the onset of symptoms is delayed and, therefore, the objective of starting treatment early is not achieved in most cases. Less than 30% of RA patients receive DMARD treatment in the first 3 months.[7,9,10] It is necessary to implement measures that act on early diagnosis and treatment of RA, through the diffusion of knowledge relating to the disease in the general population, advertising campaigns as well as an increase in the level of knowledge regarding RA in primary care physicians.

References

1. Wiles NJ, Lunt M, Barret ME, Bukhari M, Silman JA, Symons PM, et al. Reduced disability at five years with early treatment of inflammatory polyarthritis. Arthritis Rheum. 2001;45:1033–42.
2. Van der Heide A, Jacobs JW, Biglsma WA, Heurkens AH, van Booma-Frankfort C, van der Veen MJ, et al. The effectiveness of early treatment with second line antirreheumatic drugs: a randomised controlled trial. Ann Intern Med. 1996;124:699.
3. Mottonen R, Hammonnen P, Leirisalo-Rapo M, Nissila M, Kauntiamen H, Korpela M, et al. Comparison of combination therapy with single-drug therapy in early rheumatoid arthritis: a randomised trial. Lancet. 1997;350:309–18.
4. Chan A, Felson TD, Yood AR, walker MA. The lag time between onset of symptoms and diagnosis of rheumatoid arthritis. Arthritis Rheum. 1994;37:814–9.
5. Hernández-García C, Vargas E, Abásolo L, Lajas C, Bellajdell B, Morado IC, et al. Lag time between onset of symptoms and access to rheumatology care and DMARD therapy in a cohort of patients with rheumatoid arthritis. J Rheumatol. 2000;27:2323–8.
6. Zafar S, Badsha H, Mofti A, Delosantos A, Altares J, Matudio G, et al. Efforts to increase public awareness may result in more timely diagnosis of rheumatoid arthritis. J Clin Rheumatol. 2012;18:279–82.
7. Raza K, Stack R, Kumar K, Filer A, Detert J, Bastian H, et al. Delays in assessment of patients with rheumatoid arthritis: variations across Europe. Ann Rheum Dis. 2011;182:2–5.
8. Kumar K, Daley E, Carruthers DM, Situnayake D, Gordon C, Grindulis K, et al. Delay in presentation to primary care physicians is the main reason why patients with rheumatoid arthritis are seen late by rheumatologists. Rheumatology (Oxford). 2007;46:1438–40.
9. Jamal S, Alibhai SM, Badley EM, Bombardier C. Time to treatment for new patients with rheumatoid arthritis in a major metropolitan city. J Rheumatol. 2011;38:1282–8.
10. Van der Linden MP, le Cessie S, Raza K, van der Woude D, Knevel R, Huizinga TW, et al. Long-term impact of delay in assessment of patients with early arthritis. Arthritis Rheum. 2010;62:3537–46.

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Clinical Typology of Chronic Fatigue Syndrome: Classificatory Hypothesis☆

Tipología clínica del síndrome de fatiga crónica: hipótesis clasificatoria

Primary (or pure) chronic fatigue syndrome (pCFS) is a complex and severe chronic and disabling disease of unknown causes, excluding secondary chronic fatigue syndrome (sCFS) related to some other medical condition. It is characterized by intense fatigue in addition to cognitive, autonomic, neuroendocrine, immunoallergic and musculoskeletal symptoms, which are of recent appearance and that cannot be explained by other clinical reasons, lasting for at least 6 months, is non-remitting significantly with rest and which worsens with physical or mental activity, with very slow recovery and a reduction of >50% of activities of daily living previously performed by the patient.[1–4] It is diagnosed according to the 1994 Fukuda criteria,[1] the Canadian consensus document published in 2003[2] or, more recently, the international consensus criteria of 2011; with the name of myalgic encephalomyelitis that offers a review on its physiopathology, symptoms and treatment.[3] Prevalence is estimated to be between 0.5% and 2.5% of the general population.[1–3,5] In spite of it being recognized as a disease by the WHO since 1989, and classified with the code G93.3 in the ICD-10,[5,6] and that evidence accumulated from different fields during the past 2 decades, it is possible that pCFS is still largely unknown by most health professionals.

Due to the great heterogeneity in its clinical expression and the lack of standardized instruments to order its different symptoms (according to greater or lesser frequency) and clinical presentation (distinguishing between pCFS, sCFS and Idiopathic CF), we propose a classification into clusters: I, II, IIIa, IIIb and IIIc, subgrouping the main clinical conditions in a consecutive series of 199 patients (Table 1), seen in a period of time between June 2010 and February 2013 at the Chronic Fatigue Specialized Hospital Unit of the Camp de Tarragona belonging to the Hospital Universitario Joan XXIII. 84% of patients (n=167) were women (5:1). Mean age at symptom onset was 41.5 years (range 9–76). The onset of symptoms was insidious in 72.8% of patients and 71.3% had a progressive evolution of disease. At the moment of interview, 51.7% (n=103) were unemployed (65 lost their job while 38 were disabled). 8% (n=16) were retired. The pCFS criteria are valid for the diagnosis in the clinical daily practice independently of other associated criteria.[6–8] Having a classification of patients with CFS will allow us to identify more homogeneous groups of patients, candidates both for more individualized diagnostic and therapeutic guidelines and which allow for better expectations. In order to correctly classify a patient with CFS, we recommend a multidisciplinary approach. In first place, the CFS diagnosis must be confirmed (family physician, internal medicine specialist and/or rheumatologist), in order to then evaluate the existence of possible associated systemic diseases or chronic local processes that have a large differential diagnosis and, finally, to perform a precise diagnosis of the disease with a psychopathological background (psychologist and/or psychiatrist). Having a clear diagnosis in each one of these 6 areas, as well as the analysis of the chronology of symptoms or processes allows the inclusion of the patient into each one of the different classification subgroups.

Table 1
Classification Subtypes of Chronic Fatigue Syndrome.

	Classification subtypes	Primary disease (n=73/199, 36.75%)	Association autoimmune chronic thyroiditis (n=38/199, 19.1%)
Cluster I	pCFS, according to the Fukuda criteria	None, 90/199 patients (45.2%)	19/90 patients (21.1%)
Cluster II	Idiopathic CF, without having the Fukuda criteria	None, 36/199 patients (18.1%)	5/36 patients (13.8%)
Cluster IIIa	sCFS autoimmune disease	17/199 patients (8.5%) • 9 patients with primary Sjögren's syndrome[7,8] • 4 patients with polymyalgia rheumatica • 2 patients with systemic lupus erythematosus • 1 patient with Crohn's disease • 1 patient with Guillain–Barré's syndrome	7/17 patients (41.1%)
Cluster IIIb	sCFS to other medical entities	40/199 patients (20.1%) • 7 postchemotherapy patients • 6 patients due to drugs • 5 patients with severe OSA • 3 patients with a secreting hypophiseal microadenoma • 3 patients with hepatic cirrhosis • 3 patients with morbid obesity • 3 patients with severe iron deficiency • 3 patients with meopause • 2 patients with COPD • 2 patients with type TE JAK2 V617F CMPS • 1 patient with multiple myeloma • 1 patient with neuromuscular lung disease • 1 patient with severe myocardiopathy	6/40 patients (15%)
Cluster IIIc	sCFS to psychopathologic abnormalities	16/199 patients (8%) • 12 patients with depression • 3 patients with somatization • 1 patient with schizophrenia	1/16 patients (6.2%)

COPD: chronic obstructive pulmonary disease; CF: chronic fatigue; JAK2: Janus Kinase 2; OSA: obstructive sleep apnea; CFS: chronic fatigue syndrome (p: primary; s: secondary); CMPS: chronic myeloproliferative syndrome; ET: essential thrombocytosis.

References

1. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome, comprehensive approach to its definition and study. Ann Intern Med. 1994;121:953–9.
2. Carruthers BM, Jain AK, de Meirleir KL, Peterson DL, Filmas NJ, Lermer AM, et al. Myalgic encephalomyelitis/chronic fatigue syndrome: clinical working case definition, diagnostic and treatment protocols. J Chron Fatigue Syndr. 2003;11:7–115.
3. Carruthers BM, van de Sande MI, de Meirleir KL, Klimas NG, Broderick G, Mitchell T, et al. Myalgic encephalomyelitis: International Consensus Criteria. J Intern Med. 2011;270:327–38.
4. Barsky AJ, Borus JF. Functional somatic syndromes. Ann Intern Med. 1999;130:910–21.
5. Ruiz E, Alegre J, García Quintana AM, Aliste L, Blázquez A, Fernandez de Sevilla T. Síndrome de fatiga crónica: estudio de una serie consecutiva de 824 casos evaluados en dos unidades especializadas. Rev Clin Esp. 2011;211:385–90.
6. Barbado Hernández FJ, Gómez Cerezo J, López Rodríguez M, Vázquez Rodríguez JJ. El síndrome de fatiga crónica y su diagnóstico en medicina interna. An Med Interna (Madr). 2006;23:238–44.
7. Sirois DA, Natelson B. Clinicopathological findings consistent with primary Sjögren's syndrome in a subset of patients diagnosed with chronic fatigue syndrome: preliminary observations. J Rheumatol. 2001;28:126–31.
8. Nishikai M, Akiya K, Tojo T, Onoda N, Tani M, Shimizu K. Seronegative Sjögren's syndrome manifested as a subset of chronic fatigue syndrome. Br J Rheumatol. 1996;35:471–4.

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