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EDITORIAL

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

Myalgic Encephalomyelitis (ME) in the Young. Time to Repent

Myalgic encephalomyelitis (ME)/ Chronic fatigue syndrome (CFS) is a complex disease with symptoms from multiple organ systems. The severity of these symptoms ranges from mild to severe with the most severely affected confined to a dark room to achieve sensory deprivation. Two incidence peaks have been described between age 10-19 years and 30-39 years, respectively. Typically women are more often affected than men in a 3:1 ratio.[1]

In spite of such severe symptoms, ME is poorly understood and for years has been a controversial condition. However, in 2015 a paradigmatic change occurred when the Institute of Medicine (IOM), now known as National Academy of Medicine in United States, based on analysis of more than 9.000 peer-reviewed studies, concluded that ME/CFS is a serious chronic multisystem and biological disease that substantially limits the activities and quality of life of patients.[2] This report paved the way for an extensive commitment to biomedical ME research by National Institutes of Health (NIH). Four NIH-funded centres in the United States—of these, one serves as a Data Management and Coordinating Center—were established focusing on immunological, microbiological, genetic and epigenetic as well as inflammatory aspects of the illness. The NIH has tripled its research funding for ME/CFS from $5 million in 2014 to $16 million in 2018. Published data from these centres and other research groups were recently summarised by Komaroff,[3] and these results have contributed to the shift in focus from a previous psychosomatic to a biomedical understanding of ME.

Already in the 1990s, it was demonstrated that ME affects the central and autonomic nervous system. In recent years, metabolic and immunological changes have been detected. One of the most exciting findings come from very new studies indicating that low-grade neuroinflammation triggers many of the symptoms of this illness such as pain, cognitive problems and sleeping disorders.[3] In 2016, Hornig et al analysed cytokines in the cerebrospinal fluid of ME patients and concluded that the results indicate a markedly disturbed immune signature in the cerebrospinal fluid that is consistent with immune activation in the central nervous system, and a pattern associated with autoimmunity.[4] Activated microglia, elevated lactate, as well as temperature (an approximately 0.5°C increase) in the brain of ME patients [5,6] all indicate a low-grade inflammation which is compatible with how patients themselves describe their condition. What triggers the neuroinflammation is still not fully understood; however, infection, typically by herpes viruses, often precedes the manifestation of the illness. Autoantibodies have been found in some but not all of these patients; in addition, chronic stress maybe of significance. Gut microflora changes and associated inflammation maybe one peripheral trigger of neuroinflammation. Several recent metabolomics studies indicate that ME patients are in a hypometabolic state, similar to what occurs in hibernation.[3]

Other studies have demonstrated that during exercise, ME patients have a lower anaerobic threshold with lower heart rate and blood pressure. They frequently have postural orthostatic tachycardia syndrome (POTS). ME patients often have elevated lactate levels at rest, and by repeating physical stress test two days in a row, ME patients do not recuperate between the two exercise sessions, starting out with higher lactate levels the next day.[7,8]

A condition called postexertional malaise (PEM) is a hallmark of ME and should be included in all diagnostic workup of this illness. Patients experiencing PEM will often describe a «crash», relapse» or «collapse» after mental or physical exertion that was previously tolerated. It can take hours, days, a week or even longer to return to the previous baseline after a crash.[2]

One reason for the controversy regarding this disease is that investigators are applying different inclusion criteria. Definitions before 2003 when the so-called Canadian criteria were published did not include PEM. It is also important to know that modified diagnostic criteria should be applied to the paediatric ME patient group.[9] Today, there is agreement that inclusion criteria without PEM are not satisfactory. The wide variation in understanding and in prevalence reported maybe caused by different inclusion criteria. For instance, the so-called Oxford criteria, which do not include PEM, would involve a large percentage of pure psychiatric conditions and should not be applied. Many patients are in fact misdiagnosed by applying inadequate criteria, such as the Oxford criteria. Especially for paediatric patients, this may have severe implications. As pointed out recently by Geragthy and Adeniji, false positive diagnosis may lead to inappropriate labelling and improper intervention and treatment of this vulnerable patient group.[10] Further, by applying wide criteria such as the Oxford criteria, a true understanding and therefore progress for ME patients has been slowed down and even blocked.

Cognitive changes as so-called brain fog, concentration and memory problems are typical in children and adolescents with ME, with severe consequences for well-being, development, school performance and future employment. The study in this issue of Acta Paediatrica by Katherine Rowe regarding management of ME patients aged 6-18 years is therefore timely and of importance.[11] The patients from Victoria, Australia were diagnosed with ME/CFS between1991 and 2009. Questionnaires were returned from 626 patients regarding symptom management and a self-management lifestyle plan including social, educational, physical and pleasurable activity outside of home. A management plan helped these patients to regain control over their lives. Factors of importance were early

diagnosis, empathetic and informed physicians, self-management strategies and educational support helping them to function and remain socially engaged. Lack of understanding and recognition of the illness by doctors and teachers were common and expressed by one-third of the respondents as negative factors.

The study has some weaknesses. Due to the long observation period, inclusion criteria of ME changed. The first enrolled patients were diagnosed according to the so-called Holmes criteria from 1988—a purely research diagnosis that did not include PEM. Further, the study does not include the most severe ME patients who are housebound.

Based on evidence from Rowe's study and the biomedical data summarised above, there is an imminent need to avoid patients being misdiagnosed or further stigmatised by falsely equating the disease with chronic or unexplained fatigue, psychosomatic classifications, functional disorders, medically unexplained symptoms or neurasthenia.

It is, therefore, concerning that the child welfare in several countries, including my own, starts custody cases, threatening to remove young ME patients from their families into emergency placement in youth centres or foster homes. These child protection cases are based on the not updated view that ME is a functional disorder that can be addressed by ignoring physical symptoms and increasing scholarly, physical and social activity. Parents are accused of life-threatening neglect by letting their children rest in isolation. This attitude, however, ignores the international consensus definition of ME/CFS as a serious somatic disorder in which overexertion may have long-lasting or even permanent detrimental effects. To my knowledge, removing such patients from their parents has never been proven to be effective therapeutically. To the contrary, such non-evidence based practice has been shown to contribute much harm and should not be accepted.

A reorientation of the understanding and attitude to ME patients occurs worldwide. ME patients, especially the worse cases, suffer enormously. Among them, the paediatric patients are most vulnerable, representing a special challenge due to the occurrence in the midst of somatic growth and emotional development. We are waiting for a biomarker of this disease, and some are in the pipeline. And even more, we are hoping for an effective treatment. Still, it is already now time for the medical profession as well as the whole society to repent, as these patients have previously often not been treated with the respect and care they need and deserve.

CONFLICTS OF INTEREST

The author has no conflicts of interest to declare.

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