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Dickey, W.

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Chapter 2

Use of Endomysial antibody testing by family doctors

IDENTIFICATION OF COELIAC DISEASE IN PRIMARY CARE

W DICKEY, SA MCMILLAN, DF HUGHES

Departments of Gastroenterology and Histopathology, Altnagelvin Hospital, Londonderry; Regional Immunology Service, Royal Group of Hospitals, Belfast; Northern Ireland, UK

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Abstract

Background

Coeliac disease is common yet often undiagnosed because symptoms may be trivial, non-specific, or non-gastrointestinal, or because of lack of clinician awareness. Serum IgA class endomysial antibodies (EmA) have high specificity for coeliac disease and may facilitate case-finding by clinicians other than gastroenterologists. We assessed the appropriateness and diagnostic yield of requests for EmA by primary care general practitioners in a defined geographical area of Northern Ireland.

Methods

We identified patients who had EmA requests by their general practitioners during 1994-1996. Individual patient questionnaires were posted to the general practitioners concerned, seeking information on indications for testing, management following the result and final diagnosis. We compared new patient diagnosis rates in two catchment areas, one served by a large district general hospital with a medical gastroenterology facility and the other by smaller hospitals without.

Results

A total of 239 patients had coeliac profile testing by 69 of 177 general practitioners in the area. Data were available for 181 patients not previously known to have coeliac disease of whom 20 (11%) had EmA. All EmA +ve patients were referred to hospital where 19 underwent small bowel biopsy, which confirmed coeliac disease in all 19. Only 7 (35%) of the 20 had diarrhoea and there was no significant difference in EmA prevalence among patients tested with and without diarrhoea. Although the mean number of new patients (per 100,000 population per annum) diagnosed by biopsy was 11 at the large hospital compared with 5 elsewhere, the numbers identified by EmA in general practice for the two catchment areas were similar (2, 3).

Conclusion

General practitioners have an important role in the identification of patients with coeliac

disease, particularly where there is no local medical gastroenterology facility, which is made possible by EmA testing.

Introduction

Coeliac disease is common in western Europe, with population screening studies suggesting prevalences of the order of 1:150-1:300 [1-3]. However, failed or delayed diagnosis is common [4]. Although small bowel biopsy remains mandatory for diagnosis, serological testing for IgA class endomysial antibodies (EmA) has sufficiently sensitivity and specificity to allow selection of patients for biopsy [5]: EmA may be useful for clinicians other than gastroenterologists, including general practitioners in primary care. We studied the appropriateness and value of EmA requests by general practitioners in a defined geographical area of Northern Ireland using a retrospective questionnaire study.

Methods

Since 1991 the Northern Ireland Regional Immunology Service has offered EmA testing, measured by indirect immunofluorescence with titres of 1:5 or greater taken as positive [6], to all hospital clinicians and general practitioners in Northern Ireland. We studied a defined area in the west of Northern Ireland with a population of 271,400. This area has primary care services provided by 177 general practitioners working in 57 practices. As elsewhere in the United Kingdom, all patients are seen initially by their general practitioners who determine whether referral to hospital specialists is needed. One district general hospital (DGH) with a long established medical gastroenterology service provides acute medical services for approximately 58% of the population (157,800). The remaining population (113,600, 42%) is served by smaller general hospitals where most of the gastroenterology workload is managed by surgeons, with some support from consultants in general internal medicine.

From our records we identified patients for whom EmA had been requested by general practitioners in this area during the years 1994 to 1996 inclusive. In April 1997, we sent individual patient questionnaires to the general practitioners involved. Each questionnaire stated patient name, date of birth and date of testing, and requested the following data: 1. Indications for testing- presence or absences of diarrhoea; anaemia; family history of coeliac disease; skin rash (possible dermatitis herpetiformis) or assessment of known coeliac disease- with free text invited for other indications if appropriate; 2. Action taken following result-

whether or not hospital referral; small bowel biopsy; and commencement on gluten-free diet- with free text invited for other actions if taken; 3. Final diagnosis (if known). In July 1997 reminders and duplicate questionnaires were sent to GP s who had not responded, and all data received by 1 September 1997 were analysed.

Histopathology services for all hospitals within the area are provided by a single laboratory. From records we identified patients undergoing biopsy for the first time in 1994-1996 who had subtotal or total villous atrophy and thus calculated the number of new diagnoses of coeliac disease made in hospitals over the same period.

Statistical analysis used Fisher's exact test with $p< 0.05$ taken as significant.

Results

Over the study period 69 of the 177 general practitioners requested EmA on 239 patients, of whom 26 (11%) were positive for EmA. Questionnaires for 209 patients were returned by 53 (77%) general practitioners. Data on 20 patients were unavailable because they had left their practices. Thus, full data were available for 189 (79%) patients, of whom 25 (13%) had EmA. Eight patients (5 EmA +ve) had EmA testing but previous histological confirmation of coeliac disease and were excluded, leaving data of 181 patients, including 20 (11%) EmA +ve, for analysis. Seventy-nine patients (44%) tested for EmA had diarrhoea, including 16 with a family history of coeliac disease; indications in the remaining 102 comprised one or more of anaemia (42 patients), family history (23), underweight or weight loss (17), abdominal pain/bloating (15), fatigue (6), skin rash (4) and mouth ulcers (3). Only 7 EmA +ve (35%) patients had diarrhoea, and there was no significant difference in EmA prevalence between patients with and without diarrhoea (7 of 79 (9%) v. 13 of 102 (13%); $p= 0.48$). Characteristics of the 13 EmA +ve patients without diarrhoea are listed in the Table. The EmA prevalence among patients aged 30 or over was 20% (17 of 85) compared with 3% (3 of 93) of patients under 30 ($p< 0.001$); the three patients under 30 were aged 13, 17 and 19, with none of 16 patients under 10 tested having EmA. Of the 20 EmA +ve patients, all were referred to hospital where 19 had subsequent biopsy confirmation of subtotal or total villous atrophy before starting gluten free diets; one patient was seen at a general medical clinic where diet was prescribed without biopsy.

Table. Details of 13 patients with EmA and no history of diarrhoea

Patient no.	Age	Sex	Indication
1	48	Female	Bloating, constipation
2	17	Female	Anaemia
3	48	Male	Anaemia, joint pains
4	30	Male	Anaemia, family history of coeliac
5	38	Female	Family history of coeliac, no symptoms
6	45	Female	Joint pains, fatigue
7	49	Male	Anaemia
8	57	Female	Anaemia
9	55	Male	Fatigue, family history of coeliac
10	43	Male	Anaemia
11	13	Female	Abdominal pain, family history of coeliac
12	19	Female	Dermatitis herpetiformis
13	53	Female	Weight loss

Yearly figures for new patients having villous atrophy on small bowel biopsy at the DGH with medical gastroenterology were 10 (1994), 16 (1995), and 25 (1996) for a catchment area of 157,800, representing a mean 11 new cases per 100,000 population per annum. Assuming all 20 patients identified by general practitioners as EmA +ve had villous atrophy, 11 lived within the same catchment area, representing 2 new cases identified in primary care per 100,000 per annum. Comparative figures for all other hospitals without medical gastroenterology were 6 (1993), 3 (1994) and 7 (1996) for a population of 113,600- mean 5 new cases identified in hospital per 100,000 per annum: 3 new cases per 100,000 per annum were identified in primary care in the same catchment area (9 patients from a population of 113,600 over 3 years).

Of 161 EmA negative patients, 68 (42%) were referred to hospital clinics, with final diagnoses of irritable bowel syndrome in 24 (35%), inflammatory bowel disease (7;10%), diverticulosis (4;6%), neoplasia (4;6%), other diagnoses in 11 (16%) and no diagnosis in 18 (26%). Final

diagnoses among 93 patients not referred were irritable bowel syndrome (22; 24%), nonspecific self-limiting illness (17; 18%), negative family screening for coeliac disease (13; 14%), menorrhagia (10,11%), dietary deficiency (8, 9%), and toddler diarrhoea in 1 (1%) with no diagnosis in 22 (25%).

Discussion

Coeliac disease is much commoner in western Europe than previously appreciated. Population studies show prevalences for biopsy proved coeliac disease of 1:256 among Swedish blood donors [1], 1:300 in Italian secondary schoolchildren [2], and 1:150 in an adult population in Northern Ireland [3]. In two recent series from Northern Ireland less than half of patients had the "classic" textbook history of diarrhoea [4,7] and this trend has been confirmed elsewhere [8]. In particular, iron deficiency anaemia without gastrointestinal symptoms is common [9]. The diagnosis rate, as a proportion of outpatients seen, at an English DGH was threefold that of two neighbouring hospitals combined due to an increased biopsy rate among patients with haematological and other non-gastroenterological problems [10]. Accurate diagnosis is essential even if symptoms are trivial in view of the increased long-term risks of osteopenia and gastrointestinal malignancy, which are reduced by early treatment [11,12]. Although the only reliable method of confirming diagnosis is by small bowel biopsy, serological tests facilitate selection of patients particularly where symptoms are non-specific. EmA has specificity in many studies of 100% with sensitivity of 74-98% [5,6,7,13]. Our study confirms that there is already considerable awareness of the varied presentations of coeliac disease among general practitioners, with a high proportion of patients having serological testing for indications other than diarrhoea and overall 11% tested having EmA: as in other series, a minority had diarrhoea. The final diagnoses in EmA negative patients not referred to hospital imply that EmA is being used as an "insurance" before confidently diagnosing irritable bowel syndrome or attributing anaemia to poor diet or menorrhagia. This seems appropriate given the often trivial or non-specific nature of coeliac symptoms. Much of the diagnostic yield arose from testing patients over 30, with no children under 10 identified. Elsewhere in Ireland childhood coeliac disease is declining [14] though elsewhere, notably the Netherlands, it is increasing [15].

In the area studied, the incidence of biopsy proved coeliac disease at a DGH with medical

gastroenterology was over twice that of hospitals without, yet diagnosis rates in terms of general practitioner identified EmA+ve patients were similar in the two catchment areas, suggesting that a lack of awareness among hospital clinicians other than gastroenterologists accounts for the disparity rather than any epidemiological difference. Of 39 patients diagnosed as coeliac at another DGH in Northern Ireland, 14 had been referred to hospital a total of 30 times with features of coeliac disease unrecognised [4]: gastroenterologists had an 85% diagnostic success rate compared with 7% for surgeons. Our study suggests that general practitioners can help correct this deficit and have an important role in case-finding, although it must be emphasised that EmA does not have 100% sensitivity. IgA deficiency in particular is an important cause of false-negative EmA [7]. Accordingly, general practitioners should refer patients to a medical gastroenterology unit for consideration of biopsy if the presentation is suggestive even if EmA is negative.

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