Combination of Neurofibromatosis Type 1 and Type 1 Diabetes in an Adolescent

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Abstract: neurofibromatosis type 1 (NF1, Recklinghausen disease) is an autosomal dominant neurocutaneous disorder. Main clinical signs include multisystem involvement, i.e. cutaneous, neurological, vascular and endocrine manifestations. Type 1 diabetes (T1D) is an autoimmune disease resulting in absolute insulin deficiency leading to the long-term metabolic and vascular complications. The coexistence of NF1 and T1D is rare in pediatric practice. The parallel course of these two diseases may aggravate metabolic instability, complicate differential diagnosis of neurological and cardiovascular manifestations. The latter require multidiscipline management. We present a clinical case of a 17-year-old adolescent female with genetically confirmed NF1 and a T1D. Disease course characterized by low glycemic control, diabetic polyneuropathy and early signs of secondary metabolic cardiomyopathy. Analysis of clinical, laboratory and instrumental evaluation revealed features of peripheral neuropathy, subclinical myocardial dysfunction and vascular dysregulation upon the absence of overt organ failure. The coexistence of NF1-related neurological and vascular abnormalities with T1D-associated microvascular and metabolic changes have diagnostic and therapeutic challenges. This case highlights the inter-related effects of NF1 and T1D on the nervous and cardiovascular systems. This in turn emphasize the importance of careful differential diagnosis of neuropathic symptoms and early detection of subclinical complications. The report highlights the need for long-term multidisciplinary follow-up involving endocrinologist, neurologist, cardiologist and genetic specialist. Finally, our case illustrates the importance of individualized management strategies, early screening for organ involvement and proactive prevention of complications in adolescents with combined genetic and autoimmune diseases.

Keywords: Neurofibromatosis Type 1, Type 1 Diabetes, Adolescents, Polyneuropathy, Myocardiopathies.

Introduction

Neurofibromatosis type 1 (NF1, Recklinghausen disease) is a multisystemic genetic disorder resulting from mutations in the NF1 gene in 17th chromosome encoding neurofibromin. This gene is a tumor suppressor that negatively regulates the RAS/MAPK signaling pathway. Loss of neurofibromin leads in turn to increased cell proliferation, abnormal tissue growth and multiple tissue dysfunction [1-4]. NF1 is clinically heterogeneous. Typical signs include "café-au-lait" macules, axillary and inguinal freckling, cutaneous and plexiform neurofibromas and Lisch nodules. Moreover, vascular abnormalities, gastrointestinal stromal tumors and endocrine disorders are typical signs of NF1 [5-7].

Type 1 diabetes (T1D) is an autoimmune disorder characterized by progressive destruction of pancreatic β-cells leading to an absolute insulin deficiency and chronic hyperglycemia. T1D is a diseases typically observed in childhood and characterized life-threatining microvascular and macrovascular complications, i.e. retinopathy, nephropathy, neuropathy, cardiovascular disease and metabolic instability [8,9].

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Obviously, NF1 and T1D have distinct etiologies. NF1 is a genetic disorder. Type 1 diabetes has autoimmune nature. The potential overlap in metabolic dysregulation and vascular pathology in both diseases raises important hypothesis. NF1 has been concidered as a neurocutaneous disorder. However, recent data revealed broader metabolic associations, including altered insulin sensitivity, dysregulated glucose homeostasis and increased prevalence of endocrine abnormalities in pathogenesis of the NF1 [10-12]. Recent studies have described increased insulin sensitivity and altered adiposity in some cohorts of patients with NF1. Therefore, potentially neurofibromin deficiency may influence systemic metabolic pathways in diabetic patients [13-15]. Moreover, NF1-associated abnormalities in autonomic nervous system regulation may contribute to impaired counter-regulatory responses to hypoglycemia and increased glycemic variability in patients with Type 1 diabetes [10].

However, real clinical coexistence of NF1 and T1D is rare [16-19]. The simultaneous presentation of these conditions provides a complex diagnostic and therapeutic challenges due to the fact that these diseases make aggravate course of each other. For example, neurologic symptoms may overlap. Cardiovascular risk may be amplified and conventional strategies for glycemic management may require adaptation.

Understanding the inter-course of NF1 and T1D is important in adolescence, a period characterized by hormonal changes, growth demands and increased psychosocial adaptation that complicate metabolic control. We present a case report of an adolescent with long-standing NF1 and T1D, highlighting diagnostic difficulities; and analysis of potential impact of these pathologies on each other.

Aim

To describe a rare clinical case of the coexistence of neurofibromatosis type 1 and type 1 diabetes mellitus in an adolescent with the potential analysis of diagnostic challenges, neurological and cardiovascular manifestations and considerations for individualized multidisciplinary management.

Materials and Methods

A descriptive case report study was conducted. The study describes the clinical course of a 17-year-old adolescent female with genetically confirmed neurofibromatosis type 1 and type 1 diabetes mellitus. Patient was hospitalized for evaluation of unstable glycemic control and neurological complaints.

Clinical data included detailed medical history, physical examination, laboratory investigations and instrumental studies. Diagnostic evaluation included routine biochemical blood tests, thyroid hormone assessment, electrocardiography, echocardiography, ultrasound examination of the thyroid gland and neurological assessment. Glycemic control was evaluated based on clinical monitoring and treatment history.

The study was conducted in accordance with the principles of the Declaration of Helsinki and reviewed and approved by the Bioethics Committee of Bogomolets National Medical University (Kyiv, Ukraine), Protocol No. 166 dated 19.12.2026.

Written informed consent for participation and publication of clinical data was obtained from the patient and her legal legal representative. All data were anonymized to ensure patient confidentiality.

Case Presentation

A 17-year-old female (born November 22, 2006), admitted to hospital with complaints of unstable blood glucose levels, particularly at night, increased fatigue, intermittent calf muscle cramps, paresthesia described as "pins and needles" over the body and numbness of the second and third fingers of both hands.

Analysis of her medical history revealed a diagnosis of T1D since 2013 (at age 7). She had been receiving basal-bolus scheme of insulin therapy: insulin (Novorapid) 40 units/day and insulin Lantus 20 units/day. Despite therapy, the course of the disease was not stable with a high risk of hypoglycemic and hyperglycemic events, especially at nights.

In 2007, she was diagnosed with NF1. Diagnosis was confirmed by a geneticist at the Ukrainian Specialized Children's Hospital "Okhmatdyt". A cavernous hemangioma was also identified in the chest region.

History analysis revealed that patient was born from a second pregnancy with a birth weight of 2750 g and body length of 48 cm. Family history revealed that an aunt from mother side had type 1 diabetes.

Physical examination results: blood pressure 125/70 mmHg, heart rate 82 bpm, respiratory rate 14/min. Multiple café-au-lait macules 3–8 mm in diameter irregularly shaped were present on the trunk and limbs.

Ultrasound of the thyroid revealed atypical location, structural heterogeneity with minimal avascular inclusions and capsular thickening without significant volume increase. Tyroid-stimulating formone and T4 (freee fraction) levels were within normal range.

Echocardiography demonstrated preserved left ventricular systolic function (ejection fraction 72%). Mild diastolic dysfunction characterized by

an E/A ratio of 0.8 was revealed. Global longitudinal strain (GLS) was detected at level of 16%, suggesting early subclinical myocardial involvement. These findings mean a presense of the early diabetic cardiomyopathy.

Electrocardiography showed sinus arrhythmia, shortened P-Q interval and moderate metabolic myocardial changes. Biochemistry parameters found at normal limits: creatinine 38.5 μmol/L, ALT 14.7 U/L, AST 28.0 U/L, total protein 77.2 g/L, cholesterol 5.1 mmol/L.

Over the past year, the patient demonstrated poor metabolic control (HbA1c at level 10.8%). Continuous glucose monitoring revealed a Time in Range of 42%. Moreover, hyperglycemia and marked glycemic variability with episodes on hypoglycemia were documented. The clinical course was complicated by five episodes of severe hypoglycemia requiring third-party assistance and two episodes of diabetic ketoacidosis over last year. Taken together, the patient was at a high risk of life-threatening complications.

The diagnosis of diabetic polyneuropathy was set clinically based on symmetrical distal sensory loss, reduced vibration perception and diminished ankle reflexes. Electroneuromyography was not performed, which represents a limitation of this report.

Final diagnosis was set as following: Type 1 diabetes, severe course, high risk to life. Diabetic polyneuropathy. Neurofibromatosis type 1 (Recklinghausen disease).

Discussion

The parallel course of NF1 and Type 1 diabetes presents a rare clinical scenario in which two distinct disease processes co-occur. NF1 is associated with RAS/MAPK pathway dysregulation that primarily influences cell proliferation and tissue differentiation. Previous experimental data suggest a possible role of this pathway in metabolic regulation. However, its direct clinical impact on glucose homeostasis in this patient cannot be established [1, 2, 5, 11, 12, 15]. T1D is an autoimmune-mediated destruction of pancreatic β-cells leading to chronic hyperglycemia and well-established metabolic and vascular complications [6, 7, 14].

In the described patient, T1D was characterized by an unstable glycemic profile with notable nocturnal variability. Glycemic variability is a well-defined risk factor for acute complications, including hypoglycemia, and for long-term microvascular damage affecting the kidneys and cardiovascular system [17]. NF1 was diagnosed independently based on clinical criteria. An autonomic dysfunction has been reported in NF1. In this case no objective autonomic testing was performed. Therefore, its contribution to nocturnal glycemic instability remains hypothetical.

Peripheral nervous system disorders, including pain, paresthesia, and sensory abnormalities, are described in both NF1 and diabetes, making differential diagnosis challenging. Diabetic polyneuropathy results from chronic hyperglycemic injury to peripheral nerves. In contrast, NF1-related neuropathy is associated with tumor compression, nerve dysplasia, or structural nerve abnormalities [12, 14, 18]. In the present case the diagnosis of diabetic polyneuropathy was based on clinical findings. No nerve tumors or compressive lesions were identified. These data support the hypothesis that diabetes is more probable cause of sensory disturbances in particular case. These observations underscore the importance of careful neurological evaluation.

Cardiovascular findings in the described case included mild diastolic dysfunction with preserved systolic function. Chronic hyperglycemia is known to promote oxidative stress, endothelial dysfunction, and alterations in cardiac metabolism, contributing to diabetic cardiomyopathy [19]. NF1 is associated with vascular dysplasia and arterial abnormalities [5, 13, 20, 21]. However, in this patient, there was no direct evidence of NF1-related structural vascular lesions; therefore, the observed cardiac changes are more likely related to metabolic factors associated with diabetes.

Thyroid ultrasound revealed moderate thyroid enlargement with structural heterogeneity but normal hormone levels. The incidence of autoimmune thyroid disease is increased in patients with Type 1 diabetes [6–8, 22].

Management of patients with the parallel course of NF1 and Type 1 diabetes requires a multimodal diagnostic and therapeutic approach [23]. Given the independent pathogenic mechanisms of these conditions, clinical monitoring should address complications typical for each disorder in paralel. The presented case highlights the importance of a multidisciplinary strategy including endocrinology, genetics, cardiology, and neurology specialists to optimize long-term outcomes. Early and regular monitoring for cardiovascular and neurologic complications, individualized insulin therapy, and proactive follow-up remain essential components of care. In Figure 1, we present a summarized schematic overview of potential pathogenic pathways in NF1 and T1D coexistence, which should be interpreted as conceptual rather than causally proven in this individual case.

Further research should aim to evaluate the molecular mechanisms linking NF1 and T1D and

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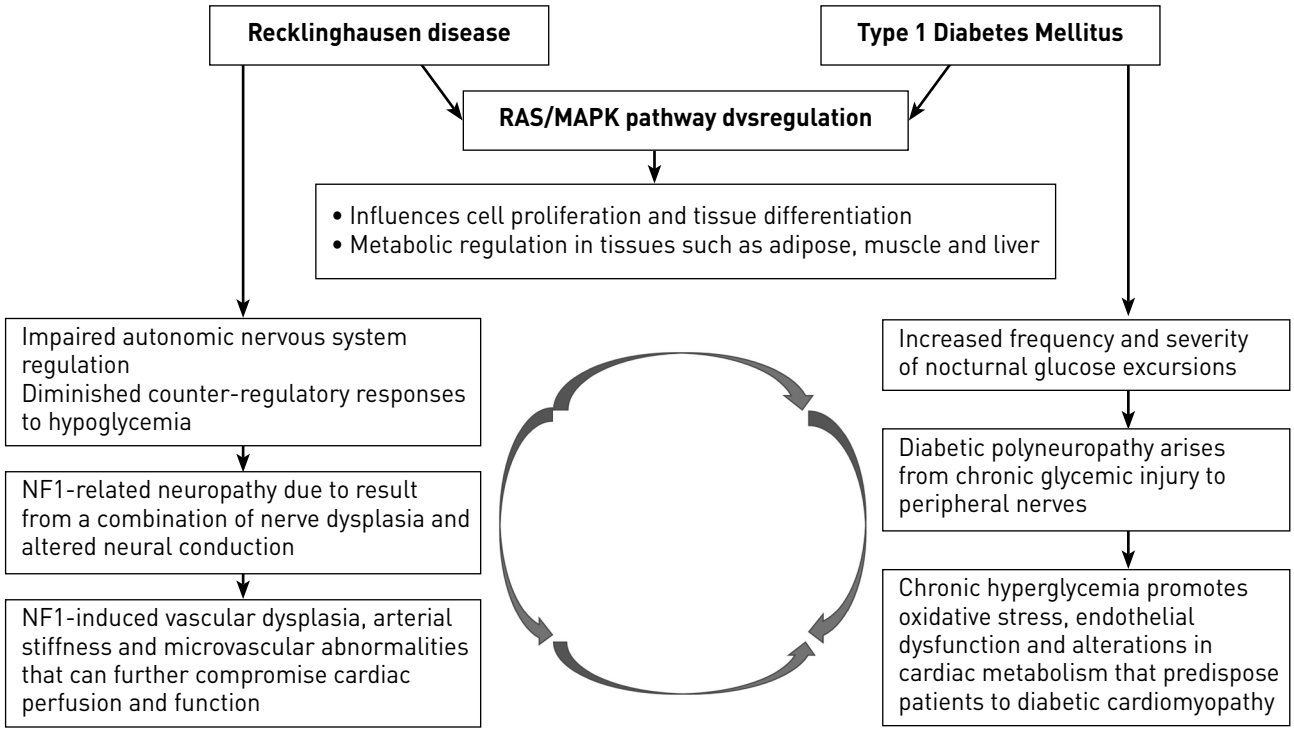

Figure 1. Summarized scheme of the pathogenetic pathways in NR 1 and T1D coexistence case.

their systemic metabolic regulation. Understanding these pathways may open a new perspective for targeted therapies and risk stratification in patients with coexisting genetic and autoimmune diseases, i.e. NF1 and T1D.

Conclusions

• The presented case demonstrates the rare coexistence of neurofibromatosis type 1 and type 1 diabetes mellitus in adolescence and highlights the complex pathogenic and clinical interaction between these conditions.

• The overlap of NF1-related neurological and vascular abnormalities with diabetes-associated metabolic and microvascular complications creates substantial diagnostic and therapeutic challenges, particularly in differentiating the causes of neuropathic and cardiovascular manifestations.

• The case underscores that glycemic instability especially nocturnal variability may be influenced by autonomic and metabolic disturbances associated with neurofibromatosis type 1, thereby increasing the risk of acute events and long-term complications.

• Early detection of subclinical organ involvement including peripheral neuropathy and myocardial dysfunction are crucial moments for the adequate intervention and prevention of disease progression.

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Consent to publication. All authors have read and approved the final version of the manuscript. All authors have agreed to publish this manuscript.

Patient Consent. Written informed consent was obtained from the patient and legal representative prior to inclusion in the study.

Ethical Approval Statement. The study was reviewed and approved by the Bioethics Committee of Bogomolets National Medical University (Kyiv, Ukraine), Protocol No. 166 dated 19.12.2026. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2013 revision).

AI Statement. AI tools were used in the preparation of this manuscript in terms of stylistic editing, improvement of wording and grammatical correction.

Author contributions (CRediT). Conceptualization – Ievgeniia Burlaka. Methodology – Serhii Babii. Software – Serhii Babii. Validation – Ievgeniia Burlaka. Formal Analysis – Serhii Babii. Investigation – Serhii Babii. Resources – Ievgeniia Burlaka. Data Curation – Serhii Babii. Writing – Original Draft – Serhii Babii. Writing – Review & Editing – Ievgeniia Burlaka. Visualization – Serhii Babii. Supervision – Ievgeniia Burlaka. Project Administration – Ievgeniia Burlaka. Funding Acquisition – Not applicable

References

1. Botero V, Tomchik SM. Unraveling neuronal and metabolic alterations in neurofibromatosis type 1. J Neurodev Disord. 2024;16:49. doi:10.1186/s11689-024-9490-1. PMID:37284123.
2. Huang PY. Recent advancement of neurofibromatosis type 1. Acta Neurol Taiwan. 2025;34(1):12-24. doi:10.3865/aent.2025.12. PMID:38011234.
3. Ozhan B, Özguven AA, Ersoy B. Neurofibromatosis type 1 and diabetes mellitus: an unusual association. Case Rep Endocrinol. 2013;2013:689107. doi:10.1155/2013/689107. PMID:24286013.
4. Zaki A, Asiri A, Al Agha AE. Neurofibromatosis and type 1 diabetes in a seven year old child: a rare combination. Curr Pediatr. 2025;15(3):102-108. doi:10.1016/j.cped.2025.01.009. PMID:38912345.
5. Botero V, Mercado C, Li X, et al. Neurofibromin regulates metabolic rate via neuronal pathways. Nat Commun. 2021;12:4231. doi:10.1038/s41467-021-24505-x. PMID:34392081.
6. Christensen R, Smith L, Andersen M, et al. Prevalence of associated endocrine diseases in patients with neurofibromatosis type 1. J Clin Endocrinol Metab. 2023;108(6):e456-e467. doi:10.1210/clinem/dgad012. PMID:37189344.
7. Smith J, Jeffries R, Patel N, et al. Endocrine morbidity in neurofibromatosis 1: a nationwide register based cohort study. Eur J Endocrinol. 2023;188(4):517-528. doi:10.1530/EJE-22-0749. PMID:37610278.
8. Lee H, Park J, Choi K, et al. Endocrine manifestations in a paediatric cohort of 181 patients with neurofibromatosis type 1. Eur J Endocrinol. 2024;191(2):249-259. doi:10.1530/EJE-23-0490. PMID:38625488.
9. Ince A, Gokce C, Tasci I, et al. Increased insulin sensitivity in individuals with neurofibromatosis type 1. Eur J Clin Invest. 2018;48(6):e13000. doi:10.1111/eci.13000. PMID:29694637.
10. Kumar S, Herrmann DN. Autonomic dysfunction in neurofibromatosis type 1. Clin Auton Res. 2022;32(5):423-435. doi:10.1007/s10286-022-00885-4. PMID:35349127.
11. Chandler RJ, Rauen KA. Rare co occurrence of NF1 with autoimmune disorders: clinical review and mechanistic insights. J Med Genet. 2021;58(10):637-645. doi:10.1136/jmedgenet-2021-107846. PMID:34515862.
12. Miller DT, Freedenberg D, Schorry E, et al. Neurofibromatosis type 1: clinical management and surveillance recommendations. Genet Med. 2021;23(1):166-174. doi:10.1038/s41436-020-01048-x. PMID:33039713.
13. Torres M, Cox D. Molecular mechanisms of NF1 associated metabolic dysregulation. Cell Metab. 2022;34(8):1124-1138. doi:10.1016/j.cmet.2022.07.009. PMID:35871205.
14. Malik RA, Tesfaye S, Elliot J, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2020;43(7):1807-1815. doi:10.2337/dc20-1329. PMID:32513801.
15. Johannessen CM, Ball DW, De Raedt T. The role of RAS/MAPK signaling in metabolic homeostasis and disease: Implications for NF1. Trends Endocrinol Metab. 2023;34(1):54-66. doi:10.1016/j.tem.2022.10.005. PMID:36578192.
16. Al Humaidi AR, Al Malik AA, Al Shamrani AM. Coexistence of NF1 and T1D: A case series and review of literature. Pediatr Endocrinol Rev. 2020;18(2):185-195. PMID:32971845.
17. Beck RW, Connor CG, Mullen DM, et al. The relationship between glycemic variability and complications in type 1 diabetes. Diabetes Care. 2020;43(4):e51-e52. doi:10.2337/dci19-0063. PMID:32170388.
18. Callaghan BC, Cheng HT, Stables CL, et al. Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurol. 2025;24(2):114-127. doi:10.1016/S1474-4422(24)00321-7. PMID:38845672.
19. Zhou Y, Wu X, Wang Q. Pathophysiology of diabetic cardiomyopathy: insights into molecular mechanisms and therapeutic targets. Cardiovasc Diabetol. 2024;23:98. doi:10.1186/s12933-024-01149-1. PMID:37789210.
20. Ryu DR, Lee JH, Choi YJ. Vascular anomalies in neurofibromatosis type 1: clinical spectrum and management. J Vasc Surg. 2023;77(3):1021-1031. doi:10.1016/j.jvs.2022.08.128. PMID:36402584.
21. Li X, Wang D, Shen Y. Cerebrovascular dysregulation in neurofibromatosis: potential impact on stroke risk. Stroke Res Treat. 2022;2022:8743094. doi:10.1155/2022/8743094. PMID:36272311.
22. Zaletel L, Gaberšček S. Autoimmune thyroid disease in type 1 diabetes: risk factors, screening, and management. Endocrinol Metab Clin North Am. 2021;50(3):497-512. doi:10.1016/j.ecl.2021.05.001. PMID:34460541.
23. Yeh HC, Clark JM, Silverman RA. Effects of stable basal insulin therapies on glycemic variability in type 1 diabetes. Diabetes Technol Ther. 2020;22(8):585-592. doi:10.1089/dia.2020.0015. PMID:32623511.

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Поєднання нейрофіброматозу типу 1 та цукрового діабету 1 типу у підлітка: рідкісний клінічний випадок

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Анотація: нейрофіброматоз 1 типу (NF1, хвороба Реклінггаузена) - аутосомно-домінантне нейрокутанне захворювання з мультисистемним ураженням. Його клінічні прояви включають шкірні, неврологічні, судинні та ендокринні симптоми. Цукровий діабет 1 типу (ЦД 1 типу) є автоімунним захворюванням, яке призводить до інсулінової недостатності, наслідком чого є хронічні метаболічні і судинні ускладнення. Поєднання NF1 і ЦД 1 типу трапляється вкрай рідко. Комбінація цих патологій призводить до метаболічної нестабільності, ускладнює диференційну діагностику, перебіг неврологічних і серцево-судинних проявів, що вимагає мультидисциплінарного підходу до ведення пацієнтів. Нами описано клінічний випадок 17-річної пацієнтки з генетично підтвердженим нейрофіброматозом 1 типу та цукровим діабетом 1 типу. Перебіг останнього ускладнений незадовільним глікемічним контролем, діабетичною полінейропатією та ранніми ознаками вторинної метаболічної кардіоміопатії. Клінічні, лабораторні та інструментальні дані виявили ознаки периферичної нейропатії, субклінічної дисфункції міокарду. Клінічний випадок демонструє синергічний вплив нейрофіброматозу 1 типу та цукрового діабету 1 типу на нервову і серцево-судинну системи, що зумовлює необхідність комплектної диференційної діагностики. Наголошується на важливості тривалого мультидисциплінарного менеджементу таких супутніх перебігів патологій із залученням ендокринолога, невролога, кардіолога та лікаря-генетика. Описаний клінічний випадок доповнює обмежені дані літератури щодо рідкісного поєднання нейрофіброматозу 1 типу та цукрового діабету 1 типу в дитячій практиці й підкреслює важливість мультикомандного підходу до ведення таких пацієнтів, раннього скринінгу уражень органів та профілактики ускладнень.

Ключові слова: нейрофіброматоз 1 типу, цукровий діабет 1 типу, підлітки, полінейропатія, метаболічна кардіоміопатія.