Clinical Study

Diagnostic Yield of Routine Duodenal Biopsies in Iron Deficiency Anemia for Celiac Disease Diagnosis

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Background. Iron deficiency anemia (IDA) is a recognised feature of celiac disease (CD) in adults and can be its only presentation. **Aim.** To define the prevalence of CD in Moroccan adult patients with IDA of obscure origin and to determine the yield of small bowel biopsy performed during routine endoscopy. **Methods.** 437 patients with IDA of obscure origin were included. 4 endoscopic mucosal biopsies were taken from the second part of duodenum and 2 biopsies from antrum and fundus, respectively. Endoscopic aspect and severity of anemia were correlated with histological diagnoses using coefficient Kappa. **Results.** 29 out of 437 patients (6.63%) had CD. Endoscopic aspect was normal in 66%, a mosaic pattern of mucosa in 17%, and scalloping of the small bowel folds in 17%. 12 patients had Marsh III, 8 had Marsh II, 6 had Marsh I, and 3 had Marsh IV lesions. There was no correlation between degree of anemia, endoscopic aspect, and severity of duodenal lesions (Kappa = -0.167). **Conclusion.** Routine duodenal biopsy gives an additional 6.63% diagnostic benefit of CD and should be indicated in all patients with IDA. The finding of normal endoscopic appearance of mucosa should not preclude duodenal biopsies.

1. Background

Occult, chronic blood loss from the gastrointestinal tract is the most common cause of iron deficiency anemia. The different lesions responsible for chronic blood loss include both upper and lower gastrointestinal tract sources with causes and incidences varying widely among different studies [1].

First described in 1888 by Samuel Gee, adult celiac disease has now been well recognized as a disease characterized by damage to the small bowel mucosa induced by gluten. Adult celiac disease can be a cause of malabsorption of several nutrients in addition to having a malignant potential. Anemia can be a presenting and/or significant feature of this disease and can occur in any age, sex, or ethnic group [1].

This autoimmune enteropathy is common not only in Europe but also in African populations, specifically in the Maghreb area. The primary aim of this study is to define the prevalence of CD in Moroccan adult patients with iron deficiency anemia of obscure origin and to determine the yield of

small bowel biopsy performed during routine endoscopy. The secondary one is to determine the correlation between degree of anemia, endoscopic aspect, and severity of duodenal lesions.

2. Methods

We retrospectively studied 437 patients with IDA of obscure origin and nonspecific gastrointestinal symptoms are collected between 2005 and 2011. All patients had a diagnosis of IDA with either hemoglobin < 12 g/dL or ferritin < 15 µg/L.

4 endoscopic mucosal biopsies were taken from the second part of the duodenum in these patients and 2 biopsies from antrum and fundus, respectively. Biopsy specimens were fixed in buffered formalin and immediately submitted for histopathology study. Histopathologic examination results of patients were stratified according to Marsh classification system: normal mucosa was defined as Marsh 0; increased number of intraepithelial lymphocytes as Marsh I;

TABLE 1: General characteristics of patients with CD.

Mean age	36 years (17–67)
Sex ratio	0.16
Mean hemoglobin	8 g/dL (6.5–10)
Ferritin	12.4 μ g/L $\pm$ 9.8

FIGURE 1: Endoscopic aspect in patients with CD.

crypt hyperplasia as Marsh II; partial or complete villous atrophy as Marsh III; incomplete development (hypoplasia) of the small bowel as Marsh IV.

Endoscopic aspect and severity of anemia were correlated with histological diagnoses using the statistical chi-squared contingency (X²) and coefficient Kappa. *P* values < 0.05 were considered statistically significant.

3. Results

437 patients with iron deficiency anemia were screened for the study. 29 out of them (6.63%) had CD.

The demographics of the study patients are summarized in Table 1. The mean age was 36 years with a range of 17–67 years. Females were predominant (25F/4M) with sex ratio = 0.16. Mean hemoglobin value and median ferritin level were 8 g/dL (6.5–10) and 12.4 μ g/L $\pm$ 9.8, respectively.

Upper endoscopic aspect was normal in 66% of patients. It showed mosaic pattern of mucosa in 17% of patients and scalloping of the small bowel folds in 17% (Figure 1).

Histopathology examination revealed 12 (41.4%) patients had Marsh III, 8 (27.5%) had Marsh II, 6 (20.7%) had Marsh I, and 3 (10.4%) had Marsh IV lesions (Figure 2).

Mean hemoglobin level was correlated to degrees of duodenal lesions, and endoscopic aspect was correlated to histologic diagnosis in patients with CD (Tables 2 and 3); there was no correlation between degree of anemia, endoscopic aspect, and severity of duodenal lesions (Kappa = -0.167).

4. Discussion

CD or gluten-sensitive enteropathy is an autoimmune enteropathy due to food gluten intolerance in genetically predisposed people [2]. It has a wide spectrum from overt malabsorption or typical gastrointestinal symptoms to clinically

FIGURE 2: Histopathologic examination (Marsh classification) in patients with CD.

TABLE 2: Mean hemoglobin level correlated to degrees of duodenal lesions.

Marsh classification	Mean hemoglobin level	<i>P</i>
Minimal lesions: I-II	11.5 g/dL $\pm$ 1.4	<0.0001
Severe lesions: III-IV	9.15 g/dL $\pm$ 1.3	

TABLE 3: Endoscopic aspect correlated to histologic diagnosis in patients with CD “Kappa = -0.167”.

	Severe lesions	Minimal lesions	Total (<i>n</i>)
Endoscopic lesions of CD	3	5	8
Normal endoscopy	11	10	21
Total (<i>n</i>)	14	15	29

silent cases [3]. IDA is a common extraintestinal manifestation of CD and has been described as the sole manifestation of the disease [4, 5].

In an extensive evaluation of the gastrointestinal tract in patients with IDA in order to identify a source of bleeding, the origin of bleeding cannot be detected in a significant minority of patients. In some of these patients, IDA could be the result of diseases that impair iron absorption in the absence of bleeding [6, 7]. Gluten-sensitive enteropathy is one of these disorders which causes chronic inflammation in the bowel surface, leading to infiltration of T lymphocytes, hyperplasia of crypts, villous atrophy, and reduction of the bowel absorption surface for various nutrients such as iron [8, 9].

The disease shows marked geographic variation, with the highest prevalence in Western Europe and in places where Europeans emigrated, notably North America and Australia [10].

The prevalence of CD in patients presenting with IDA varies from 0 to 5% [1, 10–12]. In a prospective study of 71 patients from Italy, Annibale et al. [6] diagnosed four

patients (5.7%) with CD. In a study of 114 patients with IDA, conducted in the United Kingdom, 2.6% of these patients had CD [13]. In another study, CD was present in 5.7% of patients with IDA [14]. In a study from USA, Grisolano et al. [15] identified nine cases (8.7%) in 103 patients with IDA. In our study, 6.63% of patients with IDA had CD. This disparity of prevalence could possibly be related to differences in local prevalence of CD as well as patient selection criteria.

Endoscopic diagnoses, symptoms and the prevalence of anemia were correlated with the histological diagnoses in a prospective study of 1000 patients [16]. There was no correlation between clinical symptoms, the prevalence of anemia, and the diagnosis of coeliac disease or giardiasis in this cohort. Our result is concordant with this study.

These studies emphasize the importance of the prevalence of disease in different patient groups and its effect on the predictive value of the diagnostic test. Thus, they demonstrate the important yield of upper endoscopy in the evaluation of patients with IDA.

5. Conclusion

Routine duodenal sampling during the upper endoscopic examination gives an additional 6.63% diagnostic benefit in our study (near to the most reports in the literature), and this practice should be included in the diagnostic workup of patients with IDA. Moreover, performing duodenal biopsy is still necessary even though the endoscopic appearance of the mucosa is normal.

Conflict of Interests

The authors declare no conflict of interests.

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