Fibromyalgia and coeliac disease: a media hype or an emerging clinical problem?

F. Tovoli[1], L. Giampaolo[1], G. Caio[1], M. Monti[1], M. Piscaglia[1], M. Frisoni[2], L. Bolondi[1], U. Volta[2]

[1]*Department of Medical and Surgical Sciences, University of Bologna, Bologna;* [2]*Department of Internal Medicine and Digestive Diseases, Azienda Ospedaliero-Universitaria S. Orsola-Malpighi, Bologna, Italy.*

Francesco Tovoli, MD
Luca Giampaolo, MD
Giacomo Caio, MD
Marco Monti, MD
Maria Piscaglia, MD
Magda Frisoni, MD
Luigi Bolondi, MD
Umberto Volta, MD

This study should be attributed to the University of Bologna, Department of Medical and Surgical Sciences.

Please address correspondence and reprint requests to:
Francesco Tovoli, MD,
Department of Clinical Medicine,
University of Bologna,
via Massarenti 9,
40138 Bologna, Italy.
E-mail: francesco.tovoli@studio.unibo.it

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ABSTRACT

Objective. *Fibromyalgia (FM) association with autoimmune diseases has been widely reported in literature.*
Coeliac disease (CD) is a small intestine immune-mediated disorder triggered by gluten ingestion in genetically predisposed patients.
In recent years, the Internet and the non-medical press have reported a correlation between gluten-related disorders and fibromyalgia-like symptoms.
The aim of our study was to verify a possible association between FM and CD, by assessing the prevalence of CD in a cohort of FM patients and vice versa.

Methods. *90 consecutive subjects from our Rheumatologic outpatient clinic who had been diagnosed with FM were serologically tested for CD and positive patients underwent esophagogastroduodenoscopy to obtain duodenal biopsies. A second group of 114 consecutive subjects from our Coeliac Disease outpatient clinic were investigated for the presence of FM-like symptoms through a questionnaire.*
Patients reporting chronic widespread pain were addressed to a rheumatologist for further evaluation.

Results. *The overall prevalence of CD in our FM patients was identical to that expected in general population (around 1%). In our CD group 17 patients (14.9%) reported chronic widespread pain at the questionnaire and 13 (11.4%) satisfied ACR 1990 criteria for FM. Their symptoms had not been modified by GFD.*

Conclusion. *A serological screening for CD is not recommended in FM patients but rather a case-finding strategy should be performed. At the same time, proposals of GFD in FM patients, in absence of a well-established diagnosis of CD, should be rigorously avoided.*

Introduction

Fibromyalgia (FM) is a medical condition characterised by chronic widespread pain, fatigue and sleep disorders. Disorders in central pain processing have been progressively regarded as one of the pathogenic keystones of this disease. However, the role of trigger factors such as physical and psychological traumas has also been acknowledged (1, 2).

FM, as defined by the ACR in 1990 (3), has a prevalence of 2–4% of the general population, with a high female/male ratio (4).

Association between FM and autoimmune diseases such as rheumathoid arthritis, systemic lupus erythematosus (SLE), and Hashimoto thyroiditis has been reported in literature (5, 6), but there is still a lack of studies regarding an association between FM and coeliac disease (CD) .

CD and FM share many clinical manifestations, namely abdominal pain, bloating, diarrhoea or constipation, fatigue, widespread musculoskeletal pain, depression and other mood/anxiety disorders. In a previous study by Zipser *et al.*, in a subgroup of 134 CD patients interviewed through a questionnaire, 9% of them had been diagnosed as having FM (7).

Despite the lack of studies regarding this topic, in recent years the Internet and the non-medical press have reported a correlation between gluten-related disorders and fibromyalgia-like symptoms underlining that a gluten-free diet (GFD) could be a possible treatment for muscle and joint pain, likely elicited by gluten-containing foods (8).

The aim of our study was to verify a possible association between FM and CD, by assessing the prevalence of CD in a cohort of FM patients and *vice versa*.

Methods

We analysed two different patient groups. The first group (Group A) included 90 consecutive subjects from our Rheumatologic outpatient clinic who had been diagnosed with FM according to the ACR 1990 criteria.

Patients with a concomitant systemic autoimmune disease (such as SLE and other connective tissue diseases, systemic vasculitis, rheumatoid arthritis, ankylosing spondylitis, polymyalgia rheumatica) were excluded from this study .

After having obtained informed consent, a blood sample was taken and analysed for anti-tissue transglutaminase antibodies of IgA class (IgA tTGA) and anti-deamidated gliadin peptides antibodies of IgG class (IgG DGP).

IgA tTGA were measured by a commercially available ELISA kit (EuTG IgA, Eurospital, Trieste, Italy), using recombinant human tissue transglutaminase as antigen. The cut-off value of 16 AU, provided by the manufacturer, was adopted .

IgG DGP were assessed by ELISA commercially available kits ([alpha]-glia PEP, Eurospital, Trieste, Italy) using an entirely synthetic peptide constructed in a conformationally intact manner and then selectively deamidated. According to the manufacturer's recently modified instructions, the cut-off value was set up at 16 AU.

Patients with a positive serology underwent esophagogastroduodenoscopy in order to obtain duodenal biopsies. Histology findings were evaluated according to Marsh-Oberhuber classification.

The second group (Group B) included 114 consecutive patients from our Celiac disease outpatient clinic, who were investigated for the presence of FM-like symptoms through a four-item questionnaire.

In particular, patients were asked about: a) presence of chronic musculoskeletal pain; b) symptoms present for at least 3 months; c) distribution of the symptoms both above and below the waist and contemporary presence of axial skeletal pain; d) distribution of pain in both sides of the body .

Patients who answered affirmatively to all of the aforementioned questions were addressed to a rheumatologist for further evaluation, in particular to confirm FM or to identify possible differential diagnosis or conditions mimicking FM symptoms. ACR 1990 criteria had to be satisfied and differential diagnosis ruled out in order to classify the patient as suffering from FM (3).

Table I. Demographic and clinic feature of study groups.

FM: fibromyalgia; CD: coeliac disease; GFD (gluten-free diet).

	Group A (90 FM patients)	Group B (114 CD patients)
Median age (years)	56 (24-76)	39 (14-81)
Female/Male	79/11	93/21
Median time from diagnosis (range)	4 years (1-6)	6 years (0-19)
Patients on GFD (%)	0	112 (98.2%)*

*Two patients were not following GFD suffering from asymptomatic potential CD.

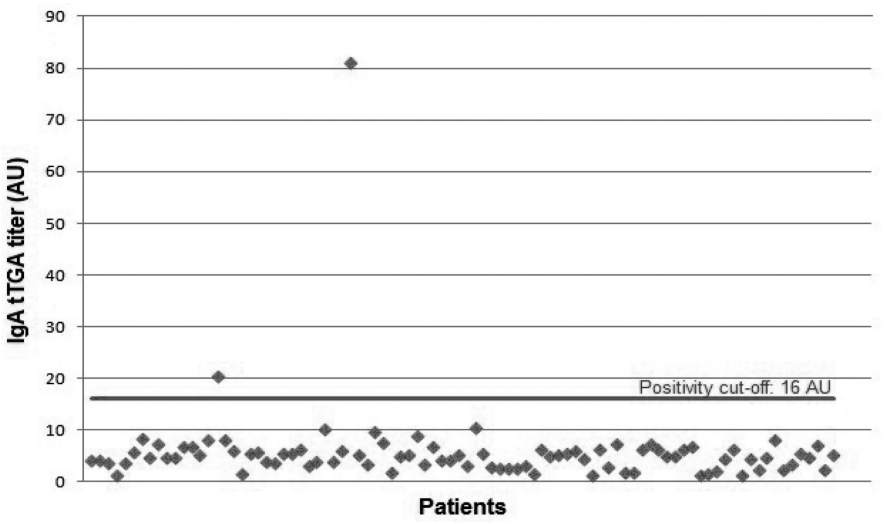

Fig. 1. Anti-tissue transglutaminase antibodies of IgA class titers (IgA tTGA) in patients with fibromyalgia.

Results

The clinical and demographic features of both groups are reported in Table I.

Group A: 88 patients (97.8%) were simultaneously negative for IgA tTGA and IgG DGP (Fig. 1).

Two patients were positive for IgA tTGA, one at a high titre (81 AU) and the other at a low titre (20 AU). DPG-AGA IgG were positive only in the first patient (52 AU).

Duodenal biopsies were obtained in both patients, showing a flat mucosa with partial villous atrophy in the first patient (grade 3b) and a normal mucosa in the latter (grade 0). The patient with flat mucosa was symptomatic for recurrent abdominal pain and iron deficiency anaemia.

Therefore only one patient was diagnosed as having CD (1.1%) starting a GFD without significant improvement of FM symptoms at a 2-year follow-up.

Group B: seventeen patients (14.9%) complained of symptoms consistent with FM. All of them underwent a rheumatologic evaluation.

Thirteen of them had pain at digital palpation in at least 11 out of 18 tender points and were diagnosed as suffering from FM.

Other rheumatologic diagnoses included: ostearthitis (2 cases), scleroderma with concomitant osteoarthritis (1 case), pain from slipped disk (1 case). Two patients suffered from autoimmune hypothyroidism: at the moment of enrolment they were adequately supplemented with levotiroxine, as documented by normal serum levels of thyroid-stimulating hormone.

All patients diagnosed with FM reported that widespread pain had begun many years before the diagnosis of CD and that their symptoms had minimal or no benefit at all from GFD.

Moreover, coeliac patients without widespread pain at the time of CD diagnosis did not develop symptoms related to FM in the follow-up after GFD.

Discussion

The availability of commercial kits for the detection of highly predictive serological markers for CD such as tTGA and DGP has marked a turning point in the clinical picture of this disorder, allowing the identification of unsuspected cases and revealing its high prevalence in the general population (around 1%) (9).

In our study only one of the two FM patients with positivity for tTGA was confirmed as having CD by duodenal biopsy. This patient showed a high tTGA titer with an associated positivity for DGP, whereas the diagnosis of CD was ruled out in the other FM patient with a low titer of tTGA and negativity for DGP.

On the basis of these data, the overall prevalence of CD in our FM patients was identical to that expected in general population (around 1%).

Correct statements about FM prevalence are more difficult as socioeconomic, ethnic, environmental, and cultural factors seem be involved in its estimate. Besides, population studies are fewer and often carried out through questionnaires. Prevalence of FM in Italy has been evaluated as high as 2.2-4.1% (10-11).

In our CD group 17 patients (14.9%) reported chronic widespread pain at the questionnaire and 13 (11.4%) satisfied ACR 1990 criteria for FM.

This finding would suggest that CD patients display a higher prevalence of confirmed FM when compared to the general population in our country.

The straight predominance of female sex in our coeliac patient group (82%) may act as a confounding factor, making difficult the comparison with other studies in the general population. In this particular case, it could determine a relative overestimate of FM prevalence, notoriously higher in female sex (4).

However, it should be underlined that such a prevalence of FM (11.4%) has never been reported up to now, probably reflecting a greater predisposition for the development of FM in CD patients.

Bonakdar lists coeliac disease as a predisposing condition for fibromyalgia and West notes that coeliac disease through the mechanism of vitamin D deficiency could cause symptoms mimicking fibromyalgia (12,13).

Vitamin D deficiency is commonly found at the diagnosis of CD, however, the association between vitamin D deficiency and non-specific musculoskeletal pain (including FM) is still controversial, as reported in recent critical analyses (14, 15).

At the diagnosis of CD all of our patients had been tested for vitamin D deficiency and, when indicated, prescribed with supplementations. However, at the beginning of the present study, recent determinations of vitamin D serum levels were available only in a few patients, thus no inferences about correlation of vitamin D deficiency and FM symptoms can be made from this study.

The high prevalence of FM in CD could be otherwise explained on one hand by the well-established association of FM with autoimmune disorders and, on the other hand by the psycho-social implications of CD (5, 6). Once the diagnosis has been established, CD remains a high social impact disease and acts as a form of psychological stress, which in its turn is regarded as a trigger event for the development and persistence of FM symptoms (2).

In conclusion, our study shows that CD patients are prone to develop FM but, conversely, prevalence of CD in patients with FM is not increased in comparison with the general population.

Consequently, a serological screening for CD is not recommended in FM patients, but rather a case-finding strategy should be performed in selected cases of FM with concomitant signs or symptoms suggestive for CD (*i.e.* diarrhoea, abdominal pain, aphthous stomatitis, iron-deficiency anaemia, unexplained hypertransaminasemia, osteopenia).

At the same time, on the basis of our data, proposals of GFD in FM patients, in absence of a well-established diagnosis of CD, represent either an incorrected clinical practice and an ineffective treatment, as FM symptoms are not usually modified by gluten withdrawal.

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