFUSE DISTRIBUTION OF ARCHITECTURAL CHANGES, CRIPTITIS AND CRYPTIC ABSCESSES. THE EPITHELIOID GRANULOMA, ONCE CONSIDERED GOLD STANDARD FOR A DIAGNOSIS OF CROHN`S DISEASE IS RARELY ENCOUNTERED ON THE TISSUE SAMPLES FROM COLONIC BIOPSIES. BASAL PLASMOCITOSIS IS PRESENT IN BOTH DISEASES, BEING A MARKER OF CHRONIC COLITIS AND HAVING NO SPECIFICITY FOR CROHN`S OR ULCERATIVE COLITIS.

KEY WORDS: CROHN`S DISEASE, ULCERATIVE PANCOLITIS, CHRONIC INFLAMMATORY COLITIS, DIFFERENTIAL DIAGNOSIS

INTRODUCTION AND AIM OF STUDY

Epidemiology of IBD is changing in Eastern Europe as population is adopting a life style similar to western countries. In Romania diagnosis and therapeutic management of patients with IBD is conducted mainly in referral centers. The national epidemiological studies show a raising

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incidence of IBD, with higher UC incidence[3]. A long diagnostic delay correlates with an increased rate of complications and also, a higher need for IBD-related surgery[4].

Although Crohn`s disease and ulcerative pancolitis have some clear distinctual characteristic, a clear separation may not be possible in 5-15 % of patients with IBD colitis[5]. More than that, 14% of patients first diagnosed with Crohn`s Disease or Ulcerative pancolitis are found to be missclassified in the subsequent years (5,6). Differentiation between these two is important because each of them associates a distinct therapeutic management and prognosis. At the moment, no single gold standard test is available[6].

The differential diagnosis between colonic Crohn`s Disease and ulcerative pancolitis based on endoscopic (macroscopic) and histologic criteria will be discussed in this paper with the purpose of identifying the features with the highest diagnostic value.

METHODS

A total of 54 patients with IBD pancolitis who presented in our clinic between 1.05.2015-1.11.2015 were reviewed from the National Romanian registry IBDPROSPECT. The group was analyzed based on the epidemiological and phenotipical features, severity of disease, mean disease duration, rate of diagnostic change and rate of postsurgical reclassification.

For the second stage of the analysis, we considered two groups according to the established diagnosis at the moment of evaluation: UC (ulcerative pancolitis) and CD (Crohn`s Disease). In each group we studied the endoscopic and histological features. As for endoscopic characteristics, Seven parameters were followed: simmetry of lesions, continuity of mucosal involvement, ulcer`s type (superficial/deep/longitudinal/confluent), hyperemia, edema, mucosal hemorrhage and association with perianal disease. As for the histological charateristics, eight parameters were followed: uniformity of inflammation, distribution of the chronic inflammation (focal/diffuse), archytectural crypt change, basal plasmocitosis, mucin depletion, crypt atrophy, cryptitis, type of granuloma encountered.

Based on the grade of diagnostic "stability" and on the percentage of misdiagnosis we identified some features with better diagnostic value than the others. We also identified some possible error factors in patients whose first diagnosis changed in time.

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RESULTS

Out of the total number of fifty-four patients, at the time of evaluation twenty six of them had an established diagnosis of UC (48.14%) and twenty eight a diagnosis of CD (51.85%) based on the endoscopical findings. The median disease duration was 5,6 years (4,15 y for UC and 7.11y for CD). In the UC group the males formed the majority (70.38%) . In the CD group, the difference between men and women was less significant (42.8 % females vs 57.15 % males). In both groups, most of the patients were found to have 17-40 years at the time of diagnosis (80,7 % in UC and 67.86 % in CD).

As for the histological characteristics we evaluated a number of 42 biopsy specimens , out of which 32 were classified as UC and 10 with UC. A high certainty of the histologic interpretation was found in 66.6 % of patients with UC and in 52.5 % of patients with CD. The remaining (36.36%) were diagnosed as Chronic IBD. In order to obtain a certain diagnosis in these patients combined evaluation according to endoscopical and clinical findings was advised.

We had a total of 9 (16.6 %) new cases (<1 year disease duration, 5 UC+ 4 CD). In the UC group 7.69% of patients had a wrong first diagnosis of CD, and 7.69% whose endoscopic pattern became discontinuous and also the pathological features became focal on treatment. This is frequently a trap in changing the diagnosis, but these changes must always be interpeted in clinical and therapeutic context of each patient. In the CD group the first diagnosis was changed in 5 (17.85%) patients, 3 of them (10,71%) with a first diagnosis of UC and 2 patients (7.14%) with a first diagnosis of indeterminate colitis. The first diagnosis changed in time in 12.96 % of all patients included in the study. Most of the misdiagnosis were established in patients with severe flares (71%).

One patient`s diagnosis of UC changed in CD after proctocolectomy and interpretation of the surgical specimen, based on the presence of transmural chronic inflammation and multiple colonic stenosis. It is important to mention that this patient also had a severe flare at the time of diagnostic endoscopy associating unresponsiveness to corticoids and anti-tnf alfa therapies. Although the postsurgical reclassification of UC into CD described in the literature is not rare, occurring in 3.5%-12% of prospective and retrospective series of procto-colectomized patients[7], we only had one patient in this situation, and this low rate (0.03%) is partially explained by the low rate of proctocolectomy performed in the study group (0.07%).

Beside the classical endoscopic characteristics for CD: assimetrical distribution of lesions which was described in 81% of patients, cobblestoning (52%) and aphtoid lesions (54%), we also observed a higher incidence of deep ulcers (25 % in CD vs 5.3 % in UC, $p<0.05$) , longitudinal and confluent ulcers (17.85% in CD vs 3.84 % in UC, $p<0.05$) and a higher severity of lesions in the right colon (28.5 % in CD vs 7.6 % in UC, $p<0.05$). The association between colonic CD and perianal disease was met in 25 % of cases.

In case of UC, the most often described endoscopical features were: continuous distribution of lesions (84.61%), hyperemia and edema (65.38%), superficial erosions (61.53%), mucosal friability (57,69%) and mucosal bleeding (on touch/spontaneous - 50%). The severity of lesions was more pronounced in the rectum and the left colon (53.84%). Discontinuous involvement of the mucosa was described in 15.38 % of cases, all of them being reported as ulcerative colitis with caecal patch.

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The following microscopic features were more often associated with UC: uniforme distribution of the inflammation (91.6%), diffuse chronic inflammation (83.3%), diffuse distortion of crypt architecture (75%) with crypt branching and atrophy (50 %) , irregular villous architecture (75%) , crypt abscesses (75%), cryptitis (83.3%) and also pronounced mucin depletion (33.33%).

Focal chronic inflammation was described in 80 % of patients diagnosed with CD, irregularly disposure of the inflammatory cells was present in 60% of cases and focal crypt irregularity (but without crypt atrophy) in 80 % of cases. Cryptits and crypt abscesses were also found in CD (40 % for each) but unlike in UC, their distribution was focal.

Epithelioid granuloma is a feature commonly found in CD but it was also described in UC in case of ruptured crypts or mucin extravasates[8]. However, we found no granuloma in the group diagnosed with UC or in the one with CD.

Basal plasmocytosis was found in UC (58.3%) but also in CD (60 %) , so it was not useful for differentiating UC from CD.

When interpreting a biopsy specimen where the granuloma was absent (as it happened in 100% of cases in this study) ,we used a number of 3 other features for establishing the diagnosis of CD (eg.: non-uniformly distribution of the inflammatory cells, focal crypt irregularity or focal inflammation).However, if the granuloma would`ve been present and the infections associated with its formation excluded then only one other feature (focal inflammation/ focal architectural abnormalities) would`ve been needed for establishing the diagnosis of CD.

DISCUSSION

When making an endoscopic differential diagnosis, attention should be given if longitudinal or deep ulcers are found or if the lesions get more severe as we progress into the proximal colon, these findings being highly suggestive of CD. Even if their presence doesn`t exclude UC, their association with the disease is rare.

As for the pathological differential diagnosis, some features are really valuable in diagnosing UC: continous and simmetrical inflammation of the mucosa, diffuse crypt distortion with crypt atrophy, irregular villous surface and mucin depletion. Cryptitis and crypt abscesses are found in both UC and CD, and only their distribution (focal/diffuse) may be important when differentiating these diseases. Basal plasmocytosis is also found with similiar frequency in CD and UC, so its role in the differential diagnosis is limited.

Even if the epithelioid granuloma is almost a hallmark for CD (when other granulomatous diseases or infections are excluded), this is rarely found on biopsy specimen and thus, the diagnosis can`t be conducted based on its presence/absence.

In case of severe flares, the chance of a misdiagnosis may be higher and a reevaluation after proper treatment should be done for diagnosis purposes.

More than that, the differential diagnosis should be made in the early phase of the disease, before any treatment is initiated, as medications change the pattern and make the differentiation difficult, if not impossible; Being aware of the changes in the disease pattern (patchiness, rectal sparing or normal mucosa) associated with medication is important and reduces the chances of a misdiagnosis.

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Despite detailed histologic and endoscopic criteria used to differentiate between pancolonic involvement of CD and UC, an accurate discrimination between these two is not yet optimal among gastroenterologists and pathologists and there is no pathognomonic feature accepted in the literature.

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