

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 Chiu 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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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 **Vertebrobasilar Ischemia and Hemorrhage** Louis R. Caplan,2015-04-02 A comprehensive review of vascular disease in the vertebrobasilar circulation by one of the world s leading authorities fully updated throughout **The Central Nervous System** Per Brodal,2004 Providing clear well illustrated descriptions of brain structures in light of their functions this cohesive and well established textbook fosters understanding of the intimate relationship between the structure and function of the nervous system Its focus on the integration of basic sciences with their clinical applications makes the book particularly well suited for medical students needing knowledge of neuroscience as a basis for clinical thinking For the third edition two new chapters have been added on the vestibular system and control of eye movements and all other chapters have been thoroughly revised *General Catalogue of Printed Books* British Museum. Department of Printed Books,1969 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 **Historical Aspects of the Neurosciences** Macdonald Critchley, Frank Clifford Rose, William F. Bynum,1982 **The ^ACentral Nervous System** Per Brodal,2010-03-29 A textbook of neuroscience for undergraduate medical students providing a concise yet critical treatment of structure function relationships as a basis for clinical thinking It aims at conveying an understanding of how the nervous system performs its tasks by using data from molecular biology to clinical neurology Stroke E-Book J. P. Mohr, Philip A. Wolf, Michael A. Moskowitz, Marc R Mayberg, Rudiger Von Kummer,2011-05-13 First published in 1986 under the editorial direction of Dr Henry J M Barnett Stroke Pathophysiology Diagnosis and Management continues to provide the dependable current answers you need to effectively combat the increasing incidence of this disease Dr J P Mohr together with new associate editors Philip A Wolf James C Grotta Michael A Moskowitz Marc Mayberg and R diger von Kummer as

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William J. Mullally,2024-07-25 To the non neurologist neurology can be one of the most intimidating fields of medicine yet it includes many common problems faced in everyday primary care practice Written specifically for the general clinician Practical Approach to the Neurological Patient A Clinician s Guide provides clear up to date and easy to understand guidance on commonly encountered issues helping you take an informed approach to patients with neurological concerns Dr William J Mullally and a team of expert contributing authors address headache dizziness stroke pain head trauma and much more making this volume an indispensable resource for primary care practitioners internists family practitioners medical specialists medical residents nurse practitioners physician associates and students Offers concise comprehensive content designed to help guide the primary care provider or non neurologist on how to manage patients with common neurological conditions Covers timely topics such as women s neurology neurogenetics pain neurology sleep disorders dementia and headache including facial pain Includes Key Points in every chapter MRI images that show brain lesions figures and tables throughout and clinical algorithms to support everyday decision making Features multidisciplinary input from physician authors who are contributors to the American Journal of Medicine as well as a nurse practitioner and physician associates

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 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 Each chapter contains a short biography a quotation from and discussion of the original publication and a discussion of the subsequent evolution and significance of the eponym within clinical neurology

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

Neuromotor Mechanisms in Human Communication Doreen Kimura, 1993-05-06 This monograph is based on 20 years of research with patients who have experienced pathology in one hemisphere of the brain It deals with brain mechanisms in human communicative behavior and with related motor functions from a broadly biological point of view In so doing the work discusses the possible evolutionary origins of human communication the relation of brain mechanisms in communicative behavior to analogous nonhuman behaviors and the neural systems involved in various levels and kinds of communication In addition noncommunicative mechanisms which parallel those used in communication such as manual and oral praxis and constructional behavior are outlined in detail Individual differences in brain organization for such functions related to hand preference and sex are also explored Although there is extensive reference to central nervous system pathology the emphasis throughout is on how the findings contribute to understanding normal brain mechanisms Much new data is presented along with the theoretical treatment of human communication which emphasizes a behavioral rather than a linguistic approach This in turn provides continuity with nonhuman primates and early hominids The work will interest psycholinguists cognitive psychologists neurologists clinical neuropsychologists speech pathologists and advanced students in these fields

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