Alimentary Tract

The diagnosis of inflammatory bowel disease is often unsupported in clinical practice

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ABSTRACT

Background: The diagnosis of inflammatory bowel disease can be challenging and requires the efforts of a multidisciplinary team. We performed a retrospective analysis with the aim of evaluating the adequacy of the prerequisites for arriving at an accurate histological diagnosis.

Methods: The following parameters were considered as prerequisites for a diagnosis of inflammatory bowel disease: clinical and endoscopic data; proper sampling and handling of biopsies; and elementary microscopic lesions. We collected 345 cases from 13 centres.

Results: The date of onset and treatment were available for 13% and 16% of the cases, respectively. Endoscopic information was accessible for 77% of the cases. Endoscopic mapping was completed in 13% of the cases. In no cases were the biopsies oriented on acetate strips. The diagnosis was conclusive in 47% of the cases. Activity, epithelial disruption and crypt distortion were described in 35% of the reports with a conclusive diagnosis.

Conclusion: Our study showed that the diagnostic prerequisites were widely unfulfilled, although approximately half of the diagnoses were conclusive for inflammatory bowel disease. Thus, in our assessment of clinical practice: (1) clinicians seldom provide suitable clinical and/or endoscopic information for a histological diagnosis and (2) histopathological diagnoses of inflammatory bowel disease are often not supported by morphology.

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1. Introduction

The incidence of inflammatory bowel disease (IBD) is increasing globally [9]. However, a definitive diagnosis of IBD vs non-IBD colitides is not always straightforward. The clinical symptoms and endoscopic patterns can be suggestive of IBD but not pathognomonic for IBD. By analogy, IBD histology shows a spectrum of architectural damage and inflammatory features that are often non-specific and may overlap with the features of the comprehensive group of non-IBD colitides [1–5]. For all of these reasons, the initial diagnostic work-up of a patient with symptoms suspicious for IBD requires the optimal integration of clinical, laboratory, endoscopic and histological data to avoid misdiagnoses and therapeutic pitfalls. International guidelines have therefore stressed that for a definitive diagnosis of IBD the pathologist requires the following: (1) a minimum set of information about the patient’s clinical history and endoscopic pattern and (2) biopsy sampling and handling procedures of adequate quality in both the endoscopy room and histology laboratory [6–11]. Previously, we proposed to adopt the term “inadequate” for cases in which these prerequisites for a histological diagnosis were not fulfilled [12].

This study aimed to estimate the proportion of cases in which the clinical, endoscopic and histological prerequisites for an accurate diagnosis of IBD, as defined by international guidelines [6–11], are met in routine clinical practice at 13 endoscopy centres in the Piedmont region of Italy. Data related to the prerequisites for diagnosis were then compared to the morphological patterns and diagnostic conclusions contained in the histological reports.

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2. Materials and methods

2.1. Study design

A retrospective analysis was conducted with the following criteria: a consecutive series of histological reports concerning endoscopic samples from patients with a clinical suspicion of IBD were selected in 13 qualified gastroenterology centres in the Piedmont region (Italy) between January 2010 and June 2013. The study required the collection of a request form for histological analysis with any supplementary report (if available). The final cohort included 345 cases.

We selected the following clinical and endoscopic parameters, which are indicated by the international guidelines to be essential for a reliable histological diagnosis: information about the reported symptoms, date of onset of clinical signs, recent or ongoing treatments, information about endoscopic pattern, laboratory tests and other instrumental examinations, complete endoscopic sampling (with biopsies from the ileum; ascending, transverse, descending, and sigmoid colon; and rectum) and positioning of biopsies on cellulose acetate filters in the endoscopic room. Then, the availability of the aforementioned parameters in the request form of each patient were recorded.

The other parameters included IBD-related histological lesions (cryptitis, crypt distortion, ulcers and basal plasmacytosis) reported in the histopathological report and the type of histological diagnosis (conclusive or inconclusive for IBD).

2.2. Statistics

A correlation analysis was performed between the clinical and endoscopic prerequisites selected for the study, the histopathological lesions detected by microscopy and the type of diagnostic conclusions reported using \( \chi^2 \) tests. The parameters available in less than 5% of the enrolled patients were excluded from further statistical analysis. All p-values calculated were two-tailed; the alpha level of significance was set at 0.05. Analyses were performed using the SPSS\textsuperscript{\textregistered} 19.0 for Windows package (SPSS Inc., Chicago, IL, USA).

3. Results

Documentation was collected for 345 patients in 13 centres. The number of patients per centre ranged from 12 to 43. The median age of the enrolled patients was 41, and 54.5% were males.

3.1. Endoscopy characteristics

Among the 345 cases, endoscopies were performed for the following reasons: in 197 cases (57.1%) for diagnostic purposes, in 94 cases (27.2%) for follow-up, and in 54 cases (15.7%) the reason for the endoscopy was not defined. The endoscopic pattern was reported to be consistent with ulcerative colitis in 120 (34.8%) cases, Crohn’s disease in 42 (12.2%) cases, IBD not otherwise specified in 125 (36.2%) cases, non-IBD colitis in 22 (6.4%) cases and in 36 (10.4%) cases the endoscopic pattern was not clearly reported.

3.2. Adequacy of the parameters on the request form and diagnostic conclusions

As shown in Table 1, among the clinical and endoscopic information, the endoscopic pattern was available for 77.9% of the request forms, whereas the symptoms, date of onset and treatments were rarely reported. Similarly, data about the laboratory tests and other imaging examinations were only reported on a few request forms. The endoscopic sampling was not adequate in 87% of the cases. Only 45 patients (13%) received a complete sampling (5 sites, including the ileum and rectum). The types of sampling were then further analysed: minimal sampling (1–2 sites) was the most frequently reported procedure (156 cases, 45.2%), whereas extended sampling without the rectum (the ileum and the four sections of the bowel) was reported in 4 cases (1.2%), and extended sampling without the ileum was reported in 51 cases (14.8%). The sampling procedure was limited by technical difficulties in 22 cases (6.4%), was atypical (discontinuous) in 52 cases (15.1%) and was unavailable in 15 cases (4.3%).

In no case were the biopsies oriented on the acetate cellulose filters.

Among the 345 cases, 163 (47.2%) had a conclusive diagnosis [Crohn’s, definite: 16 (4.6%); IBD, definite: 34 (9.9%); UC, definite: 69 (20.6%); IBD and other colitis: 1 (0.3%); longstanding inactive IBD: 17 (4.9%); normal mucosa: 7 (2.0%); non-IBD colitis: 19 (5.5%)], and 182 (52.8%) had no conclusive diagnosis [descriptive/inconclusive: 148 (42.9%); suggestive for non-IBD colitis: 14 (4.1%); suggestive for IBD: 10 (2.9%); suggestive for RCU: 5 (1.4%); suggestive for Crohn’s: 5 (1.4%)].

The frequency of a conclusive diagnosis was significantly related to the availability of suitable clinical information about the onset of symptoms and treatment (12.9% of cases with a conclusive diagnosis in the group with the aforementioned clinical information vs 3.3% of cases in the group with inadequate information; p = 0.001).

The concurrent description of active inflammation, ulcers and crypt distortion in the microscopy section of the report was statistically correlated with the availability of complete endoscopic sampling (31.1% among the cases with ileo–rectal sampling vs 13.7% in the remaining cases: p = 0.002) and with the occurrence of a specific diagnosis of IBD (35.8% of cases with a conclusive IBD diagnosis vs 6.0% of cases with an uncertain diagnostic conclusion; p < 0.001).

Basal plasmacytosis was described in 4.93% of all diagnostic reports and in 12.4% of the reports with a conclusive diagnosis of IBD.

4. Discussion

The results of this study demonstrate that the recommended guidelines for diagnosing IBD are frequently disregarded in clinical practice in our region.

For example, the time elapsed between the onset of symptoms and endoscopy was reported on only 13% of the request forms. The omission of this information, as widely stated in the literature [1–4], may lead to crucial mistakes in the interpretation of the histological pattern. For example, pathologists may not be alerted by the

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical/endoscopic information</strong></td>
<td></td>
</tr>
<tr>
<td>Reported symptoms</td>
<td>94 (27.2%)</td>
</tr>
<tr>
<td>Date of onset of the clinical signs</td>
<td>47 (13.6%)</td>
</tr>
<tr>
<td>Recent or ongoing treatments</td>
<td>58 (16.8%)</td>
</tr>
<tr>
<td>Endoscopic pattern</td>
<td>269 (78.0%)</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>16 (4.6%)</td>
</tr>
<tr>
<td>Other imaging examinations</td>
<td>4 (1.2%)</td>
</tr>
<tr>
<td><strong>Specimen quality standards</strong></td>
<td></td>
</tr>
<tr>
<td>Complete endoscopic sampling</td>
<td>45 (13.0%)</td>
</tr>
<tr>
<td>Biopsy orientation on acetate filters</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td><strong>IBD-related histological lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Activity (cryptitis)</td>
<td>199 (57.7%)</td>
</tr>
<tr>
<td>Epithelial disruption</td>
<td>103 (29.9%)</td>
</tr>
<tr>
<td>Crypt distortion</td>
<td>137 (39.8%)</td>
</tr>
<tr>
<td>Plasmacytosis</td>
<td>17 (4.9%)</td>
</tr>
</tbody>
</table>

IBD, inflammatory bowel disease.
presence of elementary histological lesions such as basal plasmacytosis, which is commonly the only finding in the first episode of the disease and appears approximately two weeks after the onset of symptoms. Furthermore, plasmacytosis was rarely described in our cohort, even in histological reports with a conclusive diagnosis of IBD (12.4% of reports).

Other clinical data that were available in the request form for a minority of cases were the results of laboratory analyses and information about symptoms and therapies, which are important in differential diagnoses involving non-IBD colitis. In this study, the pathologist was aware of the use of drugs that could give rise to lesions that mimic IBD in only 16.8% of the cases.

By contrast, the endoscopic pattern, which is of the highest importance for the histopathological interpretation of a biopsy, was much more frequently available (77.9%). However, a low rate of complete mapping (ileo-rectal) was reported at the first diagnostic endoscopy and in no cases were the samples oriented on acetate strips. Multiple biopsies permit a thorough analysis of the distribution of inflammation and are essential to recognizing dysplasia. Additionally, both in the early stage of the disease and during follow-up, the differential diagnosis between ulcerative colitis and Crohn’s disease is not always straightforward if the mapping is incomplete. Structural changes, including basal plasmacytosis and alteration of the crypt architecture, can be reproducibly assessed only if the biopsy specimens are properly oriented. Thus, minimal sampling and poorly oriented biopsies may seriously limit the process of a differential diagnosis between IBD and non-IBD colitis.

As a consequence of these factors, the primary end point that confirms the clinical instrumental hypothesis by histopathological images is lost. This analysis shows that the majority of conclusive IBD diagnoses are not based upon proper supporting information about clinical, laboratory and endoscopic analyses, and the consequences are potentially dangerous. If the diagnosis is incorrect from the beginning, it is often impossible to obtain a reliable diagnosis in subsequent follow-up biopsies because the patient is treated after the initial assessment, with consequent modifications to the endoscopic and morphological pattern.

In our opinion, the reported data highlight two hazardous behaviours. First, clinicians show a poor commitment to providing a suitable amount of information and adequate samples for histological evaluation. Second, pathologists rarely report the elementary lesions that help indicate the accuracy of the IBD diagnosis. These conclusions are consistent with the data of a previous audit on the compliance of UK pathologists with the guidelines of the British Society of Gastroenterology for the initial biopsy diagnosis. Considerable variation was found among participating UK doctors in the quality of clinical and endoscopic details received and in the information provided in the histological report [13].

Moreover, this retrospective analysis establishes that the availability of comprehensive clinical information and endoscopic samples, although rarely achieved, is closely related to reaching a definitive diagnosis. Thus, the guideline recommendations represent an effective tool for a conclusive diagnosis.

In conclusion, these data strengthen the need to ensure compliance with the recommended guidelines and to standardize the request form and histopathological report. In particular, as we previously suggested, pathologists should use a binary system of “diagnostic” or “non-diagnostic” for the final report by categorizing the adequacy of the clinical and endoscopic information, the biopsy mapping and the specimen handling (correct orientation) [12]. When these prerequisites are met, the presence or absence of unequivocal histological signs of the disease should allow for a specific diagnosis of IBD or a diagnosis that definitely rules out IBD.

We argue that multidisciplinary education should be emphasized for making an adequate diagnosis of IBD and managing the condition. Furthermore, the establishment of multidisciplinary teams, as applied in other countries [14–16], could facilitate the optimal management of patients.

Conflict of interest
None declared.

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Appendix A. Members of the Piedmont IBD group

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Quality Care Service Standards for the healthcare of people who have Inflammatory Bowel Disease (IBD)© IBD Standards Group, 2009. http://www.bsg.org.uk/attachments/160_IBD_standards.pdf