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Multisystem Features in Adult-Onset Myotonic Dystrophy Type 1: An Integrative Case Analysis

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Abstract: Myotonic dystrophy type 1 (DM1), or Steinert disease, is the most common adult-onset muscu-lar dystrophy, characterized by multisystem involvement affecting neuromuscular, cardiac, endocrine, respiratory, and cognitive domains. Clinical severity and phenotypic variability cor-relate with the size of the CTG repeat expansion in the DMPK gene. Adult-onset DM1 frequently remains underdiagnosed, particularly in individuals presenting with prominent neurocogni-tive or psychiatric manifestations. We report the case of a 56-year-old male diagnosed with DM1 in 2025 following genetic confirmation of a DMPK allele carrying >50 CTG repeats. The clinical examination revealed marked myotonia, distal lower-limb muscle atrophy, bilat-eral paraparesis (Medical Research Council grade 4/5; MRC 4/5), steppage gait, and pronounced idiomyotonic respons-es. Neurocognitive and psychiatric evaluation demonstrated a moderate neurocognitive disorder, with a Mini-Mental State Examination (MMSE) score of 22/30 and a Montreal Cognitive Assessment (MoCA) score of 19/30, alongside execu-tive dysfunction, depressive disorder with organic features, sleep disturbances, and episodic vertigo. Electromyography (EMG) confirmed myotonic discharges, while brain magnetic resonance imaging (MRI) demonstrat-ed moderate cerebral atrophy with Fazekas grade 2 leukoencephalopathy. Electrocardiography (ECG) showed a first-degree atrioventricular block. Muscle biopsy was not performed due to limited technical resources. The patient's comor-bidities included chronic liver disease, hepatitis B, benign prostatic hyperplasia, transient ischemic attack, and obstruc-tive sleep apnea. Therapeutic management consisted of neuropathic pain agents, neurotrophic therapy, anti-inflammatory and antivertigo medication, and a structured physiotherapy program. This case highlights the multisystemic complexity of adult-onset DM1 and emphasizes the importance of integrating genetic testing, neurocognitive evaluation, and comprehensive systemic assessment into routine diagnostic workflows. Cognitive and psychiatric manifestations frequently underestimated in clinical practice can markedly contribute to morbidity and should therefore be systematically evaluated in all adults suspected of DM1.

Keywords: myotonic dystrophy type 1, steinert disease, myotonia, genetic repeat expansion, neuromuscular disorders, cognitive impairment

1. Introduction

Myotonic dystrophy (DM) is a rare, progressive neuromuscular disorder and the most common form of adult-onset muscular dystrophy. Two major clinical and molecular subtypes are recognized: myotonic dystrophy type 1 (DM1) and myotonic dystrophy type 2 (DM2) [1]. Both conditions are autosomal dominant and multisystemic,

with substantial phenotypic heterogeneity. Clinical manifestations range from mild electrical myotonia to marked distal muscle weakness and functional impairment, frequently accompanied by cardiac conduction abnormalities, early cataracts, endocrine and reproductive dysfunction, insulin resistance, cognitive and behavioral impairment, respiratory compromise, and gastrointestinal dysmotility [2].

DM1 results from a CTG trinucleotide repeat expansion in the 3′ untranslated region of the DMPK gene on chromosome 19q13.3, whereas DM2 is caused by a CCTG repeat expansion in intron 1 of the CNBP (ZNF9) gene on chromosome 3q21.3 [3]. These repeat expansions produce a toxic RNA gain-of-function effect, disrupting multiple cellular pathways and explaining the disorder's multisystemic phenotype. Genetic anticipation is a characteristic feature, with progressive CTG repeat enlargement contributing to earlier onset and more severe symptoms across generations; in DM1, CTG repeat numbers may exceed 2,000 by age 20 and 4,000 by age 40 [4]. While repeat size correlates with disease severity in DM1, this relationship is weaker in DM2; CCTG repeat lengths above 75 are considered pathogenic [5,6].

DM1 is the most common muscular dystrophy among individuals of European descent, with an estimated global prevalence of 1:3,000, although certain regions (e.g., Quebec) report higher rates, up to 1:500 [7,8]. DM2 appears less frequent but is likely underdiagnosed due to its milder phenotype and later onset [9]. Myotonia, a cardinal feature of DM, presents as delayed muscle relaxation after voluntary contraction, typically improving with repeated exercise and worsening with cold exposure [1,7]. Distal muscle weakness predominates in DM1, whereas DM2 more often involves proximal musculature and is frequently associated with myofascial pain [4,8,9].

The clinical spectrum of DM1 includes congenital, mild, classic, and childhood-onset forms, each with distinct features and prognostic implications [3,6,8,10]. Evaluation of suspected cases requires an integrated diagnostic approach. Genetic testing is the gold standard, with CTG repeat expansions >50 confirming DM1 [1]. In clinically suggestive cases with negative DMPK testing, CNBP analysis is recommended to exclude DM2. Electromyography is highly valuable for identifying characteristic myotonic discharges [11,12], while muscle biopsy although it may demonstrate nonspecific myopathic changes has diminished diagnostic relevance in the molecular era [13]. Given its multisystemic nature and progressive course, DM1 requires comprehensive medical assessment and individualized symptomatic treatment, including management of myotonia, cardiac and respiratory complications, and tailored rehabilitation programs [9,14,15].

2. Case Presentation

We report the case of a 56-year-old male patient diagnosed in 2025 with DM1, confirmed through genetic testing. TP-PCR analysis identified two DMPK alleles: one normal allele with 12 ± 1 CTG repeats, and a second allele with a large pathogenic expansion (>50 CTG repeats). The clinical picture was dominated by typical signs of myotonia, including a long, myopathic "pear-shaped" facial appearance (Figure 1), myotonic handgrip phenomenon, and prolonged bilateral idiomyotonic reaction at the wrist flexors, leading to impaired grip and reduced fine motor dexterity (Figure 2). Neurological examination revealed a predominantly distal motor involvement consistent with DM1. Distal calf muscle atrophy was evident, accompanied by bilateral paraparesis with an MRC score of 4/5 in the lower limbs, while proximal muscle strength remained preserved (MRC 5/5 in both upper and lower limbs). Although muscle strength was largely maintained, movement execution was noticeably slowed, and distal weakness contributed to a bilateral steppage gait. Ambulation was possible over medium distances, with fatigability emerging after approximately 2 km of walking. Stair climbing

required lateral support. Manual dexterity was reduced due to delayed initiation and relaxation of grip.

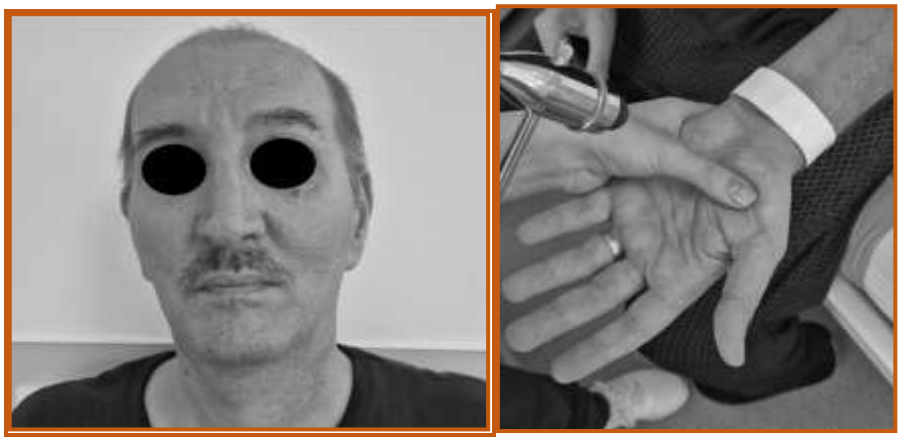

Figure 1. Characteristic facial morphology and perceptual findings: "pear shaped" facies and tenar eminence percussion myotonia

Figure 2. Evaluation of hand myotonia: repetitive hand opening and closing maneuver

Cognitive and neuropsychiatric assessment demonstrated marked CNS involvement. The patient exhibited word-finding difficulties, impaired planning and executive functioning, and psychomotor slowing. Neuropsychological testing confirmed a moderate neurocognitive disorder, with a Mini-Mental State Examination (MMSE) score of 22/30 and a Montreal Cognitive Assessment (MoCA) score of 19/30, indicating deficits in temporal-spatial orientation, attention, working memory, executive functions, and delayed recall. Psychiatric symptoms included major depressive disorder with organic features and anxiety. Vertigo episodes were intermittently present. Sleep assessment revealed clinically significant sleep-wake disturbances (Table 1).

The patient was diagnosed with sleep apnea, accompanied by chronic insomnia and severe daytime somnolence. He reported the ability to sleep only 1-2 hours during the day, despite feeling sleepy throughout most of the daytime period. Nocturnal sleep was fragmented and limited to approximately 5 hours. Daytime sleepiness was formally assessed using the Epworth Sleepiness Scale (ESS), yielding a score of 12/24, consistent with moderate excessive daytime sleepiness. He was instructed in respiratory physiotherapy, including targeted breathing exercises aimed at improving ventilatory efficiency and supporting nighttime sleep quality.

Paraclinical investigations supported the diagnosis of DM1. Electromyography demonstrated myopathic changes with characteristic myotonic discharges. Brain magnetic resonance imaging (MRI) revealed moderate global cerebral atrophy and Fazekas grade 2 leukoaraiosis.

Table 1. Summary of multisystem involvement in the presented adult-onset DM1 patient.

Clinical	Patient findings	Relevant investigations
Neuromuscular	Distal myotonia; delayed muscle relaxation; myotonic handgrip; distal muscle atrophy (calves); mild distal paraparesis (MRC 4/5); preserved proximal muscle strength; steppage gait; bradylalia (mild bulbar involvement).	Clinical examination; electromyography (EMG) showing myotonic discharges.
Cognitive & Psychiatric	Moderate neurocognitive disorder (MMSE 22/30, MoCA 19/30); executive dysfunction; depressive disorder with organic features; anxiety; psychomotor slowing.	Neuropsychological evaluation; brain MRI showing moderate cerebral atrophy and Fazekas grade 2 leukoaraiosis.
Sleep & Respiratory	Obstructive sleep apnea; chronic insomnia; excessive daytime somnolence; fragmented nocturnal sleep.	Clinical sleep assessment; respiratory evaluation.
Cardiac	First-degree atrioventricular block (PR 0.30 s); normal QRS duration; preserved left ventricular ejection fraction (LVEF 60%); mild mitral and tricuspid regurgitation.	ECG; Holter monitoring; echocardiography.
Endocrine & Metabolic	No thyroid, glycemic, lipid, or testosterone abnormalities; no clinical hypogonadism.	Standard endocrine labs.
Gastrointestinal	Chronic constipation; no dysphagia or abdominal symptoms.	Clinical history.
Hepatic	Chronic liver disease; hepatitis B infection.	Laboratory testing.
Genitourinary	Benign prostatic hyperplasia.	Clinical examination.
Ophthalmologic	Decreased visual acuity; no confirmed cataracts.	Ophthalmologic examination.
Dermatologic	Alopecia; xerosis.	Dermatologic examination.
Muscle biopsy	Not performed (technical limitations).	
Family testing	Son negative for DMPK repeat expansion.	Genetic testing.

Electrocardiography (ECG) identified a first-degree atrioventricular block with a PR interval of 0.30 seconds and normal QRS duration (Figure 3). Echocardiography demonstrated preserved left ventricular systolic function (LVEF = 60%), mild mitral and tricuspid regurgitation, and small valvular atheromatous plaques. Holter ECG monitoring confirmed first-degree AV block with a bradycardic rhythm, while ambulatory blood pressure monitoring revealed mean values of 120/70 mmHg and a heart rate of 60 bpm. The patient remained under active cardiologic surveillance. Laboratory evaluation showed a creatine kinase (CK) level of 248 U/L.

The patient engaged in a structured, individualized physiotherapy program designed to address multiple functional domains affected in DM1. The intervention focused on global muscle conditioning, distal muscle activation, and gait and balance training, with the aim of reducing fatigability and preventing functional decline. Specific emphasis was placed on respiratory physiotherapy, including diaphragmatic breathing exercises, thoracic expansion techniques, and airway-clearing maneuvers, given the presence of sleep apnea and daytime somnolence. These interventions were

reinforced through a home-based continuation program, implemented under specialist supervision to ensure proper technique, adherence, and long-term benefit. The patient reported no history of tobacco use, alcohol consumption, or illicit drug exposure, eliminating several modifiable risk factors known to exacerbate disease severity in DM1.

A muscle biopsy was not performed due to technical limitations and lack of appropriate biopsy kits at the evaluating center. Because the genetic testing results were definitive and the clinical presentation was highly characteristic of DM1, the absence of histopathological confirmation did not influence the diagnostic accuracy or subsequent therapeutic decisions and was therefore considered clinically acceptable.

The patient's medical history was notable for hepatitis B infection, chronic hepatic insufficiency, benign prostatic hyperplasia, and recurrent vertigo syndrome, all of which contributed to the overall complexity of his clinical management. His therapeutic regimen included neuropathic pain modulators, anti-vertigo medication, anti-inflammatory agents, and neurotrophic support, alongside ongoing physiotherapy and kinesiotherapy aimed at preserving mobility, minimizing muscle stiffness, and maintaining functional independence.

Given the autosomal dominant nature of DM1, genetic testing was offered to his first-degree relatives. His son underwent molecular analysis for DMPK repeat expansion, with negative results, indicating the absence of the pathological allele. This result is consistent with the variable expression and intergenerational dynamics of trinucleotide repeat disorders, and it provides important prognostic and reproductive counseling value for the family.

3. Discussion

Because DM1 is a multisystem disorder, treatment must be individualized and adapted to the specific areas affected. Clinical manifestations may involve the neurological and musculoskeletal systems, cardiac conduction pathways, respiratory function, dermatological features, endocrine and metabolic regulation, gastrointestinal motility, genitourinary function, ophthalmologic structures, and reproductive health. A coordinated multidisciplinary approach is essential to address these diverse complications and to support long-term patient outcomes.

Musculoskeletal system

The patient presented with mild distal motor dysfunction involving the forearm, hand, lower leg, and foot, characterized predominantly by slowed extension and flexion movements rather than measurable muscle weakness. Manual muscle testing showed preserved strength (MRC 5/5 in the upper limbs and MRC 4/5 in the lower limbs). Despite this, functional limitations were clinically evident, including slow gait, fatigability after approximately 2 km of walking, difficulty climbing stairs, and the need for lateral support during ascent. Mild bradylalia was also observed, consistent with subtle bulbar involvement. According to the Muscular Impairment Rating Scale (MIRS), these findings correspond to Grade 2, reflecting minimal signs with predominantly distal involvement in the absence of objective muscle weakness [16].

Although several pharmacological options exist for the symptomatic management of myotonia and pain, including mexiletine and other anti-myotonic agents [17-19], the patient is currently receiving supportive metabolic therapy consisting of B-vitamin supplementation (B1, B6, B12) and coenzyme Q10. Current rehabilitation recommendations in DM1 support moderate-intensity aerobic exercise and muscle strengthening as safe and potentially beneficial for functional endurance [20,21]. The patient completed a structured physiotherapy and education program and continues home-based therapy under professional supervision. Given the mild distal involvement, preserved muscle strength, and absence of falls, the main clinical focus remains on functional

monitoring, maintenance of mobility, gait optimization, and energy conservation strategies.

Central nervous system (CNS)

Neuropsychological assessment revealed a moderate neurocognitive disorder, with MMSE and MoCA scores of 22/30 and 19/30, respectively. Deficits were observed in temporal-spatial orientation, attention, working memory, executive function, and delayed recall. Neuroimaging demonstrated moderate cerebral atrophy and Fazekas type 2 leukoaraiosis. From an affective and behavioral perspective, the patient presented with an organic depressive disorder with anxious exacerbations and psychomotor regression, currently treated with sertraline 50 mg daily. Vertigo, managed with Arlevert, was also reported. Sleep disturbance represented a significant clinical issue, with chronic insomnia, approximately 5 hours of nocturnal sleep, and severe daytime somnolence, with the ability to sleep only 1-2 hours during the day. The patient's cognitive profile is consistent with the neurocognitive patterns described in DM1, which include impairments in executive function, attention, and memory, even in patients with moderate CTG repeat expansions [22,23].

Similarly, the presence of cerebral atrophy and white matter involvement corresponds to previously reported structural CNS abnormalities in DM1, including reduced grey matter volume and diffuse white matter changes [24,25]. The affective and behavioral manifestations observed in this patient reflect the well-documented association between DM1 and mood disturbances, including depression, anxiety, apathy, and reduced initiative [26-28].

Sleep-related complaints, when interpreted using the Epworth Sleepiness Scale (ESS) framework, correspond to a mild-to-moderate level of excessive daytime sleepiness (ESS 12/24), in agreement with the high prevalence of hypersomnolence and sleep dysregulation in DM1 [25,29].

Cardiovascular system

Electrocardiographic evaluation revealed a first-degree atrioventricular block with a PR interval of 0.30 s, while the QRS duration remained within normal limits (<120 ms), indicating preserved intraventricular conduction.

Echocardiography showed preserved left ventricular systolic function (LVEF 60%), with mild mitral and tricuspid regurgitation and the presence of small atheromatous valvular plaques. Ambulatory blood pressure monitoring demonstrated normotensive values (mean 120/70 mmHg) with a resting heart rate of approximately 60 bpm. No tachyarrhythmias were recorded. The CK level was mildly elevated (248 U/L). The patient reported no palpitations, syncope, or other cardiac symptoms.

Cardiac involvement in DM1 is well recognized, particularly with respect to conduction system disease and arrhythmias [30]. The degree of PR prolongation observed in this patient exceeds the threshold associated with increased risk of conduction progression in DM1 ($\geqslant$240 ms) [31,32], supporting the known vulnerability of the His-Purkinje system [32]. The predominantly subtle structural echocardiographic findings observed in this case are consistent with reports indicating that early-stage cardiac manifestations in DM1 are often mild and clinically silent [33,34]. At this stage, advanced cardiac imaging such as MRI was not indicated, in accordance with current practice [32].

Respiratory system

The patient was diagnosed with sleep apnea, with no additional abnormalities identified on routine respiratory assessment. There was no clinical evidence of recurrent respiratory infections, dysphagia-related aspiration, or ineffective cough. No features suggestive of nocturnal hypoventilation were documented at this stage. Respiratory involvement represents a major contributor to morbidity and mortality in DM1, accounting for more than half of DM1-related deaths in large series [36]. Symptoms may develop insidiously and remain clinically silent for prolonged periods [37].

The isolated presence of sleep-disordered breathing in this patient is consistent with the high reported prevalence of respiratory sleep disturbances in DM1, with obstructive sleep apnea affecting 52-86% of patients and central sleep apnea up to 44% [38]. The absence of overt respiratory muscle weakness or recurrent infections in this case suggests an early respiratory involvement pattern, as commonly observed in DM1. Although mechanisms such as combined peripheral respiratory muscle weakness and central ventilatory control impairment contribute to hypoventilation and infection susceptibility [39,40], these complications were not present in the current patient. Sleep apnea remains clinically relevant due to its association with daytime somnolence and increased arrhythmic risk [41,42].

Endocrinology and Metabolism

No thyroid, lipid, glucose, or gonadal abnormalities were identified in this patient, with no clinical or laboratory evidence of hypogonadism, insulin resistance, phosphocalcic disturbances, or adrenal dysfunction. Endocrine and metabolic abnormalities are a recognized component of DM1 and tend to increase with disease progression [45,46], they were absent in the present case. In men with DM1, hypergonadotropic hypogonadism represents the most frequently reported gonadal abnormality, affecting up to 80% of patients [47], this was not present in the current patient. Glucose metabolism alterations, commonly reported in DM1 and assessed by fasting glucose, glycated hemoglobin, and oral glucose tolerance testing when indicated [16], were not identified in this case. Phosphocalcic disturbances and adrenal axis alterations have also been described in DM1, with variable clinical significance [48].

Given the absence of current abnormalities, a strategy of periodic endocrine and metabolic surveillance has been adopted, including monitoring of thyroid function, gonadal hormones, glucose metabolism, and phosphocalcic parameters, in accordance with current recommendations. Lifestyle measures, including structured physical activity and dietary optimization, remain important for long-term metabolic and functional health.

Gastrointestinal system

The patient reported chronic constipation as the only gastrointestinal complaint. There were no symptoms suggestive of dysphagia, esophageal dysfunction, delayed gastric emptying, abdominal pain, diarrhea, or pseudo-obstruction at the time of evaluation. No clinical features indicating gallbladder disease or anorectal dysfunction were identified.

Gastrointestinal involvement in DM1 reflects the impact of the disease on smooth muscle function and may significantly affect quality of life [49]. Among gastrointestinal manifestations, constipation is one of the most frequent symptoms, due to reduced intestinal motility, and is fully compatible with the clinical profile observed in this patient. Oropharyngeal dysfunction and dysphagia are reported in approximately half of patients with DM1 and increase the risk of aspiration and malnutrition. Periodic screening remains important given the progressive nature of swallowing dysfunction, even though it was not present in this case. Standardized tools such as the EAT-10 question-

naire may support early detection [50,51]. Upper gastrointestinal abnormalities, including esophageal myotonia, reduced peristalsis, delayed gastric emptying, and cardia weakness, as well as lower intestinal manifestations such as alternating constipation and diarrhea or, in severe cases, pseudo-obstruction, have been well documented in DM1 [16]. Gallbladder dysmotility and gallstone formation, as well as anorectal sphincter dysfunction, have also been described and may contribute to constipation [48].

Given the presence of isolated chronic constipation, management is currently based on dietary fiber supplementation, adequate hydration, and laxative therapy when required, with periodic reassessment of symptom control [16]. Additional gastrointestinal complications were not present at this stage, ongoing clinical surveillance remains warranted to allow early detection of swallowing disorders, upper gastrointestinal dysmotility, or anorectal dysfunction, in line with the progressive nature of DM1.

Genitourinary and Reproductive systems

The patient is 56 years old and has children and grandchildren, with his reproductive history predating the diagnosis of DM1. At the time of evaluation, he showed no clinical or biochemical evidence of hypogonadism and reported no genitourinary symptoms, consistent with the typically limited urinary tract involvement in DM1 [52].

Reproductive involvement in DM1 is mainly related to endocrine and germline abnormalities, particularly hypergonadotropic hypogonadism and impaired spermatogenesis. In adult-onset DM1, reproductive histories often precede clinical recognition due to mild or unrecognized early manifestations, contributing to delayed diagnosis [27].

DM1 follows an autosomal dominant inheritance pattern, with a 50% transmission risk to offspring, and anticipation may lead to earlier and more severe disease in subsequent generations. In this case, the patient's son underwent targeted genetic testing, which confirmed the absence of a DMPK expansion, eliminating the risk of transmission in that lineage. Although the patient currently shows no evidence of gonadal dysfunction, ongoing endocrine monitoring and genetic counseling remain appropriate given the progressive nature of DM1.

Ophthalmological involvement

The patient presented with reduced visual acuity at the time of evaluation. No posterior subcapsular cataracts were documented, and there were no findings of palpebral ptosis or intraocular pressure abnormalities on ophthalmological examination. Ocular involvement is a frequent systemic feature of DM1, with posterior subcapsular cataracts representing the most characteristic manifestation, often appearing early in the adult disease course [48,53-55]. No typical DM1-related cataract changes have yet been identified, the presence of reduced visual acuity warrants continued periodic ophthalmological surveillance, given the progressive nature of ocular involvement in DM1. Routine slit-lamp examination remains essential for the early detection of posterior subcapsular cataracts [53,54].

Dermatological involvement

The patient presented with alopecia and xerotic skin changes. No pilomatricomas or cutaneous neoplastic lesions were observed on dermatological examination. Dermatological manifestations in DM1 commonly include alopecia, xerosis, seborrheic dermatitis, pilomatricomas, and features of premature aging, with reported associations to CTG expansion size and serum vitamin D levels [16]. The findings observed in this patient are consistent with those typically reported in adult-onset DM1. Although pilomatricomas have been suggested as potential early dermatological markers of systemic disease, they were not present in this case [55].

Differential diagnosis

The main differential diagnosis considered was myotonic dystrophy type 2 (DM2), given the shared presence of myotonia and multisystem involvement. DM2 was excluded based on the predominantly distal pattern of weakness, the presence of cardiac conduction abnormalities and cognitive impairment, and ultimately by genetic confirmation of a CTG repeat expansion in the DMPK gene, which is diagnostic for DM1 [56,57].

Other hereditary distal myopathies were considered due to the distal motor involvement but were regarded as unlikely given the absence of isolated muscle disease and the presence of typical multisystem features of DM1. These conditions also lack myotonia and the characteristic cardiac, endocrine, and ocular manifestations observed in this patient [58].

Non-dystrophic hereditary myotonias and other adult-onset neurological disorders were also considered early in the evaluation but were excluded based on the presence of progressive multisystem involvement and genetic confirmation of DM1 [57].

Promising therapeutic interventions

Recent research in DM1 has focused on therapies targeting the RNA-mediated toxicity caused by CTG repeat expansion in the DMPK gene, which leads to widespread splicing abnormalities and cellular dysfunction [60]. These advances have enabled the development of gene-based, RNA-targeted, and small-molecule therapeutic strategies, many of which are currently under clinical investigation. Gene editing approaches, including CRISPR-based strategies, aim to eliminate or silence the pathogenic CTG expansion at its source and have shown promising preclinical efficacy in restoring normal splicing and DMPK function [61]. RNA-targeting therapies, such as antisense oligonucleotides (ASOs) and siRNA-based compounds, seek to reduce toxic DMPK transcripts and release sequestered MBNL1, leading to splicing correction and functional improvement [62,63].

Downstream modulation of dysregulated splicing factors, particularly through GSK3β and CUGBP1 pathways, as well as correction of insulin receptor mis-splicing linked to metabolic disturbances in DM1, also represents an active area of investigation [65-69].

Among small-molecule therapies, agents such as tideglusib, erythromycin, metformin, and mexiletine have demonstrated clinical or preclinical benefits targeting neuromuscular, central nervous system, and metabolic manifestations [70-75]. Additional compounds are under study for symptomatic control, including hypersomnolence and chronic pain, and senolytic strategies have recently emerged as potential modifiers of muscle regeneration [76].

Advanced nucleic acid-based platforms, including ASOs, siRNAs, PMOs, and viral vector-based delivery systems, continue to progress through early- and late-phase clinical trials [77-84]. While these emerging therapies offer significant promise, they remain largely investigational, and current clinical management of DM1 remains centered on symptomatic and supportive multidisciplinary care.

Prevention of secondary complications

Prevention of secondary complications is a central component of DM1 management, given the progressive multisystem nature of the disease and the cumulative risks related to cardiac conduction abnormalities, respiratory dysfunction, anesthesia, and metabolic factors. In this patient, the current presentation suggests a slowly progressive disease course, with preserved cardiac systolic function, isolated sleep apnea, and

mild neuromuscular impairment, indicating a relatively stable short-term prognosis, yet with an inherent risk of long-term progression.

Perioperative and anesthetic precautions remain essential due to the increased susceptibility of patients with DM1 to respiratory depression, arrhythmias, and prolonged recovery. Succinylcholine should be avoided because of exaggerated myotonic responses, while careful selection of anesthetic agents and neuromuscular blockade protocols is required. Lifelong cardiological surveillance, with ECG and Holter monitoring, remains crucial for early detection of progressive conduction disease and for identifying candidates for pacemaker or implantable cardioverter-defibrillator therapy, which has been shown to reduce arrhythmic mortality in selected patients [60,61].

Respiratory progression may involve nocturnal hypoventilation and restrictive ventilatory decline, potentially requiring non-invasive ventilation, which has demonstrated benefit in symptomatic respiratory insufficiency [62]. Periodic respiratory reassessment is essential given the anticipated disease trajectory.

Lifestyle factors significantly influence disease progression. The absence of smoking and alcohol use, together with active participation in a structured physiotherapy program, may contribute to a slower functional decline, as adverse lifestyle factors have been associated with a more severe phenotype [63]. Ongoing aerobic conditioning, graded resistance training, respiratory physiotherapy, and speech therapy remain central to preserving mobility, ventilatory efficiency, and bulbar function.

Additional long-term monitoring includes surveillance for gastrointestinal complications, such as symptomatic gallstone disease, which occurs with increased frequency in DM1 and may require surgical intervention [64]. This patient will require lifelong multidisciplinary follow-up, with periodic reassessment of cardiac, respiratory, neuromuscular, cognitive, and metabolic function to anticipate disease progression and adapt management proactively.

4. Conclusion

This case illustrates a distinctive adult-onset DM1 phenotype in which cognitive, psychiatric, and sleep-wake disturbances emerged as prominent early features despite relatively preserved muscle strength. The patient's multisystem profile, including cardiac conduction delay, sleep apnea, chronic hepatic disease, dermatologic findings, and neurocognitive impairment, highlights the complex and frequently underrecognized presentation of DM1 in middle-aged adults. The late diagnosis at 56 years of age underscores the diagnostic challenges posed by nonmotor manifestations that may overshadow classical myotonia and distal weakness. This observation emphasizes the importance of systematically integrating neurocognitive and psychiatric assessment into the evaluation of suspected DM1, alongside timely genetic testing for accurate diagnosis. This case underscores the need for long-term multidisciplinary follow-up and greater clinical awareness of atypical adult-onset DM1 to improve patient outcomes.

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Abbreviations:

- ASO - antisense oligonucleotide
- CK - creatine kinase
- CNS - central nervous system
- CRISPR-Cas9 - clustered regularly interspaced short palindromic repeats / CRISPR-associated protein 9
- CUGBP1 - CUG-binding protein 1
- DM - myotonic dystrophy
- DM1 - myotonic dystrophy type 1
- DM2 - myotonic dystrophy type 2
- ECG - electrocardiography
- ESS - Epworth Sleepiness Scale
- GSK3β - glycogen synthase kinase 3 beta
- LVEF - left ventricular ejection fraction
- MBNL1 - muscleblind-like protein 1
- MoCA - Montreal Cognitive Assessment
- MRC - Medical Research Council scale
- MIRS - Muscular Impairment Rating Scale
- MMSE - Mini-Mental State Examination
- PMO - phosphorodiamidate morpholino oligomer

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