

A rare case of hereditary ataxia: Gordon Holmes syndrome

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ABSTRACT

Gordon Holmes syndrome is an extremely rare, autosomal recessive condition with characteristic features of cerebellar progressive ataxia, cerebellar atrophy, and hypogonadotropic hypogonadism, which was first described in 1908 by the British neurologist of the same name. Two genes have to date been frequently associated with this syndrome, RNF216 and PNPLA6.¹ A 23-year-old man presented with secondary sexual character deficiency and progressive difficulty in gait persisting for several years. He was eventually immobilized after seven years of ongoing symptoms and was definitively diagnosed with Gordon Holmes syndrome after genetic testing revealed RNF216 gene mutation.

Key words: Cerebellar ataxia, ubiquitin, RNF216, neuro-endocrinology

INTRODUCTION

Gordon Holmes syndrome, an autosomal recessive, adult-onset condition marked by progressive cognitive decline, dementia, ataxia, and chorea, in addition to hypogonadotropic hypogonadism, was first described by the British neurologist of the same name in 1908.¹ Holmes made major contributions to the study of cerebellar physiology and challenged the current conventional ideas regarding the unitary physiology of the cerebellum, even during the First World War, when he served as consultant neurologist to the British Army on the Western Front. He was subsequently awarded the CMG and CBE and was knighted in 1951. After the war, he published comprehensively in the field of neurology, and was actively engaged in neurological practice, research and education.²

Several studies have shown that the initial symptoms of this syndrome appear in early adolescence and present as difficulty in speaking.³ Mutations in either the RNF216 or PNPLA6 genes are thought to represent the underlying cause of Gordon Holmes syndrome, although there are rare instances in which no mutation has been identified. The underlying pathophysiology involves mutations in these particular genes, which cause ubiquitin to bind to healthy proteins and induce apoptotic processes, leading to cell death.⁴ This cell death may lead to progressive ataxia, hypogonadotropic hypogonadism, and structural changes in the brain such as cerebellar atrophy and white matter lesions.⁵

However, due to its rarity and frequent misdiagnosis, the prevalence of Gordon Holmes syndrome remains unknown.

A SHORT OVERVIEW OF THE RECENT LITERATURE ON GORDON HOLMES SYNDROME

Gordon Holmes syndrome, also known as autosomal recessive spinocerebellar ataxia type 16 (SCAR16), was first described in 1908.⁶ Although nearly 110 years have since passed, to our knowledge there are still only 10 case reports in the literature. The most recent reported case is located in India with homozygous mutation for RNF216, a 30-year-old male patient with progressive ataxia and hypogonadotropic hypogonadism.⁷ Neuroimaging in that case revealed hyperintensities in the white matter in FLAIR-MR images.⁸ Chio et al.⁹ described a patient from Taiwan with cerebellar ataxia and mutation in STUB1, another gene that can lead to Gordon Holmes syndrome. In 2019, another case was reported exhibiting classic Gordon Holmes syndrome symptoms of ataxia, amenorrhea, and cerebellar syndrome.¹⁰ That case was similar to that of a 26-year-old man reported in 2008, who presented with slowly progressing loss of balance and speech difficulty with hypogonadotropic hypogonadism.¹¹ However, the diagnosis was unfortunately not confirmed by

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Critchley, Frank Clifford Rose, William F. Bynum, 1982 Routledge Handbook of Motor Control and Motor Learning Albert Gollhofer, Wolfgang Taube, Jens Bo Nielsen, 2013-01-17 The Routledge Handbook of Motor Control and Motor Learning is the first book to offer a comprehensive survey of neurophysiological behavioural and biomechanical aspects of motor function Adopting an integrative approach it examines the full range of key topics in contemporary human movement studies explaining motor behaviour in depth from the molecular level to behavioural consequences The book contains contributions from many of the world's leading experts in motor control and motor learning and is composed of five thematic parts Theories and models Basic aspects of motor control and learning Motor control and learning in locomotion and posture Motor control and learning in voluntary actions Challenges in motor control and learning Mastering and improving motor control may be important in sports but it becomes even more relevant in rehabilitation and clinical settings where the prime aim is to regain motor function Therefore the book addresses not only basic and theoretical aspects of motor control and learning but also applied areas like robotics modelling and complex human movements This book is both a definitive subject guide and an important contribution to the contemporary research agenda It is therefore important reading for students scholars and researchers working in sports and exercise science kinesiology physical therapy medicine and neuroscience *Neurological Eponyms* Peter J. Koehler, George W. Bruyn, John M. S. Pearce, 2000-10-26 Neurology abounds with eponyms Babinski's sign Guillain Barre syndrome Alzheimer's disease etc Neurologists and neuroscientists however are often hazy about the origin of these terms This book brings together 55 of the most common eponyms related to the neurological examination neuroanatomy and neurological diseases The chapters have a uniform structure a short biography a discussion of and a quotation from the original publication and a discussion of the subsequent evolution and significance of the eponym Photographs of all but two of the eponymists have been included The material is organized into sections on anatomy and pathology symptoms and signs reflexes and tests clinical syndromes and diseases and defects The selection of eponyms was based on the frequency of use familiarity of clinical neurologists with the concept and the significance within neurology of the individual who coined the eponym This volume covers some of the classic ideas in the history of clinical neurology It will be of interest to neurologists neuroscientists medical historians and their students and trainees *General Catalogue of Printed Books* British Museum. Department of Printed Books, 1969 **Companion to Clinical Neurology** William Pryse-Phillips, 2009-06-03 This book is designed for the neurologist who in this day of unusually strict accountability needs to have at hand an authoritative guide to the diagnostic criteria for all conditions that he or she may be faced with in clinical practice While originally conceived as a compendium of diagnostic criteria the author has felt the need to expand the work to include definitions of practically all terms that are used in neurology today Historical elements are also provided including entries of important neurologists and neurosurgeons who have impacted the field The result is an effective representation of the tools of the trade for the neurologist in training and a concise and precise source for the practicing neurologist The

second edition was published in 2003 Since then advances in the definition of many neurological conditions have been made all of which have been incorporated in the third edition There has also been a fine tuning of the definitions and diagnostic criteria of many other conditions The author has collated over 1300 articles since the last edition in order to update many of the entries As such the entries will have the most up to date definition of diseases symptoms diagnostic tests and pearls of wisdom The third edition remains an invaluable guide to the spectrum of neurological practice and with nearly 7 000 references this truly is the bible of neurological terms and conditions

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John Hughlings Jackson Macdonald Critchley, Eileen A. Critchley, 1998-06-11 This book traces the life and scientific career of Dr John Hughlings Jackson 1835 1911 the English physician who pioneered the development of neurology as a medical specialty during the reign of Queen Victoria Jackson made a number of scientific discoveries in several areas of higher nervous activity and language and contributed greatly to the study of various types of epilepsy He isolated the form of epilepsy associated with localized convulsive seizures known as Jacksonian epilepsy His research on epilepsy stretched across a broad spectrum and included uncinat attacks intellectual auras and many other manifestations which are now collectively covered by the term temporal lobe epilepsy He was also among the first to recognize the pattern of disease of the cerebellum Jackson s research was not limited to epilepsy and encompassed studies in aphasia and neuro ophthalmology Following the concepts of the philosopher Herbert Spencer Jackson devised a hierarchy of the nervous system with positive and negative manifestations of neurological activity His work was based on a detailed insightful evaluation of the clinical symptoms of diseases of the brain coupled with meticulous repeated studies of their phenomena Jackson s observations of localized brain lesions led to the first cases of neurosurgical ablation of brain tumours Much of his original work still forms the foundation of our contemporary understanding of the dissolution of language caused by disease A straightforward comprehensive account of the life of an eminent physician John Hughlings Jackson Father of English Neurology is written as a monument to a man who aroused the deepest respect and affection in his students and colleagues Neurologists neurosurgeons psychiatrists pathologists neuroscientists residents and medical students will find this book a source of inspiration and will relish its rare description of medicine in 19th century England

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Intimate Subjects Simeon Koole, 2024-07-26 An insightful history of nineteenth and twentieth century Britain told through a single sense touch When where and who gets to touch and be touched and who decides What do we learn through touch How does touch bring us closer together or push us apart These are urgent contemporary questions but they have their origins in late nineteenth and early twentieth century Britain when new urban encounters compelled intense discussion of what touch was and why it mattered In this vividly written book Simeon Koole excavates the history of these concerns and reveals how they continue to

shape ideas about touch in the present *Intimate Subjects* takes us to the bustling railway stations shady massage parlors all night coffee stalls and other shared spaces where passengers customers vagrants and others came into contact leading to new understandings of touch We travel in crammed subway cars where strangers negotiated the boundaries of personal space We visit tea shops where waitresses made difficult choices about autonomy and consent We enter classrooms in which teachers wondered whether blind children could truly grasp the world and labs in which neurologists experimented on themselves and others to unlock the secrets of touch We tiptoe through London's ink black fogs in which disoriented travelers became newly conscious of their bodies and feared being accosted by criminals Across myriad forgotten encounters such as these Koole shows touch remade what it meant to be embodied as well as the meanings of disability personal boundaries and scientific knowledge With imagination and verve *Intimate Subjects* offers a new way of theorizing the body and the senses as well as a new way of thinking about embodiment and vulnerability today The Dagonet reciter and reader, selected from his own works by G.R. Sims George Robert Sims, 1888

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In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is actually astonishing. Within the pages of "**Selected Papers Of Gordon Holmes**," an enthralling opus penned by a very acclaimed wordsmith, readers set about an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve into the book's central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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