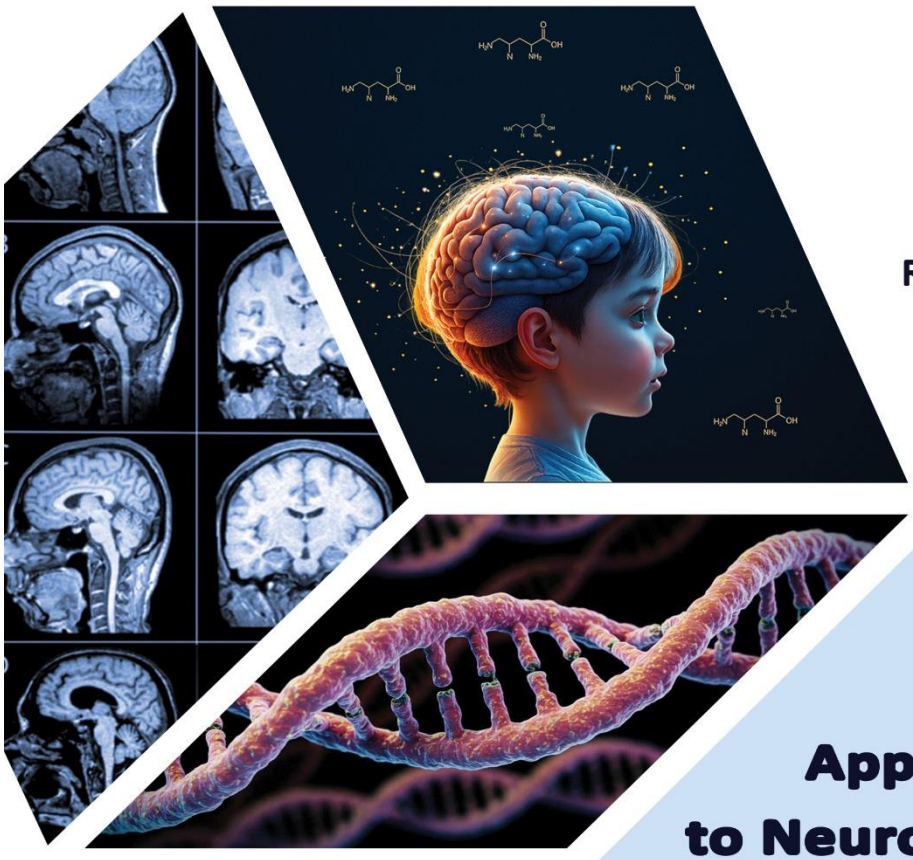

بسم الله الرحمن الرحیم

فهرست مطالب

پوستر اصلی و کارگاه های پانزدهمین کنگره سالیانه نورومتابولیک ایران

The 15th Annual Neurometabolic Congress of Iran

Iranian Neurometabolic Society



18 - 19 December 2025

Rayzan International Conference Center

Approach to Neurometabolic Disorders in View of Clinical Finding

021 - 22909559

Neurometabolic.ir

Neurometabolic.irnmd@gmail.com

Tehran, Niavaran, Kashank, before Ajodanieh intersection, Rayzan International Conference Center


پانزدهمین کنگره سالیانه
نورومتابولیک ایران
آزمایشگاه ژنتیک پزشکی و پاتوبیولوژی
نیل
Iranian Neurometabolic Society
سخنران
دکتر ثمره پنجه شاهی
متخصص ژنتیک پزشکی
دکتر سید محمد میریونسی
متخصص ژنتیک پزشکی
دکتر محدثه فتحی
دکتر شیدا خلیلیان
دبیر علمی
دکتر سید محمد میریونسی
چهارشنبه۲۶– آذر۱۴۰۴
(۱۰ الی ۱۲)
شناسه بازآموزی: ۲۴۵۹۹۴
کارگاه آزمایش های ژنتیک: از درخواست تا تفسیر بالینی مؤثر
(نگاهی بالینی به نقش آزمایش های ژنتیک در تشخیص و تصمیم گیری پزشکی)
محل برگزاری: کاشانک نرسیده به سه راه آجودانیه
مرکز همایشهای بین المللی رایزن – تالار سخن

پانزدهمین کنگره سالیانه نورومتابولیک ایران

Iranian Neurometabolic Society

کارگاه تکنیک ها و روش های نوین آزمایشگاهی در تشخیص اختلالات متابولیک ارثی

سخنران

دکتر سامان ناهید (بیوشیمیست)

دکتر علی طالع (فوق تخصص غدد و متابولیسم کودکان)

دکتر مریم کچویی (فوق تخصص اعصاب کودکان)

چهارشنبه ۲۶– آذر ۱۴۰۴ (۸ الی ۱۰)

شناسه بازآموزی: ۲۴۶۱۵۸

محل برگزاری: کاشانک نرسیده به سه راه آجودانیه
مرکز همایشهای بین المللی رایزن – تالار سخن

پیام رئیس کنگره

پانزدهمین کنگره سراسری نورومتابولیک ایران در تاریخ ۲۶ لغایت ۲۸ آذر ماه ۱۴۰۴ برگزار گردید. در این کنگره تعداد ۱۰ پانل علمی توسط اساتید محترم دانشگاه های علوم پزشکی کشور مدیریت و ارائه شد. هر پانل علمی با عنوان یکی از مباحث مهم به عنوان رویکرد به بیماری نورومتابولیک در نظر گرفته شده بود: مانند مشکلات بینایی، مشکلات شنوایی، مشکلات پوستی، پریفرال نوروپاتی، میوپاتی، اختلالات سایکتری، تشنج و اپی لپسی و . . . . لذا با استفاده از هرکدام از یافته های فوق ورود به بیماری های نونورومتابولیک صورت گرفته و در نهایت تشخیص قطعی می گردد. خوشبختانه در سال های اخیر پیشرفت های قابل ملاحظه ای در مباحث نورومتابولیک صورت گرفته که تمام این تلاش ها منجر به تشخیص زودرس و به موقع و درمان به موقع بیماران خواهد گردید.

حاصل تلاش اساتید محترم در پانل های علمی و سخنرانی ها در قالب کتابچه پیش رو تقدیم می گردد.

دکتر پروانه کریم زاده

رئیس کنگره نورومتابولیک

پیام دبیر علمی کنگره

بنام خداوند قلم

ایزد منان را سپاسگزاریم که توفیق برگزاری پانزدهمین کنگره سالیانه نورومتابولیک حاصل شد. این کنگره با محوریت تظاهرات مختلف بیماریهای نورومتابولیک در دوروز و در محل مرکز همایشهای بین المللی رازی و در قالب ۱۰ پانل فوق تخصصی و با حضور نزدیک به پنجاه نفر از اساتید و صاحب نظران این حیطه برگزار می شود.

ضمن اینکه طی فراخوانی از تمام علاقمندان دعوت به ارسال مقالات مربوط گردید که به تبع آن ۱۳ مقاله به دبیرخانه کنگره ارسال و از این میان مورد بدلیل عدم انطباق موضوعی حذف، سه مقاله به انتخاب کمیته علمی بعنوان مقالات منتخب قابل ارائه بصورت Oral presentation برنامه ریزی شد. ۷ مقاله باقیمانده بصورت E Poster در محل برگزاری همایش جانمائی گردید.

امید آن داریم با انتخاب بر اساس نیاز سنجی بحث ها، زمانبندی و نظم در اجرای برنامه ها و ارائه مطالب بروز و کاربردی گامی در جهت ارتقا خانواده نورومتابولیک برداشته باشیم.

در خاتمه بر خود فرض می دانم از حمایتهای همیشگی استاد کریم زاده هنرگوار، استاد اشرفی گرانقدر و زحمات همکار عزیزم سرکار خانم دکتر قناعتی و تیم اجرائی هدل و یکدستان سپاس ویژه ای داشته باشم.

دکتر فرزاد احمدآبادی

دبیر علمی کنگره نورومتابولیک

پیام دبیر اجرایی کنگره

پانزدهمین کنگره سالیانه نورومتابولیک از تاریخ ۲۶ لغایت ۲۸ آذرماه در مرکز همایش های رازین برگزار می شود و جمعی از اساتید، متخصصین نورولوژی کودکان، فوق تخصص های متابولیک، متخصصین ژنتیک و همکاران آزمایشگاهی را گرد هم می آورد تا تازه ترین دستاوردهای علمی این حوزه را مورد بحث و بررسی قرار دهند.

در روز نخست، کارگاه های علمی با محوریت نقش آزمایشگاه های بیوشیمی و ژنتیک در تشخیص بیماری های نورومتابولیک برگزار می شود. در این کارگاه ها، بر اهمیت تشخیص زودهنگام، تفسیر دقیق یافته های آزمایشگاهی و بهره گیری از روش های نوین مولکولی تاکید می شود و تعامل سازنده میان تیم های بالینی و آزمایشگاهی به عنوان یکی از ارکان اصلی مدیریت بیماران مورد توجه قرار می گیرد.

در دو روز بعدی، پانل های علمی متعددی برگزار می گردد که با هدف ارتقای دانش همکاران نورولوژی کودکان طراحی شده اند. در این پانل ها، تازه ترین مباحث تشخیصی و درمانی، چالش های بالینی، رویکردهای نوین مدیریتی و تجربه های مراکز مختلف مطرح می شود و فضای علمی پویا و تعاملی شکل می گیرد.

این کنگره بستری برای هم افزایی علمی، توسعه همکاری های بین رشته ای و تقویت پژوهش های ملی فراهم می کند و بر ضرورت حرکت به سوی ایجاد شبکه های منسجم تشخیصی، رجیستری های تخصصی و پروژه های چندمرکزی تاکید می نماید. نگاه حاکم بر این رویداد، نگاهی رو به آینده است؛ آینده ای که در آن تشخیص های دقیق تر، درمان های هدفمند تر و مراقبت های ساختاریافته تر کیفیت زندگی بیماران نورومتابولیک را ارتقا می دهد.

اینجانب به عنوان دبیر اجرایی کنگره، ضمن قدردانی از اعضای محترم کمیته علمی، سخنرانان و شرکت کنندگان گرامی، امیدوارم که این گردهمایی علمی مسیر پیشرفت مستمر دانش نورومتابولیک کشور را ترسیم کند و زمینه ساز شکل گیری همکاری های پژوهشی گسترده تر در سال های پیش رو باشد.

دکتر فائزه قناعتی

دبیر اجرایی کنگره نورومتابولیک

درباره انجمن

پایه گذاری **انجمن علمی نورومتابولیک ایران** از سال ۱۳۹۱ در بیمارستان کودکان مفید صورت گرفت لیکن فعالیت اصلی انجمن پس از تصویب از سال ۱۳۹۴ آغاز و پی ریزی شد. اهداف انجمن شامل اهداف آموزشی، پژوهشی و درمانی بوده و استراتژی طوالنی مدت در راستای اهداف انجمن طراحی شده است. در راستای این اهداف استراتژیک چشم انداز آینده انجمن برای سال ۱۴۰۵ رسیدن به رتبه بهترین و بالاترین انجمن کشور از نقطه نظر پژوهشی و آموزشی می باشد. این انجمن با اعضای تایید شده ۷۵ نفری و اعضای در انتظار تایید ۸۰ نفری خود یکی از انجمن های بین رشته ای می باشد که می تواند پاسخگوی قسمتی از نیازهای آموزشی و پژوهشی رشته های مغز و اعصاب، ژنتیک و غدد باشد. ضمن اینکه ارتباط تنگاتنگی با رشته های رادیولوژی، پاتولوژی و علوم تغذیه و طب فیزیکی و توان بخشی دارد. در رابطه با عملکرد انجمن برگزاری جلسات هفتگی معرفی Case که به صورت مستمر در سه سال اخیر بدون وقفه ادامه یافته است، جلسات ماهیانه نورومتابولیک و نهایتا ۱۱ دوره کنگره سالیانه نورومتابولیک است که حتی پیش از شروع به کار رسمی انجمن از سال ۱۳۹۱ برگزار گردیده است.

لیست اعضای هیئت مؤسس انجمن: خانم دکتر پروانه کریم زاده، آقای دکتر محمودرضا اشرفی، آقای دکتر فرزاد احمدآبادی، آقای دکتر مسعود هوشمند ویژه، آقای دکتر محمدرضا عالیی، آقای دکتر سعید طالبی، خانم دکتر فاطمه سرخیل، خانم دکتر مرجان شکیبا

اعضای کمیته علمی

۱. دکتر پروانه کریم زاده
۲. دکتر محمودرضا اشرفی
۳. دکتر فرزاد احمدآبادی
۴. دکتر فائزه قناعتی
۵. دکتر محمود محمدی
۶. دکتر رضا شروین بدو
۷. دکتر مهران بیرقی طوسی
۸. دکتر حسین اسلامیه
۹. شهریار نفیسی
۱۰. دکتر مرتضی حیدری
۱۱. مهدی اکبری
۱۲. دکتر تکتم موسویان
۱۳. دکتر مرجان شکیبا
۱۴. دکتر آزیتا توسلی
۱۵. دکتر محمدمهدی تقدیری
۱۶. دکتر سرور اینالو
۱۷. دکتر نرجس جعفری
۱۸. دکتر فاطمه عبدی
۱۹. دکتر علی طالع
۲۰. دکتر حمیده نژادبیگلری
۲۱. دکتر شهرام نصیری
۲۲. دکتر حسین نجم ابادی
۲۳. دکتر یلدا نیلی پور
۲۴. دکتر مسعود قهوه چی
۲۵. دکتر غلامرضا زمانی
۲۶. دکتر مرضیه بابایی
۲۷. دکتر محمدوفایی شاهی
۲۸. دکتر آریانا کریمی نژاد
۲۹. دکتر شاداب صالح پور
۳۰. دکتر هدیه صانعی فرد
۳۱. دکتر پریناز حبیبی
۳۲. دکتر محمدمهدی ناصحی
۳۳. دکتر ساسان ساکت
۳۴. دکتر میترا خلیلی
۳۵. دکتر فخرالدین شریعتداری
۳۶. دکتر محمد روحانی
۳۷. دکتر مهری سالاری
۳۸. دکتر علی نیک خواه
۳۹. دکتر میثم بابایی
۴۰. دکتر محسن جوادزاده
۴۱. دکتر کتایون رازجویان
۴۲. دکتر سعید انوری
۴۳. دکتر آیدین تبریزی

اعضای کمیته اجرایی

۱. دکتر فائزه قناعتی
۲. دکتر پروانه کریم زاده
۳. دکتر فرزاد احمدآبادی
۴. سرکار خانم فرزانه نوریاران
۵. سرکار خانم مهشاد دلاوری
۶. سرکار خانم فاطمه روح الامینی
۷. سرکار خانم الهه خاری
۸. سرکار خانم هستی فدوی
۹. سرکار خانم سعیده امین زاده
۱۰. سرکار خانم کیانا نقوی
۱۱. سرکار خانم روژان اسماعیلی
۱۲. سرکار خانم تارا اسدی
۱۳. سرکار خانم پریا مهدوی
۱۴. سرکار خانم آیدا عباسی
۱۵. جناب آقای ارد جلالی خلیل ابادی
۱۶. جناب آقای رسا ازاد

پانزدهمین سمینار سالیانه نورومتابولیک ایران

طیف علائم بالینی در بیماریهای نورومتابولیک

رئیس سمینار: دکتر پروانه کریم زاده دبیرعلمی سمینار: دکتر فرزاد احمد آبادی دبیر اجرایی سمینار: دکتر فائزه قناعتی

روز اول – ۲۷ آذر

زمان	عنوان پانل	اعضا
08:00-08:15	قرآن و سرود	
08:15-08:30	کلیپ کنگره	
08:30-09:00	خیر مقدم و افتتاحیه	ریاست انجمن: دکتر محمودرضا اشرفی ریاست کنگره: دکتر پروانه کریم زاده دبیر کنگره: دکتر فرزاد احمدآبادی
09:00-10:10	Seizure in Neurometabolic Disorders	دکتر محمود محمدی دکتر رضا شروین بدو دکتر مهران بیرقی طوسی دکتر حسین اسلامیه

دکتر شهریار نفیسی) دکتر مرتضی حیدری دکتر مهدی اکبری دکتر تکتم موسویان	Neurometabolic Hearing loss &Bulbar dysfunction	10:10-11:20
Break		11:20-11:50
دکتر پروانه کریم زاده دکتر مرجان شکیبا دکتر آزیتا توسلی دکتر فاطمه عبدی	Ophthalmic presentation of Neurometabolic Disorders	11:50-13:00
دکتر فرزاد احمدآبادی دکترعلی طالع دکتر حبیبه نژاد بیگلری دکترشهرام نصیری	Dermatological presentation of Neurometabolic Disorders	13:00-14:10
نهار و نماز		14:10-15:10
دکتر محمودرضا اشرفی دکترحسین نجم ابادی دکتریلدا نیلی پور دکتر مسعود قهوه چی	Myopathic presentation of Neurometabolic Disorders	15:10-16:20
دکترغلامرضازمانی دکتر نرجس جعفری دکتر مرضیه بابایی دکتر محمد وفایی شاهی	Neuropathic presentation of Neurometabolic Disorders	16:20-17:40

روز دوم– ۲۸آذر

زمان	عنوان پانل	اعضا
08:15-09:30	Dysmorphism in Neurometabolic diseases	دکتر آریانا کریمی نژاد دکتر شاداب صالح پور دکتر هدیه صانعی فرد دکتر فائزه قناعتی دکتر پریناز حبیبی
09:30-10:40	Stroke & stroke like in Neurometabolic Disorders	دکتر محمدمهدی ناصحی دکتر ساسان ساکت دکتر میترا خلیلی دکتر فخرالدین شریعتمداری
10:40-11:15	Break	
11:15-12:20	Movement disorders and ataxia in IEMs	دکتر محمد روحانی دکتر مهری سالاری دکترعلی نیک خواه دکتر میثم بابایی
12:20-13:30	Psychiatric presentation of Neurometabolic Disorders	دکتر محسن جوادزاده دکتر کتایون رازجویان دکتر سعید انوری دکتر آیدین تبریزی
13:30-15:00	نهار و نماز	
15:00-15:10	مقاله منتخب: "Neurologic manifestation of Tyrosinemia, interesting cases and review"	دکترسرور اینانلو
15:10-15:20	مقاله منتخب: "Inborn error of copper metabolism: Menkes, Wilson, and MEDNIK"	دکترسیمین خیاط زاده
15:20-15:30	مقاله منتخب: "WDR45 Mutation Presenting as Leigh -Like Encephalopathy in a male: Expanding the Phenotypic Spectrum of Beta-Propeller Protein-Associated Neurodegeneration"	دکترنرگس هاشمی
15:30-16:00	CPC	دکتر محمدمهدی تقدیری

برگزار کنندگان

Iranian Neurometabolic Society

انجمن علمی نورومتابولیک ایران

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انجمن علمی اعصاب کودکان

دانشگاه علوم پزشکی تهران

حامیان کنگره

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tekaje
beyond generics

Skin Manifestations of Neurometabolic Disorders

F Ahmadabadi[1*]

[1*] Associate Professor of Pediatric Neurology, Pediatric Neurology Research Center, Shahid Beheshti university of medical sciences

Abstract

Neurometabolic disorders comprise a heterogeneous group of inherited conditions in which defects of cellular metabolism lead to progressive neurological dysfunction. Beyond the nervous system, the skin often serves as an early and accessible window into these disorders. Cutaneous manifestations may precede neurological symptoms, coincide with disease progression, or signal metabolic decompensation, making them valuable diagnostic clues.

This lecture reviews the spectrum of skin findings associated with major neurometabolic disorders, emphasizing their pathophysiological basis and clinical relevance. Characteristic manifestations include pigmentary abnormalities, photosensitivity, alopecia, ichthyosis, angiokeratomas, xanthomas, connective tissue changes, and distinctive hair shaft abnormalities. Representative conditions such as lysosomal storage disorders, mitochondrial diseases, peroxisomal disorders, aminoacidopathies, and disorders of cholesterol and lipid metabolism will be highlighted.

Through a pattern-based approach and illustrative clinical examples, the lecture underscores how recognition of specific dermatologic signs can guide targeted metabolic evaluation, reduce diagnostic delay, and facilitate earlier intervention. Increased awareness of these cutaneous clues among neurologists, pediatricians, and dermatologists can significantly improve diagnostic accuracy and multidisciplinary care in patients with neurometabolic diseases.

Keywords

- Neurometabolic
- skin manifestation
- Dermatological manifestation

Brown-Vialetto-Van Laere Syndrome: Case Report of Dramatic Response to Riboflavin

Morteza Heidari[1], Masood Ghahvechi Akbari[1], Golazin ShahbodaghKhan[2,3], Masoud Garshasbi[4,5], Reza Shervin Badv[1], Hossein Yousefimanesh[6]

[1] Pediatrics Center of Excellence, Department of Pediatric Neurology, Children's Medical Center, Growth and Development Research Center, Tehran University of Medical Sciences, Tehran, Iran

[2] Department of Pediatrics, Division of Pediatric Neurology, Children's Medical Center, Pediatrics Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran

[3] Myelin Disorders Clinic, Pediatric Neurology Division, Children's Medical Center, Pediatrics Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran

[4] Genetics Research Center, University of Social Welfare and Rehabilitation Sciences, 19857 Tehran, Iran

[5] Department Human Molecular Genetics, Max Planck Institute for Molecular Genetics, 14195 Berlin, Germany

[6] Department of Medicine, Shiraz Medical Students Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Brown-Vialetto-Van Laere syndrome (BVVL) is a rare neurodegenerative disorder caused by riboflavin transporter genes SLC52A2 and SLC52A3 variants. It manifests as a combination of cranial nerve palsies and sensorineural hearing loss. This study presents the case of a 5.5-year-old boy with progressive swallowing difficulties, ptosis, severe hearing loss, and a progressive speech disorder. Remarkably, he showed a significant response to high-dose riboflavin supplementation. Subsequent genetic testing confirmed the diagnosis. Whole exome sequencing identified a homozygous missense variant, [c.239G>A; (p. Gly80Asp)], in the SLC52A3, consistent with BVVL 1. It is essential to remember that BVVL is a set of sensorineural hearing loss and a variety of cranial nerve palsies. Riboflavin should be started as soon as possible because it has a crucial role in neuronal preservation and even reverses the disease.

Keywords

Neurometabolic Disorders and Their Impact on The Auditory and Balance Systems

Mehdi akbari[1]

1 Associate Professor of IRAN university of medical science

Abstract

Neurometabolic disorders are a complex area of medicine and a challenging process due to their broad impact on the sensory and motor systems, requiring a multidisciplinary approach to brain and nervous system function. Neurometabolic disorders are a group of genetic diseases that result from genetic mutations that alter the body's genetic code and disrupt the normal functioning of cellular metabolism. These diseases can have significant effects on daily activities, growth, and physical-motor function. For example, mitochondrial diseases can lead to muscle weakness, neurological disorders, and multisystem problems. Symptoms include mental retardation, behavioral problems, and decreased motor skills, and usually begin in early childhood. Neurometabolic disorders can cause a wide range of symptoms that vary depending on the type of disease and the age of the patient. These symptoms may include: uncontrolled seizures, loss of motor or cognitive skills, abnormal movements and muscle weakness, vision problems, hearing impairment, and abnormal head growth, including microcephaly or macrocephaly.

As of 2021, dozens of genes have been identified with disorders that include both neuromuscular dysfunction and SNHL. These disorders often present with developmental delay, hypotonia, epilepsy, or ataxia. When neurons and metabolism are combined, these two elements naturally interact functionally, so many normal sensory and motor activities and physical skills are known to be coordinated. The auditory and vestibular systems are among the most important senses in developing life skills. Numerous studies on people with neurometabolic disorders indicate the prevalence of hearing and balance disorders. In a study conducted by Daniel Orang et al. (2025) between 2021 and 2025, they looked at 38 genes that had the greatest impact on hearing and the developmental system. The most notable point in their study and suggestions was that: The symptoms emphasize that hearing loss can serve as

an early marker of systemic neurogenetic disease, which may provide the best opportunity for timely intervention. A study that consecutively enrolled 100 children with profound-severe sensorineural hearing loss (SNHL) reported neurodevelopmental disabilities in 48% of the children, including motor and cognitive disabilities [7]. These findings demonstrate how the development and function of the auditory system are intertwined with the central and peripheral nervous systems[^] .

Neurometabolic disorders can cause neuropathy in the auditory system, in which case the first symptoms of the patient are expected to be hearing loss, speech comprehension, and auditory processing difficulties. For this purpose, a series of subjective and objective tests of the auditory system, including pure tone audiometry, tympanometry, and a series of auditory processing tests, and auditory brainstem response tests, otoacoustic emissions, etc., should be used. Given the proximity and coordination between the two auditory systems and the vestibule and the prevalence of balance disorders co-occurring with hearing problems, balance examinations are also essential.

Discussion

Hearing and balance problems in metabolic disorders can be the first and main symptom and clue to diagnosis in certain IMDs. Therefore, HL evaluation can be useful when IMD is suspected, especially for diseases that are difficult to diagnose. In studies, the cause of approximately 50% of SNHL is unknown. On the other hand, . Most IMDs present with SNHL. These problems are associated with neuronal demyelination, polyneuropathy, or accumulation of molecules in inner ear structures (e.g., inner and outer hair cells, spiral ganglion nerve, supporting cells). The reviewed studies suggest that HL should be considered in the child for IMD evaluations at the same time as other evaluations. For this reason, it is important to recognize and manage all symptoms that occur, including HL, and balance problems. Overall, HL is not uncommon in IMD and should be considered as part of a diagnostic strategy.

Conclusion

Recent advances in gene discovery have revolutionized our understanding of the molecular basis of neurogenetic disorders associated with hearing loss and balance. Most importantly, the auditory and neural systems have unique metabolic and structural requirements that make them particularly susceptible

to disorders, especially metabolic disorders.
Clinically, the findings emphasize the diagnostic value of hearing loss as a warning factor and a core feature of multisystem neurodevelopmental syndromes.

Keywords

Challenges in Neurometabolic Etiology in Childhood Seizures

Mahmoud Mohammadi[1]

[1] Professor of Pediatric Neurology, Pediatrics Centre of Excellence, Department of Pediatric Neurology, Children's Medical Centre, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Childhood epilepsy is a complex neurological disorder with a diverse etiological landscape. While advances in neuroimaging and genetics have improved diagnostic yields, a significant number of cases remain cryptogenic. Among the identified causes, inborn errors of metabolism represent a critical, yet often overlooked, category in the differential diagnosis of pediatric seizures. This webinar focuses on the profound challenges associated with recognizing and diagnosing neurometabolic disorders as the underlying cause of seizures in children.

The clinical presentation of neurometabolic seizures is notoriously heterogeneous and nonspecific. Seizures can be the inaugural sign, appearing in the neonatal period or later in childhood, and may manifest as infantile spasms, myoclonic, tonic, or intractable focal seizures. The primary challenge lies in their phenotypic overlap with more common conditions, such as hypoxic-ischemic encephalopathy, structural malformations, or genetic epileptic encephalopathies. Missing these disorders without a high index of suspicion can lead to critical delays in targeted management. Key diagnostic red flags that will be discussed include a family history of unexplained neonatal death or consanguinity, developmental regression, multisystemic involvement, specific triggers, and a lack of response to conventional antiseizure medications.

This session will provide a practical framework for the clinician, outlining when to suspect a neurometabolic etiology. We will learn about the interpretation of crucial diagnostic clues from neuroimaging, such as symmetric basal ganglia abnormalities or leukodystrophy, and electroclinical patterns like burst-suppression on EEG. Furthermore, we will navigate a complicated pathway from initial metabolic screening—including blood gases, ammonia, lactate, and urine organic acids—to advanced confirmatory testing like genomic sequencing. Ultimately, this webinar aims to empower clinicians

to overcome these diagnostic challenges, facilitating earlier intervention, which is paramount for improving neurological outcomes in this vulnerable patient population.

Keywords

Maternal Hyperphenylalaninemia and Infant Microcephaly: A Case Report

Saeed Anvari [1]

[1] Department of Pediatrics, Division of Pediatric Neurology, Milad Hospital, Social Security Organisation, Tehran, Iran

Abstract

We report a case of a male infant born with microcephaly, whose mother was found to have severe hyperphenylalaninemia. The infant, born at 2,230 g with a head circumference (HC) of 31 cm, showed only modest HC growth during follow-up. Brain CT was normal. A second sibling similarly exhibited poor head growth. Maternal serum phenylalanine exceeded 30 times the normal level during pregnancy, and dietary adherence was suboptimal. This case highlights the teratogenic effects of maternal phenylalanine on fetal neurodevelopment and underscoring the importance of strict metabolic control during pregnancy.

Keywords

Introduction

Maternal phenylketonuria (mPKU) syndrome occurs when women with hyperphenylalaninemia or PKU have elevated phenylalanine (Phe) levels during pregnancy. High maternal Phe acts as a teratogen, causing microcephaly, intrauterine growth restriction, congenital heart defects, and neurodevelopmental abnormalities in the offspring. Early and strict dietary control including a low-phenylalanine diet significantly reduces these risks (Koch et al., 1991; Harding et al., 2006). Microcephaly is defined as a head circumference more than two standard deviations below the mean for age and sex. In cases of maternal PKU, microcephaly may occur even in the absence of obvious structural brain anomalies, as in our patient, who had a normal CT scan.

Case Presentation

A one-month-and-four-day-old male infant was referred for evaluation of microcephaly. Birth weight was 2,230 g, and HC at birth was 31 cm, increasing to 31.2 cm at first follow-up. The patient was the first child of a non-consanguineous couple, born via spontaneous vaginal delivery. Postnatally, he was hospitalized for 7 days to evaluate the cause of microcephaly. Family history revealed two cousins with gait abnormalities. By 8 months, HC measured 38.4 cm.

Laboratory evaluation revealed that the mother had severe hyperphenylalaninemia (serum Phe >30× normal). Although a low-Phe diet was recommended during pregnancy, adherence was poor. A second sibling was subsequently born and similarly showed restricted head growth, confirming a maternal metabolic effect rather than purely genetic microcephaly.

Discussion

This case exemplifies maternal PKU syndrome. The teratogenicity of elevated maternal phenylalanine has been well-documented, even in mothers with normal intelligence . Strict dietary control prior to conception and throughout pregnancy is crucial. Poor adherence, as in this case, can lead to microcephaly, growth restriction, and neurodevelopmental deficits in the offspring .

Our patient's normal brain CT suggests that microcephaly may occur without major structural anomalies detectable on routine imaging. The recurrence in a second sibling reinforces the role of maternal metabolic environment as the primary etiologic factor.

This case underscores the importance of prenatal metabolic monitoring, dietary counseling, and patient education for women with hyperphenylalaninemia or PKU to prevent maternal PKU syndrome.

Metabolic Myopathies

Mahmoud Reza Ashrafi [1]

[1] Professor of Pediatric Neurology . Children's Medical Center, Pediatrics Center of Excellence, Tehran University of Medical Sciences

Abstract

Metabolic myopathies are a rare group of phenotypically and genotypically heterogeneous disorders characterized by abnormalities in skeletal muscle bioenergetics leading to impaired adenosine triphosphate (ATP) production. They are individually rare and several have received the 'orphan disorder' status.

Impairments in glycolysis/glycogenolysis (glycogen-storage disease), fatty acid transport and oxidation (fatty acid oxidation defects), and the mitochondrial respiratory chain (mitochondrial myopathies) represent the majority of known defects. Mitochondrial disorders, with a frequency of 1/8000 population, are the commonest cause of metabolic myopathies.

The major energy sources for muscle contraction are Glycogen, Glucose, and Fatty acids depending on the type, intensity, and duration of exercise. Skeletal muscle relies on different fuel sources at different times and circumstances . Resting muscle in the fed state uses fatty acids as the primary fuel. Glucose from the blood and derived from muscle glycogen is used during short-term intense exercise. Fatty acids predominate during fasting and prolonged exercise.

The two major distinct syndromes of muscle metabolic disorders are exercise intolerance and rhabdomyolysis +/- myoglobinuria and weakness +/- hypotonia .

Clinically, metabolic myopathies usually cause dynamic and reversible skeletal muscle dysfunction related to exercise.

Non-reversible changes/deficits leading to progressive limb girdle weakness mimicking limb girdle muscular dystrophy (LGMD) can occur.

Specific therapies depend on the precise location and nature of the metabolic blockade.

Enzyme replacement therapy is commonly used in GSD II, providing the

missing GAA enzyme to muscle cells . Similarly, the administration of nucleosides is meant to ameliorate the motor performance of patients with TK2 deficiency .

Pre-exercise oral sucrose administration has been shown to improve symptoms in McArdle disease .

Steroids given at the very beginning of CK elevation may be beneficial to avoid the often-fatal consequences of rhabdomyolysis in lipin-1 deficiency .

Bezafibrate and triheptanoin have been used in FAOD with mitigated outcomes.

Riboflavin supplementation often results in spectacular outcomes in patients with RR-MADD .

As for gene therapy in general, it remains in the preliminary stage.

The efficacy and sustainability of pharmacological interventions in mitochondriopathies are debatable.

Cocktails of vitamins associated with or without L-carnitine and CoQ10 can help .

Keywords

13- Year-Girl with Refractory Seizure and Hearing Loss

Aina Riahi [1]

[1] Pediatric Neurology, Aliasghar Children Hospital, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Abstract

A 3 years old girl with myoclonic seizure and microcephaly was visited in neurologic clinic. She was the third child in family. Her delivery was NVD and term with BW:2200 gr and 9 days addition in NICU in first days of life because of GI bleeding.

The parents had consanguinity. The weight was 7 Kg and head circumference was 41 Cm. She had severe head lag and poor fix and follow. The DTR was 1^{+} and she had severe bilateral hearing loss. She had developmental regression from 9-month-old. The seizure type was myoclonic. The global developmental delay was quite clear.

In brain MRI there was bilateral signal in caudate and putamen nucleus. In laboratory tests, 3 methyl glutaric acid was high in urine organic acids.

The patient was hypoton and she had 20 times myoclonic seizures in a day and EEG had severe abnormal generalized epileptiform discharges.

We requested WES with the impression of genetic disorders and in WES, mutation SERAG1 homozygote, pathogen and autosomal recessive, that was confirmed in patient's SANGER sequencing.

The diagnosis was: 3 methyl glutaric aciduria with deafness, encephalopathy and leigh like syndrome.

Keywords

VLCFA Levels and Peroxisome Biogenesis Disorders in Pediatric Populations

Mehran Beiraghi Toosi [1]

[1] Rare Pediatric Neurological Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

Peroxisome biogenesis disorders (PBDs) are a genetically heterogeneous group of metabolic diseases caused by impaired peroxisome assembly and function. PBDs exhibit striking clinical variability, ranging from lethal neonatal forms to milder childhood-onset presentations such as rhizomelic chondrodysplasia punctata. While elevated very long-chain fatty acids (VLCFAs) remain a key diagnostic feature, unusual cases with normal plasma VLCFA levels highlights the limitations of relying solely on this biochemical marker for diagnosis. Recent studies further implicate dysregulated pexophagy - a targeted autophagic degradation of peroxisomes- in the underlying disease mechanisms. This review underscores the necessity for a multifaceted diagnostic approach that combines thorough clinical assessment, detailed biochemical evaluation, and advanced molecular genetic testing to improve diagnostic accuracy and patient care, particularly in pediatric populations. Advancement in identifying novel biomarkers and targeted therapies offers promise for tailored interventions, underscoring the importance of precision medicine in optimizing outcomes for pediatric PBD patients.

Keywords

- Peroxisome Biogenesis Disorders
- Biomarkers
- VLCFA
- Precision Medicine

A Case of Canavan Disease with A Presentation of Microcephaly: A Case-Report

Parvaneh Karimzadeh[1], Danyal Isapour[2*], Elham Hatami[2], Faeze Ghannati[2]

[1] Department of Pediatric Neurology, School of Medicine, Pediatric Neurology Research Center, Research Institute for Children Health, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2] Pediatric Neurology, Pediatric Neurology Research Center, Shahid Beheshti University of Medical, Sciences, Tehran, Iran.

Abstract

Introduction: Canavan disease is a hereditary neurodegenerative leukodystrophy characterised by the spongiform degeneration of cerebral white matter. CD is defined by mutations in the gene that encodes aspartoacylase (ASPA), the enzyme responsible for hydrolyzing N-acetylaspartic acid (NAA) into acetate and aspartate. Increased NAA and subsequent acetate deficit associated with this condition result in progressive neurological manifestations, including macrocephaly, visuocognitive impairment, and psychomotor retardation. Although CD is a rare disease, microcephaly is extremely rare in these patients. In this report, we presented a case of Canavan disease who was referred to us with microcephaly.

Case presentation: An 8.5-month-old girl of relative parents was referred to us due to developmental delay and microcephaly. The birth head circumference was 35 centimetres. Head circumference at the physical examination was 43 centimetres. Global developmental delay and inability to control head motions, to walk, and to roll over were observed. Hypotonia, inability to sit, inability to phonetize, and inability to fix and follow were found in the infant. Deep tendon reflexes were hyperactive. Magnetic resonance imaging (MRI) and MR spectroscopy (MRS) showed diffused white matter with U-fibre involvements. MRS showed an NAA peak. A high level of NAA was found in the urine analysis. High-performance liquid chromatography (HPLC) of amino acids

was normal. The infant was diagnosed based on these manifestations.

Conclusion: Although Canavan disease is rare, microcephaly can be one of the presentations of this disease, in contrast to the diagnostic criteria of the disease that include macrocephaly.

Keywords

- Canavan disease
- Microcephaly
- Magnetic Resonance Spectroscopy
- N-acetylaspartic acid

Combined Oxidative Phosphorylation Disorders: An Overview

Hosein Eslamiyeh[1]

[1] Associate professor of pediatric neurology, division of neurology, department of pediatrics ,shahid sadoughi university of medical sciences , Yazd, Iran

Abstract

Introduction

Combined oxidative phosphorylation deficiency disorders represent a challenging and heterogeneous group of mitochondrial diseases which include 55 subtypes .In these disorders more than one complex of the mitochondrial respiratory chain is impaired. Because the respiratory chain is essential for producing ATP,these disorders can affect many organs, particularly those with high energy demands such as the brain, heart, liver, and muscles. Unlike single-complex mitochondrial defects, combined OXPHOS disorders indicate broader dysfunction within mitochondrial metabolism, often leading to more severe clinical features and earlier onset of symptoms.

Methods and materials:

The search was conducted in the electronic databases pubmed, Cochrane Database of Systematic Reviews and google scholar addressing term of combined oxidative phosphorylation deficiency was used. A total of 11000 articles were found during our review.

Results:

Combined oxidative phosphorylation deficiency syndromes include 55 subtypes with thousands of reports about their clinical features .based on the article at first , we introduce the steps of oxidative phosphorylation and then it causes.

Oxidative phosphorylation occurs inside mitochondria and involves:

- The **electron transport chain (ETC)**: Complexes I–IV
- **ATP synthase (Complex V)**
- **Numerous assembly factors and cofactors**
- **Mitochondrial DNA (mtDNA)** and **nuclear DNA (nDNA)** genes that encode proteins required for these complexes

When multiple complexes are affected, ATP production drops significantly, resulting in cellular energy deficiency.

Keywords

Causes of Combined OXPHOS Disorders

1. Genetic Mutations

Both nuclear and mitochondrial genes contribute to OXPHOS function. Causes include:

- mtDNA depletion syndromes → markedly reduced mtDNA copy number
- Mutations in nuclear genes involved in:
  - mtDNA replication (e.g., *POLG*, *TK2*)
  - Mitochondrial ribosomal proteins
  - Assembly factors for complex I, III, IV, or V
- Defects in mitochondrial translation → impaired synthesis of multiple ETC protein

2. Abnormal mitochondrial biogenesis

Genes that regulate the formation of new mitochondria (e.g., *PGC-1α*, *TFAM*) can be affected.

Clinical Features

Symptoms vary widely, but combined OXPHOS disorders often present in infancy or childhood with multisystem involvement.

Common manifestations

- **Neurological symptoms**: developmental delay, seizures, ataxia, hypotonia

- **Muscle involvement**: weakness, exercise intolerance, myopathy
- **Cardiac dysfunction**: cardiomyopathy, arrhythmias
- **Liver disease**: hepatomegaly, liver failure (especially in mtDNA depletion syndromes)
- **Failure to thrive**
- **Lactic acidosis**: buildup of lactate due to impaired aerobic metabolism

The severity depends on the specific genetic defect and the tissues most affected.

Diagnosis

Diagnosing combined OXPHOS disorders is complex and its diagnosis is based upon clinical evaluation and laboratory tests including elevated blood or CSF lactate ,elevated pyruvate ,abnormal amino acids, organic acids, or acylcarnitine profiles. also, Tissue biopsy especially muscle biopsy may show Ragged-red fibers (in some but not all cases)and low mtDNA content in mtDNA depletion syndromes, finally genetic study including whole exom sequencing and mtDNA copy-number analysis can accurately confirms the diagnosis

Treatment and Management

There is **no universal cure**, but supportive and targeted treatments can improve symptoms and quality of life.

Supportive therapies

- Nutritional support
- Physical and occupational therapy
- Management of seizures or cardiac issues
- Avoiding mitochondrial toxins (e.g., valproic acid)

Mitochondrial “cocktail” supplements (variable evidence)

According to the type of the disorder, the patient responds to treatment variably. In some types these combinations can contribute in improvement of symptoms and in the others ,they may have lesser effect . These medications often include**:**

- Coenzyme Q10, Riboflavin (B2), L-carnitine, Thiamine (B1), Alpha-lipoic acid, Antioxidants and creatin monohydrate

Emerging therapies

- Gene therapy approaches for specific nuclear mutations
- Nucleoside therapy for certain mtDNA depletion syndromes (e.g., *TK2* deficiency)
- Mitochondrial replacement therapy (in reproductive settings)

Prognosis

The prognosis varies widely. Early-onset combined OXPHOS disorders, especially mtDNA depletion syndromes, often have a poor prognosis. Milder forms due to partial enzyme defects or certain nuclear mutations may allow survival into adolescence or adulthood.

Conclusion:

Combined oxidative phosphorylation disorders represent a challenging and heterogeneous group of mitochondrial diseases. Their complexity arises from the involvement of multiple components of the respiratory chain, diverse genetic causes, and wide variation in clinical manifestations. While current treatments are primarily supportive, advances in genetics and mitochondrial biology offer hope for more targeted therapies in the future.

Metabolic Myopathies

Masood Ghahvechi[1]

[1] Pediatrics Center of Excellence, Department of Pediatric Neurology, Children's Medical Center, Growth and Development Research Center, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Metabolic myopathies (MMs) are a heterogeneous group of metabolic disorders characterized
by defects of enzymatic pathways involved in myocyte metabolism (inborn errors of metabolism).
MMs can affect the skeletal muscle exclusively, or the muscle plus other organs or tissues (metabolic
myopathy plus (MM+), collateral myopathy).
EDX studies are most useful to diagnose a myopathy when further data are needed to exclude alternative diagnoses, confirm the presence of a muscle disease, and narrow down the differential.
EMG may also add diagnostic information relating to the location, type, and severity of the underlying process.
Finally, EMG may be useful in identifying target muscles for biopsy.

Keywords

WDR45 Mutation Presenting as Leigh-like Encephalopathy in a Male: Expanding the Phenotypic Spectrum of Beta-Propeller Protein-Associated Neurodegeneration

Narges Hashemi[1,2], Reza Nejad Shahrokh Abadi[3,4], Mehran Beiraghi Toosi[1,2], Farrokh Seilanian Toosi[5]

[1] Rare Pediatric Neurological Diseases Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

[2] Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

[3] Hakim Hospital, Neyshabur University of Medical Sciences, Neyshabur, Iran.

[4] Clinical Research Development Unit, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

[5] Department of Radiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract

An 8-month-old boy presented with recurrent seizures and developmental regression following sequential episodes of infectious gastroenteritis and pneumonia accompanied by high-grade fever. He was born at term via normal vaginal delivery with a birth weight of 2800 grams and a normal Apgar score. There were no perinatal complications or significant antenatal concerns. Apart from neonatal jaundice, his early postnatal course was unremarkable. The child was the third offspring of consanguineous parents, and there was no family history of neurological, metabolic, or genetic disorders. On neurological assessment, the patient exhibited generalized hypotonia, brisk deep tendon reflexes, and divergent strabismus (exotropia), while fundoscopy was normal. His medications included baclofen and Levetiracetam for spasticity and seizure control. Baseline hematological, biochemical, and metabolic investigations were within normal limits, excluding common metabolic encephalopathies.

Brain MRI revealed T1-weighted hypointensity in the thalami and T2-weighted hyperintensities in the dentate nuclei, pons, substantia nigra, globus pallidus (with edema), and thalami. Diffusion-weighted imaging showed restricted diffusion in the bilateral globus pallidus, substantia nigra, and sub-thalamic nuclei. These findings initially suggested a mitochondrial encephalopathy, particularly Leigh syndrome, due to symmetrical involvement of deep grey matter structures. Comprehensive genetic testing with whole-exome sequencing revealed a hemizygous likely pathogenic variant in the WDR45 gene (ChrX:49075862TCAC>T), confirming a diagnosis of beta-propeller protein-associated neurodegeneration (BPAN; OMIM 300894), an X-linked form of neurodegeneration with brain iron accumulation (NBIA). BPAN accounts for approximately 5–7% of NBIA cases, with around 30 reported male cases of the 160 globally confirmed. The WDR45 gene, located at Xp11.23, encodes a beta-propeller scaffold protein essential for autophagic regulation and neuronal survival. Interestingly, despite the genetic confirmation, no significant iron deposition was observed on MRI, suggesting that radiological iron accumulation in BPAN may develop later in childhood. This likely reflects early lysosomal and mitochondrial dysfunction secondary to defective autophagy, occasionally mimicking Leigh syndrome. This case highlights the importance of considering WDR45-related disorders in infants with Leigh-like encephalopathies, even in the absence of iron accumulation, and highlights the value of genetic testing and longitudinal MRI monitoring using iron-sensitive sequences.

Keywords

- WDR45 Mutation
- Beta Propeller Protein Associated Neurodegeneration
- Neurodegeneration with Brain Iron Accumulation
- Leigh-like Encephalopathy
- Mitochondrial Dysfunction

Neurologic Manifestation of Tyrosinemia Interesting Cases and Review

Soroor Inaloo [1]

[1] professor of pediatric neurology, Shiraz university of medical sciences

Abstract

Tyrosinemia is a genetic disorder characterized by problems breaking down the tyrosine, which is a building block of most proteins. If the condition is untreated, tyrosine and its byproducts build up in tissues and organs, which can lead to serious health problems.

There are three types of tyrosinemia, distinguished by their symptoms and genetic cause. Tyrosinemia type I is the most severe form of this disorder and usually begins in the first few months of life with failure to thrive, diarrhea and vomiting, jaundice, bleeding tendency and liver and kidney failure, some affected children have repeated neurologic crises.

Tyrosinemia type II often begins in early childhood and affects the eyes, skin, and mental development.

Tyrosinemia type III is the rarest of the three types. The characteristic features of this type include intellectual disabilities, seizures, and periodic loss of balance and coordination (intermittent ataxia)

We present 3 case of tyrosinemia with different neurologic presentation: (acute flaccid paralysis, seizure and intellectual disorder) as first clinical presentation. We will discuss clinical presentation of cases and review of clinical presentation and management of tyrosinemia.

Keywords

Inborn Error of Copper Metabolism: Menkes, Wilson, And Mednik

Simin Khayatzadeh Kakhki[1]

[1] Division of Pediatric Neurology, Bahrami Children's Hospital, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Copper is an essential trace element involved in numerous enzymatic and physiological processes, including oxidative phosphorylation, connective tissue formation, neurotransmitter synthesis, and antioxidant defense. Inborn errors of copper metabolism represent a heterogeneous group of rare genetic disorders characterized by disrupted copper transport, distribution, or excretion, leading to either copper deficiency or toxicity. The three major inherited diseases in this category are **Menkes disease**, **Wilson disease**, and **MEDNIK syndrome**.

Menkes disease, caused by mutations in the *ATP7A* gene, results in defective intestinal copper absorption and systemic copper deficiency, leading to progressive neurodegeneration, connective tissue abnormalities, and characteristic "kinky" hair. In contrast, **Wilson disease**, due to mutations in the *ATP7B* gene, is marked by impaired biliary copper excretion and copper accumulation primarily in the liver, brain, and cornea, producing hepatic failure and neuropsychiatric manifestations. **MEDNIK syndrome** (Mental retardation, Enteropathy, Deafness, Neuropathy, Ichthyosis, Keratoderma) , a much rarer and newly recognized disorder resulting from mutations in the *AP1S1* gene, exhibits features overlapping both copper deficiency and overload, reflecting combined impairment of copper transport pathways.

Recent advances in molecular genetics and biochemical diagnostics have improved early detection and understanding of these disorders, allowing for more targeted therapeutic interventions such as copper histidine supplementation in Menkes disease and chelation or zinc therapy in Wilson disease. Continued research into these syndromes—particularly the emerging mechanisms underlying MEDNIK—offers valuable insight into copper homeostasis and potential novel therapeutic strategies.

Keywords	
	• Copper metabolism • Menkes disease • Wilson disease • Mednik syndrome • Atp7a • Atp7b • Ap1s1 • Trace element disorders

Electrodiagnostic Characterization and Pathophysiological Correlates of Peripheral Neuropathy in Hereditary Neurometabolic Disorders

Marzieh Babaee[1]

[1] Associate professor of physical medicine and rehabilitation, Physical medicine and rehabilitation research center, Shahid Beheshti university of medical sciences.

Abstract

Background:
Hereditary neurometabolic disorders encompass a heterogeneous group of rare genetic conditions characterized by enzymatic defects, mitochondrial dysfunction, or transport failures that result in the accumulation of toxic metabolites or energy failure within the peripheral nervous system. Unlike the common metabolic neuropathies associated with diabetes mellitus, these disorders—including Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE), Refsum disease, and Metachromatic Leukodystrophy (MLD)—present unique diagnostic challenges. This abstract examines the neurophysiological signatures of these disorders, aiming to differentiate them from acquired immunologic neuropathies which they often mimic.
Pathophysiology and Clinical Phenotype:
The prototype of this category, MNGIE, is an autosomal recessive disorder caused by mutations in the TYMP gene, leading to thymidine phosphorylase deficiency. This results in the toxic accumulation of thymidine and deoxyuridine, causing mitochondrial DNA depletion and instability. Clinically, patients present with a tetrad of severe gastrointestinal dysmotility, cachexia, ophthalmoparesis, and peripheral neuropathy. Similarly, Refsum disease involves the accumulation of phytanic acid due to a defect in alpha-oxidation. In these conditions, the nerve pathology is driven by the disruption of Schwann cell metabolism (causing demyelination) or direct axonal energy failure.

Electrodiagnostic (EDX) Findings:
Electrodiagnostic testing plays a pivotal role in phenotyping these complex disorders. In MNGIE, nerve conduction studies (NCS) typically reveal a sensorimotor polyneuropathy with prominent demyelinating features. Key findings include:
Conduction Velocities: Generalized, uniform slowing of motor and sensory conduction velocities, often in the demyelinating range (<70% of lower limit of normal).
F-Waves: Prolonged F-wave latencies, reflecting proximal nerve root involvement.
Compound Muscle Action Potentials (CMAP): While slowing is prominent, secondary axonal loss often leads to reduced CMAP amplitudes distally.
Needle EMG: Electromyography may show fibrillation potentials and positive sharp waves indicating active denervation, alongside neurogenic motor unit action potential (MUAP) changes.
Crucially, the electrophysiological pattern in MNGIE mimics Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). However, unlike CIDP, MNGIE neuropathy lacks conduction blocks or temporal dispersion, presenting instead with uniform rather than multifocal slowing.
Differential Diagnosis via EDX:
The abstract contrasts MNGIE with other neurometabolic profiles. Acute Intermittent Porphyria (AIP), for instance, presents with a strictly axonal motor neuropathy, characterized by reduced CMAP amplitudes with preserved conduction velocities, often mimicking Guillain-Barré syndrome. Conversely, Metachromatic Leukodystrophy (MLD) presents with profound, uniform slowing of conduction velocities (often <20 m/s) due to sulfatide accumulation in myelin sheaths.

Conclusion:
Hereditary neurometabolic disorders must be considered in the differential diagnosis of patients presenting with undefined sensorimotor polyneuropathy, particularly when systemic features (GI issues, retinitis pigmentosa) are present. Electrodiagnostic evaluation is essential for categorization. The identification of a "pseudo-CIDP" pattern—demyelination without conduction block—should raise suspicion for MNGIE or metabolic leukodystrophies.

recognizing these specific electrophysiological signatures is critical to avoid misdiagnosis and the inappropriate administration of immunomodulatory therapies, guiding clinicians instead toward genetic confirmation and metabolic management.

Keywords

- MNGIE
- Hereditary Neurometabolic Disorders
- Electrodiagnosis
- Demyelinating Neuropathy
- Nerve Conduction Studies
- Refsum Disease

Familial Co-Segregation of the Arylsulfatase A Variant: Nine Carriers and Three Affected in an Iranian Kurdish Pedigree

Meisam Babaei[1]*,Fatemeh Arab[2], Mahsa Boogari[3]

[1] Department of Pediatrics, North Khorasan University of Medical Sciences, Bojnurd, Iran.

[2] Department of Advanced Technologies, School of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran.

[3] Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background: Metachromatic leukodystrophy (MLD) is an autosomal recessive neuro-metabolic disorder caused by deficient activity of the arylsulfatase A (*ARSA*) enzyme, resulting in severe motor disability, developmental regression, seizures, deafness, and death. The disease presents as a late-infantile, juvenile, or adult form.

Case: We describe a consanguineous Iranian Kurdish family with three affected children (ages 2, 4, and 9 from two sibships. All presented with developmental regression, seizures, cognitive and behavioral decline, and elevated cerebrospinal fluid protein. Brain MRI showed symmetric periventricular hyperintensities in the 4- and 9-year-old patients and asymmetric posterior periventricular hyperintensities in the 2-year-old patient.

Methods: To investigate the genetic basis, we first performed whole-exome sequencing in the affected children. Subsequently, we used Sanger sequencing to assess family segregation and identify carrier members.

Results: We identified a homozygous *ARSA* splice-site variant (c.465+1G>A) in all affected children. Both parents were confirmed carriers, which is consistent with autosomal recessive inheritance. Sanger sequencing analysis showed that in this family nine individuals were carriers. The variant is a pathogenic zero-allele (r.(0)), expected to abolish normal splicing and *ARSA* function, aligning with the early and severe clinical course observed.

Conclusions: Family-based testing established the diagnosis in this pedigree and highlights the utility of segregation analysis. The splice-site variant c.465+1G>A has been reported in Western European populations and among Jerusalem Arabs, with haplotype evidence suggesting a shared founder origin. These findings underscore the importance of targeted testing to expedite diagnosis and to inform carrier counseling, reproductive planning, and prenatal testing.

Keywords

- Metachromatic leukodystrophy
- Arylsulfatase a
- Whole-exome sequencing
- Neuro-metabolic disorder

Metabolic Disorders Leading to Pediatric Stroke: A Contemporary Review (2020–2026)

Sasan Saket[1]

[1] Pediatric Clinical Neurophysiology and Epilepsy Fellowship, Assistant Professor of Child Neurology at Iranian Child Neurology Center of Excellence (ICNCE), Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, IRAN.

Abstract

Introduction

Although pediatric stroke occurs far less frequently than stroke in adults, its consequences are often profound and long-lasting, leading to significant neurological morbidity. Established etiologies include congenital heart disease, coagulation disorders, infections, and structural vascular abnormalities. In recent years, however, metabolic disorders have emerged as an important and distinct cause of stroke in children. These conditions may manifest either as true ischemic strokes—commonly related to endothelial dysfunction or hypercoagulable states—or as stroke-like episodes, particularly in mitochondrial diseases, where neuroimaging abnormalities do not respect conventional vascular territories.

Metabolic Disorders Associated with Pediatric Stroke

A) Mitochondrial Disorders

MELAS syndrome (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) is a prototypical example, in which neuronal and endothelial energy failure, lactic acidosis, and oxidative stress culminate in recurrent stroke-like events. MRI typically reveals lesions that extend beyond defined vascular distributions and are often precipitated by systemic stressors such as infection or metabolic decompensation.

In *Leigh syndrome*, a progressive neurodegenerative disorder predominantly affecting the basal ganglia and brainstem, stroke-like manifestations may occur during metabolic crises, further complicating the clinical picture.

B) Disorders of Amino Acid Metabolism
Homocystinuria, caused by cystathionine β-synthase deficiency, is strongly associated with true ischemic stroke. Elevated homocysteine levels lead to endothelial injury and a marked prothrombotic state, predisposing affected children to both arterial and venous cerebrovascular events.
C) Urea Cycle Disorders
Deficiencies in enzymes such as *carbamoyl phosphate synthetase I* or *ornithine transcarbamylase* result in hyperammonemia. Excess ammonia causes astrocytic swelling, cerebral edema, and neuronal toxicity, which may give rise to secondary stroke-like episodes during metabolic decompensation.
D) Organic Acidurias
Conditions including *methylmalonic acidemia* and *propionic acidemia* may present with acute metabolic strokes, particularly during periods of catabolic stress. These episodes are often characterized by seizures, altered consciousness, lethargy, and focal neurological deficits.
E) Lysosomal and Other Metabolic Disorders
In disorders such as *Fabry disease* and certain *gangliosidoses*, accumulation of toxic metabolites leads to progressive vascular endothelial dysfunction, thereby increasing the risk of ischemic stroke even in childhood.

Pathophysiology
In mitochondrial disorders, impaired ATP production and oxidative stress disrupt cerebral autoregulation and regional blood flow. In homocystinuria, elevated homocysteine directly damages the vascular endothelium and promotes thrombosis. In urea cycle disorders, hyperammonemia induces cerebral edema and widespread neuronal injury. Distinguishing true ischemic stroke from metabolic stroke mimics is therefore a critical challenge in this population.

Clinical Assessment and Diagnosis
Neuroimaging plays a central role, with MRI and MR spectroscopy often demonstrating lesions outside classical vascular territories and, in some cases, lactate peaks. Laboratory evaluation should include blood and cerebrospinal fluid analysis for lactate, ammonia, and amino acids, alongside targeted

metabolic and genetic testing for nuclear or mitochondrial mutations. Identifying potential triggers—such as infection, prolonged fasting, or other catabolic states—is essential for both diagnosis and management.

Management

Acute management focuses on supportive care, including rapid correction of metabolic disturbances, seizure control, and management of intracranial pressure when indicated. Disease-specific treatments are equally important, such as pyridoxine or folate supplementation in homocystinuria, dietary protein restriction in urea cycle disorders, and cofactor or supportive therapies in mitochondrial diseases. Long-term prevention relies on avoidance of catabolic stress, close metabolic monitoring, and appropriate genetic counseling for affected families.

Conclusion

Metabolic disorders represent a critical yet frequently under-recognized cause of pediatric stroke, with presentations ranging from true ischemic events to stroke-like episodes. Early identification, prompt metabolic stabilization, and tailored disease-specific interventions are essential to improve outcomes and minimize long-term neurological disability. Pediatric neurologists should maintain a high index of suspicion for metabolic etiologies, particularly when clinical features or neuroimaging findings are atypical.

Keywords

- Pediatric stroke
- Metabolic disorders
- Stroke-like episodes

Neurometabolic Diseases Presenting with Peripheral Neuropathy: How to Recognize, Diagnose, and Manage Them

Gholamreza Zamani[1]

[1] Pediatric Neurologist, Children's Center of Excellence, Tehran University of Medical Sciences.

Abstract

Background

Neurometabolic disorders are inherited conditions that disrupt biochemical pathways essential for healthy nerve and muscle function. Because peripheral nerves rely heavily on stable energy production, proper myelin maintenance, and removal of toxic metabolites, these disorders often present first—or most prominently—through various forms of neuropathy. For some patients, neuropathy may be the earliest warning sign. Early recognition is critical, as several neurometabolic disorders have targeted treatments that can prevent long-term neurological damage.

Objectives

To understand how neurometabolic disorders present with neuropathy, clinicians must identify key examination findings that suggest a metabolic cause, use a structured diagnostic approach, and implement disease-specific treatments when appropriate while managing symptoms and preventing complications.

The following elements are essential:

Common neuropathy patterns (motor, sensory, small-fiber, autonomic).

Systemic clues such as visual abnormalities, organ enlargement, developmental issues, or myopathy.

A stepwise diagnostic approach: metabolic labs (lactate, VLCFA, amino/organic acids), neurophysiology, MRI/MRS, and genetic testing.

Treatment options including enzyme replacement therapy, dietary

interventions, crisis-prevention strategies, and mitochondrial support therapies. Different neurometabolic disorders tend to produce recognizable neuropathy patterns:
Mitochondrial diseases often cause length-dependent axonal neuropathy with exercise intolerance.
Peroxisomal disorders such as Refsum disease and X-ALD may produce sensory or demyelinating neuropathies with visual or adrenal involvement.
Lysosomal storage disorders like Fabry disease or MLD commonly lead to burning pain, autonomic dysfunction, or progressive demyelination.
Organic acidemias and fatty-acid oxidation defects may trigger neuropathy during metabolic crises.
A structured diagnostic pathway improves accuracy and reduces delays in care. Once the underlying diagnosis is identified, effective treatments—such as enzyme replacement therapy, dietary modification, adrenal management, and metabolic stabilization—can be initiated, making early recognition essential.

Conclusion

Neuropathy is often more than an isolated symptom; it may be a vital clue to an underlying neurometabolic disorder. A careful history, targeted neurological examination, and strategic use of metabolic and genetic tests can lead to early diagnosis and appropriate intervention. Because many neurometabolic neuropathies are treatable, timely recognition can significantly improve patient outcomes. Clinicians should suspect a neurometabolic cause whenever neuropathy coexists with multisystem involvement, developmental abnormalities, or episodic metabolic decompensation.

Keywords

- Neurometabolic
- Neuropathy
- Diagnostic approach

Overview of Genetic Mutations Causing Adrenoleukodystrophy: A Case-Series Study

Mohadeseh Fathi[1,2], Sheyda Khalilian[1,2], Arezu Sayad[2,3], Parvaneh Karimzadeh[4], Farzad Ahmadabadi[4], Soudeh Ghafouri-Fard[2*], Mohammad Miryounesi[2,3*]

[1] Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2] Department of Medical Genetics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[3] Genomic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[4] Department of Pediatric Neurology, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

X-linked adrenoleukodystrophy (X-ALD) is a genetic disorder resulted from mutations in the *ABCD1* gene located at the Xq28 locus. This gene encodes a transporter protein responsible for importing very-long-chain fatty acids into peroxisomes. This research seeks to elucidate the clinical manifestations linked to various mutations in the *ABCD* gene among Iranian patients with X-ALD, considering the diverse severity of symptoms observed in this disease. Totally, six variants, including three novel variants (c.1538A>G, c.1781-1G>C, and c.1781-47G>A) were identified in the *ABCD1* gene in the patients. While all variant were identified to be pathogenic/likely pathogenic, c.1781-47G>A was classified as a variant of uncertain significance. This study broadens the spectrum of *ABCD1* mutations among Iranian patients, providing applicable information for appropriate genetic counseling in the affected families.

Keywords

- Adrenoleukodystrophy
- ABCD1
- Iran

Decoding the Neuro-Metabolic Signature of Epilepsy: Pathway-Based Insights into Genetic Determinants and Therapeutic Potentials

Sima Binaafar [1]

[1] University of Applied Sciences & Technology, Tehran, Iran

Abstract

Metabolic epilepsies constitute a genetically and biochemically distinct subset of epileptic disorders, predominantly manifesting in infancy or early childhood and often embedded within complex neurological or systemic phenotypes. Of 2,946 epilepsy-associated genes, 609 are specifically linked to metabolic epilepsies, corresponding to 609 inborn errors of metabolism among 1,904 characterized disorders. Representing roughly 20.7% of all epilepsies and 42% of monogenic forms.

These data place clinicians at a diagnostic red line, highlighting the multiplicity of implicated genes and the resulting involvement of diverse pathways. Such genetic complexity underlies pronounced phenotypic heterogeneity and variable disease trajectories, and likely contributes to the wide spectrum of treatment responsiveness, with therapeutic outcomes largely determined by the reversibility and specific nature of the affected pathways.

It appears that integrated diagnostic strategies combining biochemical, genomic, and transcriptomic profiling may represent a promising approach for precision medicine. In silico analyses, including tissue-specific expression mapping (Human Protein Atlas) and functional pathway annotation (Reactome), complement experimental and clinical studies, refining interpretation and identifying potential therapeutic targets. Integration of metabolomic, genomic, and clinical datasets accelerates and enhances in vitro and in vivo research, while bioinformatics insights further clarify disease mechanisms and guide precision medicine approaches. Collectively, this framework advances the capacity to translate complex genetic and metabolic information into effective patient-centered interventions.

Keywords	
	• Neurometabolic • Metabolic Epilepsy • Inborn Errors of Metabolism • Molecular Genetics • Omics • In Silico Analysis • Pathway Analysis

Dystonia as A Prominent Movement Abnormality in Children with Neurometabolic Disorders

Ali Nikkhah [1]

[1] Pediatric Neurologist (Imam Khomeini Hospital Complex, Tehran University of Medical Sciences)

Abstract

Dystonia is a common hyperkinetic movement disorder in children. Dystonia is revealed as abnormal, involuntary, repetitive movements and/or postures due to sustained or intermittent muscular contractions. Dystonia is a common manifestation in some neurometabolic disorders. There are a few neurometabolic disorders which dystonia is a prominent abnormality in them. These disorders are Wilson disease (WD), neuro-degeneration with brain iron accumulation (NBIAs), dopa-responsive dystonia (DRD), hypermanganesemia with dystonia (HMNDYT), leigh syndrome (LS), Glut1 deficiency, and glutaric asicuria1 (GA1).

Early diagnosis of treatable neurometabolic disorders is very important and early medical intervention based on disease can prevent irreversible neurodegeneration in these patients. So, in this brief lecture, I will talk about timely diagnosis based on characteristics of dystonia in common treatable neurometabolic disorders.

Keywords