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THE DIAGNOSTIC PROCESS IN INFLAMMATORY BOWEL DISEASE: PRINCIPLES AND PITFALLS, THE RESULTS OF A LOCAL STUDY

Gabriella Canavese, MD*, Vincenzo Villanacci, MD ^, Anna Sapino, MD *, Rodolfo Rocca, MD °,
Marco Daperno, MD °, Renzo Suriani, MD °, Francesca Maletta, MD *, Paola Cassoni, MD, PhD *
and the Piedmont IBD group.

(*), Pathology Department, Azienda Ospedaliera Città della Salute e della Scienza di Torino, Via
Santena, 7 10126 Turin, Italy

(°), Gastroenterology Department, Ospedale Mauriziano, Largo Turati 62, - 10128 Turin, Italy

(^), Pathology Department, Spedali Civili di Brescia, P.le Spedali Civili, 1 25123 Brescia, Italy

The authors have no conflicts of interest to disclose.

Address for correspondence and reprints: Gabriella Canavese, MD, Pathology Department, Azienda
Ospedaliera Città Della Salute di Torino, Via Santena, 710126 Torino, Italia.

Phone: +39 011 6334783

E-mail: gcanavese@cittadellasalute.to.it

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Abstract

Background and Aims:The diagnosis of IBD can be challenging and requires the efforts of a multidisciplinary team. This study aimed to evaluate the adequacy of the clinical, endoscopic and pathological prerequisites for arriving at an accurate histological diagnosis of IBD.

Methods:The following parameters were considered as prerequisites for a diagnosis of IBD: clinical and endoscopic data;the sampling of, handling of and procedures forbiopsies and elementary microscopic lesions. These data were collected from request forms and histological reports of 345 cases obtained from 13 centers in Piedmont.

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

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

Key words: Inflammatory Bowel Disease, diagnosis

Introduction

The incidence of Inflammatory Bowel Disease (IBD) is increasing globally ^[9]. However, a definitive diagnosis of IBD or 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 histologic data to avoid misdiagnosis and therapeutic pitfalls. International guidelines have therefore stressed that for a definitive diagnosis of IBD the pathologist requires: (1) a minimum set of information about the patient's clinical history and endoscopic pattern and (2) an adequate quality of biopsy sampling and handling 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 are 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 centers in the Piedmont region of Italy. Data related to the prerequisites for diagnosis were then compared to the morphologic patterns and diagnostic conclusions contained in the histological reports.

Materials and methods

Case cohort

The survey was conducted in 13 qualified gastroenterology centers in the Piedmont region (Italy) and required the collection of the following records: (1) the request form for histological analysis with any supplementary report (if available) and (2) the relative histopathological report of biopsies taken from patients with a clinical suspicion of IBD. The final cohort included 345 cases. The presence or absence of the clinical and endoscopic parameters required for the correct interpretation of the biopsy (symptoms, date of onset, treatment, endoscopic pattern, laboratory tests and other instrumental examinations) in the request form, the type of sampling (complete or incomplete) and the correct orientation of the biopsy specimen (present or absent) were assigned for each case. The other parameters included the presence or absence of a description of IBD-specific histological lesions (cryptitis, crypt distortion, ulcers and basal plasmacytosis) in the pathological report and the type of histological diagnosis (conclusive or inconclusive for IBD).

Statistics

A correlation analysis was performed between the clinical and endoscopic parameters and the histopathological lesions described by pathologists with the type of diagnostic conclusions. Statistical analyses were performed using the ISSP® software package. The p values were generated with χ^2 tests.

Results

Characteristics of endoscopies

Among 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.

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 instrumental examinations were only reported on a few request forms. The endoscopic sampling was not adequate in 87% of cases. Only 45 patients (13%) received a complete sampling (5 sites, including the ileum and rectum). The types of sampling were then further analyzed, as reported in table 2. Minimal sampling (1–2 sites) was the most frequently reported procedure (45.2%), whereas extended sampling without rectal sampling was reported less frequently (1.2%). In no case were biopsies oriented on acetate cellulose filters.

Among 345 cases, 163 (47.2%) had a conclusive diagnosis and 182 (52.8%) had no conclusive diagnosis. The different types of diagnoses are reported in table 3.

The occurrence 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; $p = 0.001$).

Active inflammation, ulcers and crypt distortion were statistically correlated with the availability of complete endoscopic sampling (31.1% among 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 reports with a conclusive diagnosis of IBD.

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 literature ^[1-4], may lead to crucial mistakes in the interpretation of the histological pattern. For example, pathologists may not be alerted by the 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 this survey, 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 the differential diagnosis with non-IBD colitis. In this survey, only in 16.8% of cases was the pathologist aware of the use of drugs that could give rise to lesions that mimic IBD.

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 recognize 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 or alteration of the crypt architecture, can be reproducibly

assessed only if the biopsy specimens are properly oriented. Minimal sampling and poorly oriented biopsies may thus seriously limit the process of 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. In this survey, it was evident that the majority of conclusive IBD diagnoses are not based upon proper supporting information about clinical, laboratory and endoscopic analyses, with the risk of dangerous consequences. 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.

The findings of this local survey highlight two important problems. First, clinicians show a poor commitment to providing a suitable set of information and adequate samples for histological evaluation. Second, pathologists rarely report the elementary lesions that help indicate the accuracy of the IBD diagnosis. The results of this study 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].

This survey establishes that the availability of a complete set of clinical information and endoscopic samples, although rarely achieved, is closely related to the arrival at a definitive diagnosis. Thus, the guideline recommendations represent an effective tool for reaching a conclusive diagnosis.

In conclusion, these data strengthen the need to ensure compliance with the recommended guidelines and standardization of the request form and histopathological report. In particular, as

we previously suggested, pathologists should use a binary system of diagnostic or not diagnostic for the final report, by categorizing the adequacy of clinical and endoscopic information, biopsy mapping and specimen handling (correct orientation) ^[12]. When these prerequisites are met in a high quality manner, 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.

Members of the Piedmont IBD group: MARCI Valerio Ospedale S.Luigi Orbassano, SAMBATARO Angela Ospedale S.Luigi Orbassano, TARAGLIO Stefano Ospedale M.Vittoria Torino, RIELLA Paola Ospedale Valdese Torino, RAVIZZA Mauro Ospedale Valdese Torino, CHIUUSA Luigi Ospedale Molinette Torino, CERA Giovanni ASL CN1, OLIVERO Francesca ASL CN1, MERLO Renato ASL5 Moncalieri, GHIDONI Palmira ASL5 Moncalieri, FRAIRE Flavio ASL CN2 Alba Bra, VANNI Riccardo ASL CN2 Alba Bra, EMIDI Roberto ASL VCO, IANDOLO Maria ASL TO3 Pinerolo, GROSSO Stefano ASL TO3 Pinerolo, PAGANO Marco ASL CN1 Savigliano, FORNARA Maria Grazia ASL CN1 Savigliano, BERNARDI Paolo Ospedale Aosta, VALLE Francesca Ospedale Aosta, FORTUNATO Mirella Ospedale S.Croce Cuneo, PULITANO' Raffaella Ospedale S.Croce Cuneo, DEMARCHI Andrea Ospedale S.Giovanni Bosco, MOSSO Luciano Ospedale Mauriziano, NIOLA Paolo ASL AT, RICCI Daniele ASL AT, SURIANI Adolfo Ospedale M.Vittoria Torino, DAVID Ezio Ospedale Molinette Torino

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