

Chapter 18

Childhood Neurodegenerative Disorders

Lal Devayanivasudevan Nair
Saveetha Medical College, India

ABSTRACT

Neurodegenerative disorders (NDs) are a group of disorders with the deterioration of attained skills often with no solutions, usually ending with death or crippling disabilities. This chapter contains a classification for childhood NDs as well as an algorithmic approach for easy management of these disorders. Genetic defects and pathophysiology of disorders like Canavan, Krabbe, subacute sclerosing panencephalitis (SSPE), etc. are written in detail. Suggestions regarding management of some of these conditions are described as a lifecycle approach, from birth to death, to enable those who are taking care of such kids. Allogeneic hematopoietic stem cell transplantation (HSCT), gene therapy, combination therapy, and other experimental therapies have enlarged the scope of diagnosis and treatment options for these disorders. The author aims to brush up the existing and latest possibilities in NDs, including those at the experimental stage, for an easy understanding and for further research, especially as treatment options.

INTRODUCTION

Childhood NDs are neglected group of central nervous system (CNS) disorders by clinicians, as much of these disorders have no answers and hence any investigations to find out cause of a developmental problem due to NDs are mainly of academic interest. Fresh interest among clinicians in this is kindled by recent advances in molecular diagnosis and neurosciences, in addition to newer modalities on treatment. Childhood NDs are mainly genetic mutations resulting in either enzyme deficiencies or formation of abnormal products in nervous system (Marder, K et al, 1998). Most of the disorders, where definitive mutations and abnormal products have been identified in CNS, have significant variations in their clinical presentations. The knowledge about the cause of this individual variations is however limited. Individuals who carry the same mutation in the same disease-causing gene may display a range of different clinical symptoms (Kwon, 2016). This chapter gives a bird's eye view of the common NDs in children and tries

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to bridge the gap between research and possible application of the knowledge in real life. It shall be the authors endeavor to put in approaches where ever such new knowledge can be inserted to find new ways of analyzing these disorders clinically. In this process author tries to bring in an algorithmic model utilizing the existing and new knowledge to find easy clinical approaches that also serves as a clinical classification. Where ever possible the author puts in life cycle approach, i.e., birth to death, to solve the difficulties these children undergo. Recent advances and possible areas of new researches are also added in this chapter, along with each disorder. The main objective of this chapter is to consolidate the existing knowledge from diverse sources to help in easy understanding to facilitate clinical management and bring out to fine tune the ideas and possibilities from the new options emerging out of researches.

BACKGROUND

NDs are a group of disorders often associated with constellations of findings suggesting loss of acquired skills, loss of memory; impairment of intellect; personality and behavioral changes, in addition to definite neurological signs like vision and hearing loss, changes in tone, seizures etc. However quite many NDs are due to identifiable causes like genetic, biochemical defects, chronic viral infections. With the advent of better imaging techniques and biochemical and molecular markers, a specific diagnosis is possible in many case; but thorough history and clinical examination still give chances to suggest a possible diagnosis (Kwon, 2016).

Most of the NDs of childhood are neurometabolic disorders. Often multisystem involvement with CNS signs and regression of attained milestones points to a neurometabolic disorder affecting the CNS. The age of onset, progression of the disease process and primary finding helps one to determine whether we are dealing with white matter or grey matter disorders (GM) (Kwon, 2016). Increasing spasticity and Upper Motor Neuron signs is a pointer towards white matter (WM) disease while seizures, visual impairment, loss of memory and executive functions are pointers to grey matter injury. This over simplification cannot explain the reason behind behavioral changes occurring in WM lesions. In fact, WM lesion often results in neurobehavioral disconnection syndromes due to disruption in nerve bundle connecting 2 cortical areas (Schwachman et al, 2008).

With the differentiation between presentation of GM and WM disorders decreasing and newer magnetic resonance imaging (MRI) evidences blurring these distinctions, a newer method of classification based on abnormal molecules or mutations is warranted. Even when options are limited, work up for a diagnosis is still needed for the promotion of preventive care in subsequent pregnancies. Advances in enzyme therapies can be of use only if diagnosed at an early age. This scenario necessitates the consolidation of emerging knowledge at different domains, including animal research, and linking it with existing ones.

CLASSIFICATION OF CHILDHOOD NEURODEGENERATIVE DISORDERS

The classification offered in some textbooks based on site involved is too simplistic and often confusing as mixed presentations are seen (Shu et al, 2017).

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