

INTEGRATING PAIN MANAGEMENT IN A PATIENT WITH CYSTIC FIBROSIS AND FIBROMYALGIA: A CASE REPORT

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- Background:** Chronic pain is increasingly recognized in individuals with cystic fibrosis (CF), especially as survival improves. However, the coexistence of CF and fibromyalgia—a centralized pain syndrome—has not been previously reported and presents a unique diagnostic challenge.
- Case Report:** A 26-year-old woman with confirmed CF presented with chronic, widespread musculoskeletal pain unresponsive to CF-specific treatment. Evaluation revealed neuropathic features and positive findings on fibromyalgia screening tools. Management included duloxetine, pregabalin, Pilates-based rehabilitation, and reflexology-based manual therapy. With consistent care, the patient achieved significant symptom control and improved quality of life.
- Conclusion:** Our case highlights the importance of individualized, multimodal pain management in CF, particularly when symptoms suggest overlapping centralized pain syndromes. Clinicians should consider fibromyalgia in CF patients presenting with persistent, widespread pain unresponsive to standard treatment.
- Key words:** Cystic fibrosis, fibromyalgia, chronic pain, rare diseases, case report

BACKGROUND

Cystic fibrosis (CF), a rare, life-limiting autosomal recessive disorder, is characterized by chronic respiratory infections, pancreatic insufficiency, and progressive multisystem dysfunction (1,2). While advances in therapy have dramatically improved life expectancy in individuals with CF, this increased longevity has also led to the emergence of comorbid conditions more commonly seen in the general population, including chronic pain syndromes (3-7). Traditionally, clinical management of CF has focused on pulmonary and digestive complications; however, pain—including musculoskeletal pain—has gained recognition as a substantial contributor to overall disease burden (8,9). The etiology of pain in CF is often multifactorial, underscoring its

complex, multidimensional nature and the need for comprehensive pain assessment and management in this growing patient population (8).

Fibromyalgia, a complex and often underdiagnosed centralized pain disorder, is characterized by widespread musculoskeletal pain, persistent fatigue, and cognitive disturbances (10,11). While fibromyalgia is relatively common in the general population (12), its coexistence with CF is exceedingly rare and, to our knowledge, has not been reported in the published literature. The intersection of these 2 chronic conditions introduces a unique diagnostic and therapeutic challenge, particularly in distinguishing between pain related to CF—often nociceptive or inflammatory in nature (13)—and the neuropathic or centrally mediated pain associated with

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fibromyalgia (14). Recent guidelines (13) around pain in CF emphasize its multifaceted mechanisms necessitating coordinated input from multiple clinical disciplines.

In our report, we present a rare case of a patient with both CF and fibromyalgia, highlighting the individualized, multimodal pain management strategies implemented and their clinical outcomes. Our case underscores the importance of integrated care models for complex, comorbid conditions—models that prioritize both symptom control and long-term functional improvement (15). The patient provided written informed consent for the inclusion of her clinical details in our case report and for the publication of this research.

CASE PRESENTATION

Our report is based on a 26-year-old female patient diagnosed with both CF and fibromyalgia. The patient was evaluated at the Pain and Palliative Care Clinic of the Athens Medical Center, in Greece (16), where she first presented on November 13, 2023, for specialized assessment and management of chronic, widespread pain. The diagnosis of fibromyalgia was supported by both the patient's history and the presence of tenderness in 8 characteristic fibromyalgia points, consistent with the diagnostic criteria established for centralized pain syndromes (17).

Medical History, Diagnosis, and Management of CF

The patient, born in February 1999, exhibited classic gastrointestinal manifestations of CF from birth, including failure to thrive, steatorrhea, and abdominal distension. Despite these early symptoms, a formal diagnosis of CF was not established in infancy or childhood.

By the age of 10, the patient experienced chronic daily coughing and frequent respiratory infections, suggestive of evolving pulmonary involvement characteristic of CF. These symptoms persisted and worsened over time.

At 14 years old, the patient developed arthritis affecting both small and large joints, initially misdiagnosed as juvenile idiopathic arthritis. Retrospectively, this presentation was likely a consequence of systemic inflammation secondary to untreated CF, rather than a primary autoimmune process.

The correct diagnosis of CF was eventually made at the age of 21, in June 2020, following a clinical workup initiated due to an emergency cholecystectomy. Imaging studies revealed fatty infiltration of the pancreas, prompting a genetic evaluation, which confirmed the diagnosis of CF.

In July 2020, the patient began CF-specific therapy (Table 1), which led to a marked clinical improvement. Symptoms, including arthritis, respiratory infections, chronic cough, and gastrointestinal disturbances (such as bloating and unformed stools), significantly regressed. This underscored the importance of early and targeted intervention in CF management, even when diagnosis is delayed.

In July 2023, the patient initiated on CF transmembrane conductance regulator (CFTR) modulator therapy (ivacaftor and ivacaftor/tezacaftor/elexacaftor) (Table 1), designed to enhance CFTR protein function and reduce systemic inflammation, thereby improving pulmonary function, nutritional status, and overall quality of life. At the time, this escalation in therapy was also evaluated for its potential impact on musculoskeletal symptoms, including hip (trochanteric) pain and cervicalgia, which were still present. However, the persistence of these musculoskeletal symptoms despite CFTR modulator therapy suggested that they were not solely related to CF. This led to further evaluation and the eventual confirmation of a secondary diagnosis of fibromyalgia.

Diagnosis and Management of Fibromyalgia

Symptom Onset and Clinical Course

The first symptoms suggestive of fibromyalgia emerged in December 2022, following a severe lower respiratory tract infection accompanied by thoracic pain and fever. By January 2023, the patient reported persistent bilateral trochanteric pain, followed by cervicalgia in April 2023, which temporarily improved with the use of a cervical collar for 2 weeks (August to September 2023). From mid-2023, she also experienced neuropathic-like symptoms, including burning and numbness in the quadriceps, along with intermittent sacroiliac joint discomfort.

Formal Diagnosis

A formal diagnosis of fibromyalgia was made in September 2023 by a rheumatologist, based on clinical criteria that included widespread pain, fatigue, and tenderness in 8 fibromyalgia-specific points. The diagnosis was further supported by neurosensory disturbances and a lack of inflammatory or structural abnormalities on examination. On November 13, 2023, this diagnosis was confirmed at the Pain and Palliative Care Clinic, where a comprehensive pain history and examination were performed. Clinical findings were confirmed via the Visual Analog Scale (with a score ranging between

Table 1. Pharmacological management.

Medication	Start	End	Dose/Frequency
CF			
Inhaled Antibiotics and Other Respiratory Treatments			
Tobramycin (inhaled)	Jul 20	Nov 20	28 mg/cap, 4 caps bid
Colistimethate sodium (inhaled) and aztreonam lysine (nebulized)	Dec 20	Dec 22	1.66 M IU bid/ 75 mg tid
Colistimethate sodium (nebulized)	Jan 23	Ongoing	2 M IU bid
Recombinant human deoxyribonuclease 1 (nebulized)	Jul 20	Ongoing	2.5 mg daily
Fluticasone furoate/vilanterol (inhaled)	Dec 20	Ongoing	92/22 mcg daily
Azithromycin	Jul 20	Ongoing	500 mg daily x 3/week
CFTR Modulator Therapy			
Ivacaftor	Jul 23	Ongoing	150 mg daily
Ivacaftor/tezacaftor/elixacaftor	Jul 23	Ongoing	2 (75/50/100 mg) tabs daily
Nutrition and Metabolic Complications			
Pancreatic enzymes	Jul 20	Ongoing	Varied
Ursodeoxycholic acid	Jul 20	Ongoing	500 mg bid
Calcium carbonate/citrate	Jun 23	Ongoing	500 mg bid
Cholecalciferol (vitamin D3, 3,000 IU) and multivitamin tailored for CF with fat-soluble vitamins (A, D, E, K)	Jul 20	May 24	1 tab daily
Fibromyalgia			
Duloxetine	Sep 23	Sep 24	30 mg daily
Duloxetine	Sep 24	Ongoing	60 mg daily
Pregabalin	Nov 23	Nov 23	Gradual increase from 25 mg to 50 mg daily
Pregabalin	Nov 23	Jan 24	75 mg daily
Pregabalin	Jan 24	May 24	100 mg daily
Pregabalin	May 24	Ongoing	125 mg daily
Pilates-based exercise program	Sep 23	Jul 24	3 sessions weekly
Pilates-based exercise program	Aug 24	Ongoing	2 sessions weekly
Manual pressure therapy targeting reflex zones (reflexology-based therapy)	Feb 24	Jul 24	1 session weekly
Manual pressure therapy targeting reflex zones (reflexology-based therapy)	Aug 24	Ongoing	1 session every 2 weeks

Abbreviations: CF, cystic fibrosis; CFTR: CF transmembrane conductance regulator.

6 and 9, out of 10, which indicates high pain levels), and via the Fibromyalgia Rapid Screening Tool (with 100% positive responses, indicating the existence of fibromyalgia) (18).

Pharmacological Management

Initial pharmacologic therapy included duloxetine at 30 mg/d, initiated on September 16, 2023, targeting both mood and centralized pain mechanisms. Duloxe-

tine uptake was eventually increased to 60 mg/d from September 2024 onward. Pregabalin was started on November 14, 2023, at 25 mg/d and titrated upward over the following months: 75 mg/d by November 2023, resulting in moderate improvement; 100 mg/d in January 2024, following a symptom flare; and, 125 mg/d in May 2024, after a short discontinuation of physical therapy triggered symptom recurrence. This

pharmacological management resulted in near-complete symptom control with good tolerability (Table 1).

Nonpharmacological Interventions

The patient began a Pilates-based exercise program in September 2023 (3 sessions per week), which significantly reduced trochanteric and sacroiliac pain. In January 2024, she resumed the Pilates-based exercise program at a more consistent frequency (3 sessions per week), which played a critical role in pain control and preventing relapses. A brief interruption in May 2024 led to symptom recurrence, emphasizing the importance of continuity. From August 2024 onward, the frequency changed to 2 sessions per week without any relapse occurring (Table 1).

Manual pressure therapy targeting reflex zones (reflexology-based therapy) was introduced in February 2024 (one session per week), further supporting pain and sensory symptom management. It also helped alleviate myofascial tightness during a period of increased muscle stiffness (March 2024). After the first 6 months, the frequency of reflexology-based therapy sessions was reduced to one every 2 weeks.

Treatment Response and Current Status

Overall, the patient achieved stable symptom control with only minor, short-lived fluctuations. More specifically, the patient's symptoms varied across specific time periods: from June to September 2024, mild quadriceps burning occasionally reoccurred during the first 2-3 days of her menstrual cycle, but resolved spontaneously. From October 2024 to February 2025, the patient's trochanteric pain worsened, especially during the first 2 days of menstruation. From March to April 2025, the pain intensified around the middle of the menstrual cycle. From May to June 2025, no clear correlation was observed between the pain and the menstrual cycle. These patterns occurred within the broader context of sustained improvement in quality of life, functional mobility, and pain levels—attributed to the combined effects of pharmacologic, physical, and complementary therapies.

DISCUSSION

Our case highlights the unique clinical and therapeutic challenges posed by the coexistence of CF and fibromyalgia, 2 chronic conditions with distinct yet overlapping pain mechanisms, which comprise a rare and diagnostically challenging combination.

Clinical Overlap and Diagnostic Complexity

As survival in CF improves, comorbidities, such as chronic pain and musculoskeletal complications, are becoming more prevalent (13,19,20). In this patient, musculoskeletal pain initially attributed to CF-related inflammation persisted despite appropriate CF management. The diagnosis of fibromyalgia underscored the necessity of expanding the differential diagnosis, particularly when the clinical presentation includes widespread, multifocal pain and neuropathic features, such as burning, paresthesias, or hypersensitivity. While CF-related pain is typically localized and arises from identifiable sources, such as chronic coughing, inflammatory arthritis, infections, or bone disease (21,22), the emergence of generalized pain patterns with centralized or neuropathic characteristics signals the need to consider alternative or overlapping conditions (23). Without broadening the diagnostic lens, there is a significant risk that all pain will be misattributed solely to CF complications, delaying the correct identification and treatment of coexisting syndromes, such as fibromyalgia, which require distinct management strategies, including neuromodulatory medications, physical rehabilitation, and nonopioid multimodal approaches (24).

Pain Phenotype and Mechanisms

Pain in CF patients has been widely documented across age groups, with studies (9,21) showing that over 70% of adolescents and adults report pain, most commonly in the chest, back, joints, and head. Our patient exhibited a complex pain profile encompassing both nociceptive and neuropathic elements, characteristic of overlapping chronic inflammatory and centralized pain syndromes (25). Localized discomfort in the trochanteric, cervical, and sacroiliac regions suggested mechanical and postural contributors, commonly observed in CF due to chronic coughing and musculoskeletal strain (9,21). Concurrently, the presence of burning sensations in the quadriceps and symptom exacerbation during menstruation indicated central sensitization—a hallmark of fibromyalgia—where the central nervous system amplifies pain signals, leading to heightened sensitivity and widespread pain (26). Notably, the hormonal fluctuations during the menstrual cycle have been implicated in intensifying the central sensitization.

While pain is common in CF, central sensitization may persist independently of peripheral nociceptive input and represents a core mechanism of fibromy-

algia (27). In our patient, earlier pain manifestations were temporally associated with CF-related inflammatory disease and improved following CF-specific therapy, suggesting a predominantly peripheral driver at that stage. The later emergence of widespread pain, fatigue, neuropathic-like sensory symptoms, persistence despite optimized CFTR modulator therapy, and response to centrally acting agents support a shift toward a centralized pain phenotype consistent with fibromyalgia rather than ongoing CF-related peripheral pain alone.

Multimodal and Stepwise Pain Management

Effective management required a multimodal approach combining pharmacological and nonpharmacological interventions. The pharmacologic regimen combining duloxetine, a serotonin-norepinephrine reuptake inhibitor, and pregabalin, an anticonvulsant, has previously demonstrated enhanced efficacy in reducing fibromyalgia symptoms (28) and was also shown to be effective in our case study. The patient's duloxetine and pregabalin dosage titration, in response to symptom severity, underscoring the importance of individualized dosing strategies (29).

Nonpharmacological interventions played a pivotal role in the patient's pain management. Regular sessions of Pilates-based exercises contributed to improved musculoskeletal flexibility and reduced postural strain. Studies (30) have shown that Pilates-based exercises can effectively alleviate pain and enhance quality of life in individuals with fibromyalgia. Additionally, the incorporation of reflexology-based therapy sessions provided neuromuscular relaxation, further mitigating pain flare-ups, confirming findings that reflexology-based therapy is associated with significant reductions in pain intensity among fibromyalgia patients (31).

Importantly, recent CF studies (13) emphasize that

without tailored multimodal strategies, pain can interfere with essential disease management tasks, such as airway clearance and exercise, ultimately compromising long-term outcomes.

Impact of Treatment Adherence and Continuity

The relationship between pain, psychological burden, and health outcomes has been well established in CF populations, where higher pain levels are associated with increased pulmonary exacerbations and worse health-related quality of life (9,22,32). Our case vividly illustrates how even brief interruptions in therapy (e.g., a 2-week break from the Pilates-based exercise program) can lead to symptom relapse, reinforcing the critical need for sustained adherence to both pharmacological and rehabilitative regimens (33). The prompt reinstatement of exercise routines and adjustment of pharmacologic therapy led to rapid symptom amelioration, emphasizing the dynamic nature of fibromyalgia management and the necessity for ongoing, multidisciplinary care strategies.

CONCLUSIONS

To the best of our knowledge, this is the first documented case report describing the co-occurrence of fibromyalgia in a patient with CF. While chronic pain is increasingly recognized in adults with CF, no prior publications have specifically addressed the diagnostic or therapeutic challenges posed by overlapping centralized pain syndromes, such as fibromyalgia in this population.

Our case underscores the importance of early pain recognition, cross-disciplinary collaboration, and structured nonpharmacologic interventions in managing rare disease comorbidities, such as fibromyalgia in CF. With the right therapeutic framework, long-term symptom control is achievable even in diagnostically complex cases.

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