Journal of
Rheumatology and Arthritis

Research Article Open Access

A Case for Autoimmnunity as the Cause of Fibromyalgia

Le Goff[1*] and Youinou[2]

[1]Emeritus Professor of Rheumatology, (INSERM research Unit) at the European Brest University of Brittany, Brest, France
[2]Emeritus Professor of Immunology (INSERM research Unit) at the European Brest University of Brittany, Brest, France

[*]**Corresponding author:** Le Goff, Emeritus Professor of Rheumatology, (INSERM research Unit) at the European Brest University of Brittany, Brest, France, Tel: 0298801821, E-mail: legoff.paul@orange.fr

Citation: Le Goff, Youinou (2022) A Case for Autoimmnunity as the Cause of Fibromyalgia. J Rhemat & Arth 1: 1-3

Introduction

Fibromyalgia syndrome (FMS), a long-known but generally neglected disease, associates widespread pain, emotional distress and moderate, mild or great tenderness [1]. It is worth empha- sizing that some experts think of as a psychological disorder [2]. This is primarily a diagnosis of exclusion, so that all other causes of joint and muscle pain have first to be ruled out. However, based on the study of 293 patients with bona fide primary or secondary FMS and 255 controls with disor- ders that could have been confused with FMS, classification criteria have been proposed by 25 re- search groups [3]. A severity symptom scale has then been constructed [4], and the original criteria recently revised by the American College of Rheumatology [4]. Unfortunately, the currently avai- lable therapies of this puzzling disorder remains modest. To go any further, we must thetefore focus on its pathophysiopathology. To this end, the hypothesis of a muscle disease has been intensively explored [5], and small fiber abnormalities characterized on muscle biopsies [6], but there was no advance in therapy.

To gain further insights into the pathophysiology of FMS, new informations should be obtained, not only from analysis of neurolological and muscular disorders, but also on what we learn about immunological dysregulation. An exciting hypothesis has recently been put forward, speculating that the immune system contributes to the development of the disease. In this field, accumulation of clues has indeed drawn our attention. They have been gained from autoimmunity- related observations. For example, the markedly increased prevalence of FMS in patients with autoimmune rheumatological conditions, such as rheumatoid arthritis, systemic lupus erythematosus or Sjogren(s syndrome [7], the demonstration that some complex regional pain syndromes are caused by antibodies (Ab) to the self [8], and the report that autoAb bind to neuronal and glial cells (NGC) surface receptors, potentially impairing signaling processes. Among them, are Ab to N-Methyl-D-aspartate (NMDA) receptor, Ab to gamma-aminobutyric acid A (GABA) receptor and Ab to alpha-amino-3-hydroxy-4-isoxazolepropionic (AMPA) receptor. The discovery of these autoAb may offer an antigen (Ag)-specific model linking autoimmunity to psy- chopathology [9]. Whorthwhile to note is that most of these recently discovered autoAb bind to sur- face receptors in the central nerval system. The other way round, autoimmune-associated ence- phalitis often encompasses psychiatric symptoms as its first manifestations. One step ahead, novel guidelines distinguish autoimmune psychosis from autoimmune encephalitis [10]. Various psychiatric symptoms, including mood disordres and sleeping dysfunction, have thus been shown to be associated with synaptic and/or neuronal serum or cerebrospinal fluid (CSF) autoAb. Interestingly, the clinical pictures differ among pathologies based on Ab targets, but the heterogeneity of these autoAb improves our understanding of the variable neurological symptoms in FMS. An impaired blood-CSF barrier function might, however, be a prerequisite for autoimmune- mediated psychological symptoms. It is also most intriguing that Ag-specific cytotoxic T lymphocytes have been claimed to play a role in neuronal damages [11].

Despite the total absence of inflammation in FMS, a thus-far unknown autoimmune process may give rise to a painful disease. To help in our interpretation of this complex condition, there is a need for animal models with symptoms mimicking the human disease. They have recently been developed [12]. Before working out the models, two issues had hitherto to be adressed. The first problem was to trigger off FMS-like symptoms in rodents by transfering patholo-gical human samples. To this end, sera from FMS patients and from healthy controls (HC) were introduced into normal mice. The ensuing pain-like behavior was examined. Its easurement in animals was precisely the second problem to be solved. The Randall-Selitto paw pressure test, the tactile and thermal sensitivities, the forelimb grip strenght and the locomotor acitivities were thus assumed to reproduce human FMS. In addition, nocireceptor excitability, intraepithelial fiber density and the tissue localization of putative autoAb and their binding to murine and human NGC after passive transfer, could also be determined. Importantly, normal mice trated with IgG from FMS patients, but neither with IgG-depleted serum from these patients, nor with IgG from HC, exhibited hypersensitivity. Patients IgG bound to NGS. Despite the resort to a proteome-wide microarray screen using 42,000 amino-acid human peptides made of 50-150 amino-acids, their target Ag has still to be identified. Taken together, these finding temtingly suggest that immune dysregulation is implicated.

The autoAb may help in the early detection of FMS, and thereby its early therapy.This improvement does not necessarily imply that they are involved in the pathophysiology. Whatever are the intimate mechanisms, therapeutic interventions would be facilitated. Conceivably, treat- ments could be effective by rituximab-induced depletion of pathogenic B lymphocytes, by reduction of the global level of IgG, using e.g. plasmapheresis, immunoabsorption through a pro- tein A column, or immunoabsorption with protein A. Even better, but requiring identification of the target Ag, should be the selective removing of pathogenic IgG by immunoadsorption. Though being a T cell-mediated autoimmune disease, FMS might benefit from B cell depletion, as was the case for multiple sclerosis.

To conclude, needless to say that, in this rerspect, we have to establish a cause and effect relationship between immunological dysregulation and the development of FMS. It is difficult to achieve, but this is a research area worthy of pursuit in the future.

References

1. Clauw DJ (2014) Fibromyalgia, a clinical review. JAMA 311: 1547-55

2. Klauss K, Fischer S, Doerr JM, Natu UM, Mewes RL (2017) Classifying fibromyalgia syndrome as a mental disorder? An ambulatory assessment study. Int J Behav Med 24: 230-8

3. Wolfe F, Smythe HA, Yunus MB et al. (1990) The American College of Rheumatology criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 33: 160-72

4. Wolfe F, Clauw DJ, Fitzcharles MA et al. (2010) The American College of Rheumatology preliminary criteria for fibromyalgia ans measurement of disease severity. Arthritis Care Res (Hoboken) 62: 600-10

5. Wolfe F, Clauw DJ, Fitzcharles MA et al. (2016) revision of the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum 46: 319-29

6. Le Goff P (2006) Is fibromyalgia a muscle disease? Joint Bone Spine 73: 239-42

7. Bonaeda RP, Downey DC, Bennett RM (1995) An association of fibromyalgia with Sjogren's syndro- me, a prospective study of 72 patients. J Rheumatol 22: 132-6.

8. Li WW, Guo TZ, Shi X et al. (2014) Autoimmunity contributes to nociceptive sensitization in a mouse model of complex regional pain syndrom. Pain 155: 2377-89

9. Mantere O, Saarela M, Kineseppä et al. (2018) Anti-neuronal antibodies in patients with early psycho- sis. Schizophr Res 192: 404-7

10. Tanaka K, Kawamura M, sakimura K, Kato N (2020) Significance of autoimmune encephalitis in rela- tion to antigen localization: an outline of frequently reported autoantibodies with a non-systematic review. Int J Mol Sci 21

11. Grosse L, Carvalho LA, Birkenhager TK et al. (2016) Circulating cytotoxic T cells and natural killer cells as potential predictors for antidepressant response in melancolic depression. Restoration of T regulatory cell population after antidepressant therapy. Psychopharmacology (Berl) 33: 1679-88

12. Goebel O, Knock E, Gentry C et al. (2021) Passive transfer of fibromyalgia symptoms from patients to mice. J Clin Invest 131