The 2013 Dr. Kenneth J. Friedman Vermont CFIDS Medical Scholarship

Individuals with Chronic Fatigue Immune Dysfunction Syndrome (CFIDS) are faced with prolonged illness and disability that has substantial impact on their lives and the lives of their families. The widely used term Chronic Fatigue Syndrome does not adequately reflect the debilitating nature of this condition. CFIDS is characterized by severely disabling physical and mental fatigue with malaise, headaches, concentration and memory impairment, sleep disturbances, and musculoskeletal pain [1]. The fatigue has been described as "an overwhelming and specific lack of energy, comparable to the impression of an empty battery or a blown fuse" [2]. With no pathognomonic physical signs or laboratory abnormalities, the condition is difficult to diagnose and at present, has no known cure. Sadly, a common complaint among CFIDS patients is a general dissatisfaction with the quality of medical care received. Patients experience a pattern of being misunderstood, accused of malingering and receiving psychiatric misdiagnoses [3-8].

CFIDS is poorly recognized by health professionals and the general public. Many healthcare providers remain skeptical about the disease [9-11] and do not feel comfortable making the diagnosis or managing the condition [9,12]. The aim of this paper is to discuss the diagnosis and management of CFIDS and outline a proposal for ways to effectively educate medical students about this chronic debilitating disease. Our medical education is the foundation of our ability to provide good medical care. Educating future healthcare providers in the evaluation, diagnosis and treatment of CFIDS is a step toward legitimizing the disease and improving the care available to patients.

CFIDS is relatively common, plaguing 0.2-0.4% of the population - over one million Americans and thousands of Vermonters [1,13]. Despite its prevalence, there is little-to-no mention of it in the University of Vermont (UVM) medical school curriculum (known as the Vermont Integrated Curriculum, VIC); there is vague instruction to include "Chronic Fatigue Syndrome" as part of the differential diagnosis for a patient presenting with the chief complaint of fatigue, and a reference to the disease in a lecture on psychopathology in the first-year neural science course. Regardless of the context in which it is presented, including CFIDS in a lecture on psychopathology reinforces the misconception that it is a mental disorder.

The integration of CFIDS into the VIC should include basic education about CFIDS, an outline for proper evaluation of suspected cases, diagnostic criteria, and discussion of management strategies. These same objectives have been followed in continuing medical education programs used to increase awareness about CFIDS among healthcare providers and to improve provider understanding for the significant impact CFIDS has on patient lives [14].

An important part of medical education is learning what is normal and what is abnormal. Labeling a condition as a disease has important implications for clinician attitudes about management and treatment of the condition. If a condition is not considered by the clinician to be a disease, effective treatment may not be pursued. Similarly, conceptualizing a non-disease condition as a disease may result in unnecessary treatment. Defining a disease is straightforward in some cases, but in other situations, the labeling of certain conditions as diseases is controversial, as it has been historically for CFIDS [15].

Medical students are at a unique stage in their training during which opinions about diseases are more malleable than the opinions of those further along in their medical careers.

Classifications and attitudes toward illness are flexible as students acquire more knowledge and clinical experience. There are implications for how students are taught about conditions, especially those conditions for which there are uncertainties in disease classification among practitioners. The terms used to refer to specific diseases also have implications. For example, a study indicated that medical students were more likely to classify "myalgic encephalomyelitis" (another term used for CFIDS) as a disease than they were to classify Chronic Fatigue Syndrome as a disease, even though the terms are descriptions of the same entity [15].

During the first course of the VIC (entitled Introduction to Clinical Decision Making, ICDM), it would be valuable to discuss the concept of disease vs. non-disease and the implications of such classifications. As part of this lecture, students should be challenged to think about what defines a disease and how that distinction affects the management of a condition from a medical perspective. CFIDS can be used as an example of a multifactorial illness defined by medically unexplained symptoms and functional impairments. Friedberg et al. (2008) designed a similar lecture to examine how an interactive seminar focusing on CFIDS (the term Chronic Fatigue Syndrome was used for this research) and fibromyalgia influenced medical student attitudes toward these complex conditions. Their thought was that if medical students can be taught the fundamentals of diagnosis and management of these conditions, they will be better equipped to help their patients. The researchers found that after the seminar, students had significantly more favorable attitudes toward CFIDS; students supported more CFIDS research funding and flexible clinical hours for patients, viewed CFIDS not as a primarily psychosocial condition, and demonstrated increased perception of the disability associated with the disease [16].

Following the presentation about classification of diseases in the ICDM course, problem-based learning of selected cases in small groups would be an appropriate way to ensure that the controversies over classification of medical conditions are adequately discussed [15]. A survey could be performed at the start of the VIC and then again upon its completion to assess how medical student perceptions change as students become more informed about complex diseases like CFIDS.

A formal introduction to CFIDS should be provided to medical students during the second-year Connections course. The second-year medical school curriculum focuses on clinical presentations of illnesses, developing differential diagnoses, and managing medical conditions. The introduction to CFIDS should include an overview of the condition, how to make the diagnosis, and current theories on the etiology of the condition. Suggested pertinent information to be included in the VIC is described throughout this paper.

CFIDS is defined as chronic or relapsing fatigue for more than six consecutive months. Before a diagnosis of CFIDS can be made, medical and psychiatric causes of chronic fatigue must be excluded. The fatigue must have a specific onset and must interfere with occupational, social, or personal functioning. The fatigue must not be the result of ongoing exertion or be significantly relieved by rest. In addition, there must be persistence or recurrence of four or more of the following symptoms during the six months of the illness: 1) cognitive dysfunction (impairment of short-term memory or concentration that interferes with activities, difficulty with information processing, planning, or word-finding), 2) sore throat, 3) painful lymph nodes, 4) muscle or joint pain without evidence of inflammation, 5) new-onset headaches, 6) disturbed sleep (insomnia, hypersomnia, unrestful sleep), 7) post-exertional malaise lasting longer than 24 hours, and 8) exacerbation of symptoms with physical or mental exertion [1]. Symptoms of CFIDS vary in severity and quality over time, and are different for every patient.

Patients have described receiving the diagnosis of CFIDS to be the single most helpful event for them in management of their condition [6,17]. The importance of early diagnosis and management of CFIDS is critical because early intervention can improve patient outcomes [18]. Unfortunately, the mean time to diagnosis of CFIDS has been reported as 3.7 years [3]. Contributors to this delayed diagnosis, as alluded to earlier, include the complexity of the condition and breadth of symptoms, poor recognition of the disease by medical professionals, lack of formal training in management of CFIDS as part of medical education, loosely-defined diagnostic criteria, and absence of specific disease markers or laboratory tests to confirm the diagnosis.

Many possible etiologies of CFIDS have been investigated including immunologic, neurological, endocrine, genetic, psychiatric, and infectious causes. Upper respiratory and flu-like infections often precede the onset of CFIDS. Bacterial and viral infections like Epstein-Barr virus, Coxiella burnetti, parvovirus B19, and Mycoplasma pneumoniae are well known triggers [19].

The body normally responds to infection by increasing pro-inflammatory cytokines that act in the brain to induce common symptoms of sickness such as decreased appetite, sleepiness, fever, aching joints, psychomotor retardation and fatigue [20]. This sickness behavior is an acute adaptive response: a state of energy conservation that serves to enhance recovery from an illness or injury. Deviating from the normal physiology, it is thought that CFIDS is a disorder in which pathologic chronic activation of immuno-inflammatory and oxidative pathways result in deficits in energy production. The depletion of energy leads to the early exhaustion and the wide range of disabling sickness symptoms seen in CFIDS [21]. The cognitive and affective symptoms (like confusion, impaired memory, decreased motivation, anxiety and depression) seen in CFIDS are also seen in other chronic inflammatory and infectious diseases [22].

CFIDS can be introduced in the Connections course by incorporating it into the series of lectures about adaptive and innate immune response and other rheumatologic conditions like fibromyalgia, lupus, rheumatoid arthritis and Lyme disease. There is on-going research into the role of immune dysfunction in patients with CFIDS. Identified immune system abnormalities include diminished natural killer t-cell function, increased pro-inflammatory cytokine levels, and up-regulation of Th1 and Th2 responses [23-26].

Acute and chronic infections, environmental factors, and medical disorders that cause pro-inflammatory states may all increase susceptibility to CFIDS and contribute to its development. Psychosocial stressors have been found to cause elevated levels of inflammatory cytokines and reactive oxygen/nitrogen species. Increased stress is therefore associated with increased sickness symptoms, and has been shown to increase frequency of relapses in patients with CFIDS and cause general worsening of symptoms [27,28]. In educating patients and providers about CFIDS and the role of psychosocial stressors, it is important to emphasize that a psychosomatic component of an illness does not minimize the legitimacy of the disease.

The essence of understanding CFIDS lies in hearing first-hand accounts of the illness from patients. In addition to presenting an overview of symptoms, diagnostic criteria, and possible etiologies, the introduction of medical students to CFIDS should include a panel of individuals with CFIDS to speak about their experiences with the condition and with the health care system. Listening to a panel of patients speak about their experiences would help students to better understand the disabling nature of the disease [29].

Patients usually report that prior to the onset of their illness they were healthy and led busy, active lives. The illness is described as “an extreme and abnormal depletion of energy compared to life as before illness onset” [8]. Patients who manage to continue working often have to eliminate all other activities of daily life to conserve energy. Communication skills essential in the work place are compromised; social relationships often suffer [8]. Some patients compare the disease to having the flu every day for decades; one patient describes “if I managed to prepare dinner, I could not manage to sit at the table and eat it. I could not lift my arm holding the fork before having rested” [2].

It is important for students to be prepared to provide newly diagnosed patients with realistic information about the prognosis of CFIDS in a sensitive, well-informed manner. Some patients will have symptomatic improvement over time and be able to return to work and normal daily routines. Others, however, will continue to experience symptoms, relapse, or remain severely debilitated by the condition [17]. About 25% of people with CFIDS in the United States are home-bound, unemployed, or receiving disability because of the illness [18,29,30].

Students should be counseled on management of CFIDS during orientation to the Outpatient Internal Medicine Clerkship, during the third year of medical school. This rotation emphasizes incorporating pathophysiologic reasoning and evidence-based knowledge into patient-centered care. Beyond performing a physical exam, students must be able to communicate effectively with patients, families, and members of the health care team to ensure that the patient receives optimal care. While on this rotation, students work with patients who have a variety of chronic issues. It is essential that students understand the emotional, physical, and health needs of patients with chronic conditions like CFIDS. In comparison with other chronically-ill populations, research suggests that CFIDS patients are strikingly disabled, demonstrating more significant impairment in functioning than seen in other medical or psychiatric disorders. Social responsibilities are substantially compromised, while emotional functioning and mental health were found to be relatively preserved [31].

Management of CFIDS is challenging, as it is for many other chronic conditions for which pathophysiology is not well-understood and treatment options are minimal. Recommendations emphasize early accurate diagnosis and patient-centered care with a focus on the patient's individual needs and symptom management. In working with patients who have CFIDS, it is important that healthcare providers acknowledge the reality and impact of the disease and its symptomatology. In addition, professionals should provide patients with information about possible etiologies of the illness, the natural course of the condition, and interventions and management strategies [4,8,17]. Knowing more about the condition is considered by patients as critical to cope with the uncertain nature of the disease. Education about the illness helps them to develop strategies for hope and recovery, and to reestablish a sense of self that is compromised by unremitting invalidation, skepticism and judgment by others [8]. In the context of insufficient services and resources, physicians must be prepared to offer patients everything that *is* available.

In the management of CFIDS, clinicians are encouraged to help patients accept their diagnosis and limitations, emphasize stress management techniques, and teach patients about self-care and how to adapt their activity pace. In addition, pain, sleep disturbances and emotional distress should be targeted with appropriate pharmacotherapy. No single treatment has been identified for CFIDS, but there is ongoing research into approaches for coping with the devastating illness. Understanding the final goal in treatment of CFIDS is important: improving a patient's quality of life and ability to effectively cope with the condition is a more feasible and realistic goal than full recovery [32].

Cognitive behavioral therapy and graded-exercise therapy are widely used in the management of CFIDS and have been shown to benefit patients by improving symptoms [33]. Studies generally show that antidepressant medications and analgesics have poor efficacy in the management of CFIDS symptoms [11], but there is ongoing research into other possible pharmacologic therapies. Focusing on the immunologic aspect of CFIDS, treatment with CoenzymeQ10 may have anti-inflammatory effects and ameliorate oxidative stress, significantly improving fatigue and exercise intolerance in CFIDS patients [34]. Medications that interfere with inflammatory cytokines and are widely used in autoimmune diseases, such as rituximab, etanercept, and infliximab, may also have the potential to improve symptoms and the quality of life in CFIDS patients [35,36].

Medical students are receptive to acquiring productive attitudes and new knowledge about medically unexplained illnesses like CFIDS [16]. Integrating CFIDS into the medical school curriculum at UVM will serve to increase awareness and educate students about this poorly recognized illness.

In summary, the following are recommendations for how to incorporate CFIDS into the VIC: 1) Survey incoming students regarding the classification of certain conditions as disease vs.

non-disease; 2) revisit the concept of disease classification in small groups during ICDM using case studies for problem-based learning; 3) introduce CFIDS and its clinical presentation, diagnosis and etiology as part of the discussion of immune system regulation and rheumatologic conditions during the second-year Connections course; 4) invite a panel of CFIDS patients to speak to students about their experiences with the disease; 5) clinical aspects of CFIDS and approach to communication and care of patients should be readdressed and reinforced during the third-year Outpatient Internal Medicine Clerkship; and 6) prior to graduation from medical school, resurvey students to assess perceptions of commonly misunderstood medical conditions, and their approach to diagnosis, management and care of these conditions.

By including CFIDS in the Vermont Integrated Curriculum, graduates from the UVM College of Medicine will be better prepared as future physicians to confidently diagnose and manage CFIDS. Students will not only be in a position to effectively advocate and provide compassionate care for their own patients with CFIDS, but they will also be able to educate other professionals, and improve the overall quality of health care available to this vulnerable patient population.

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