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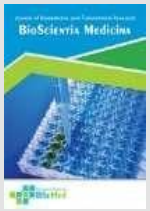

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Presumed Polymyositis in Chronic Hepatitis C: Navigating Diagnostic Uncertainty and Therapeutic Imperatives in Recurrent Myopathy

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A B S T R A C T

Background: Polymyositis (PM) is a cell-mediated inflammatory myopathy for which viral triggers, particularly the Hepatitis C virus (HCV), are increasingly recognized. The convergence of these conditions creates a formidable clinical scenario, often compelling urgent therapeutic intervention despite incomplete diagnostic data. This report explores the management of such a case, highlighting the pragmatic decision-making required when definitive investigations are deferred. **Case presentation:** A 48-year-old male with untreated chronic HCV infection (Genotype 1b, viral load 2.8 x 10^6 IU/mL) presented with a debilitating relapse of severe, symmetric proximal muscle weakness, three years after a similar episode. He exhibited profound weakness (Medical Research Council grade 2/5 in hip flexors) and marked myonecrosis (Creatine Kinase 8,572 U/L). Although comprehensive myositis-specific autoantibodies were negative, a strong clinical and biochemical profile led to a presumptive diagnosis of an acute PM exacerbation. Definitive diagnostics, including muscle biopsy, were deferred by the patient. Empirical treatment with high-dose corticosteroids and azathioprine was initiated, predicated on a careful risk-benefit analysis concerning immunosuppression in active viral infection. This strategy resulted in rapid and significant clinical and biochemical improvement. The patient was subsequently scheduled for direct-acting antiviral therapy to address the underlying viral trigger. **Conclusion:** This case underscores the critical challenge of managing severe, presumed autoimmune disease in the face of diagnostic ambiguity. It demonstrates that a therapeutic strategy guided by strong clinical evidence can be effective for controlling acute, disabling flares. Furthermore, it champions a necessary dual-paradigm approach: acute immunomodulation to preserve function, followed by targeted antiviral therapy to eradicate the probable etiological trigger, thereby aiming to prevent future recurrence and achieve durable remission.

1. Introduction

The idiopathic inflammatory myopathies (IIMs) represent a sophisticated and heterogeneous constellation of systemic autoimmune diseases, united by the cardinal feature of chronic muscle inflammation leading to progressive weakness and potential disability.[1] These conditions, while rare, pose substantial diagnostic and therapeutic challenges due to their overlapping clinical presentations and complex immunopathogenesis. The contemporary classification of IIMs encompasses several distinct clinical and histopathological subtypes, including dermatomyositis (DM), the recently defined immune-mediated necrotizing myopathy (IMNM), sporadic inclusion body myositis (IBM), and the classic entity of polymyositis (PM).[2] Polymyositis is characterized

clinically by a subacute, symmetrical, and progressive weakness that predominantly targets the proximal musculature of the limbs, neck flexors, and pharynx, often culminating in significant functional impairment, dysphagia, and a diminished quality of life.[3]

The immunopathological paradigm of PM is understood to be a highly specific, cell-mediated autoimmune process orchestrated primarily by cytotoxic CD8+ T-lymphocytes.[4] The cascade is believed to be initiated when an unknown trigger, such as an environmental exposure or infectious agent, incites an aberrant and diffuse upregulation of Major Histocompatibility Complex class I (MHC-I) molecules on the surface of myofibers.[5] This abnormal expression transforms the sarcolemma into an immunological target. Clonally expanded, antigen-specific CD8+ T-cells recognize endogenous peptides presented by these MHC-I molecules, infiltrate the muscle endomysium, and directly invade non-necrotic myofibers. Upon engagement, these cytotoxic T-cells release granules containing perforin and granzymes, inducing a targeted apoptotic cascade that results in myofiber destruction, the hallmark of the disease process. This targeted cellular assault manifests clinically as profound weakness and biochemically as the release of muscle enzymes into the circulation.

While the precise autoantigens that trigger this cytotoxic T-cell response remain largely unelucidated, the etiology of PM is unequivocally multifactorial, arising from a complex interplay between host genetic susceptibility—involving specific HLA haplotypes—and a variety of environmental triggers.[6] Among these environmental factors, infectious agents have long been implicated as potent disruptors of self-tolerance, capable of initiating autoimmune disease through mechanisms such as molecular mimicry, bystander activation, and persistent immune stimulation.

A particularly compelling and well-documented association exists between chronic Hepatitis C virus (HCV) infection and a broad spectrum of extrahepatic autoimmune phenomena. HCV, a lymphotropic RNA virus, establishes a persistent, lifelong infection in a majority of infected individuals, thereby creating a state of continuous, low-grade immune activation and systemic inflammation.[7] This chronic antigenic stimulation can lead to widespread immune dysregulation, including polyclonal B-cell activation, cryoglobulinemia, and the generation of autoantibodies, contributing to a generalized loss of self-tolerance. The link between HCV and myositis is increasingly recognized, with the virus proposed to initiate muscle-directed autoimmunity through various pathways, including molecular mimicry between viral proteins and skeletal muscle antigens or through bystander activation of autoreactive T-cells within the inflammatory milieu of the infected host.[8] The identification of HCV Genotype 1b, as seen in the present case, is particularly noteworthy, as this genotype has been specifically associated with a higher prevalence of extrahepatic autoimmune manifestations.[9]

This confluence of a presumed autoimmune disease and a chronic viral infection introduces a profound layer of complexity to clinical management. The standard therapeutic approach for an acute PM flare involves aggressive immunosuppression with high-dose corticosteroids and steroid-sparing agents to quell the destructive T-cell-mediated inflammation.[10] However, deploying such potent immunosuppressive agents in a patient with a high viral load carries the theoretical risk of exacerbating viral replication and accelerating HCV-related liver disease. This creates a significant therapeutic dilemma, forcing clinicians to weigh the immediate need to prevent irreversible muscle damage against the potential long-term risks of unchecked viral activity.

This report aims to present a comprehensive, in-depth case of a severe, recurrent myopathy with a clinical and biochemical phenotype highly characteristic of polymyositis, occurring in the context of untreated, high-titer chronic Hepatitis C virus infection. The primary novelty and educational value of this report lie in its detailed illustration of a critical and common clinical challenge: the imperative to

make urgent, high-stakes therapeutic decisions in the absence of gold-standard diagnostic confirmation from a muscle biopsy. This case serves as a powerful clinical lesson in managing a presumed autoimmune catastrophe based on a robust synthesis of clinical presentation, historical context, and biochemical evidence, especially when a persistent and plausible viral trigger is identified. It highlights the diagnostic uncertainty that clinicians must expertly navigate and underscores the necessity of a pragmatic, sequential therapeutic paradigm that first addresses the acute autoimmune flare to preserve organ function and then targets the underlying viral trigger to prevent long-term disease recurrence.

2. Case Presentation

Three years prior to the current admission, the patient, then a 45-year-old male with a medical history significant only for medically-controlled hypertension, experienced the insidious onset of a progressive and symmetrical muscle weakness. He initially reported functional difficulties with tasks requiring proximal muscle strength, such as rising from a low chair, climbing stairs, and lifting objects overhead. Over a period of several weeks, this weakness progressed to become significantly debilitating, affecting both his upper and lower extremities. This was accompanied by the development of dysphagia for solid foods and mild dysarthria, suggesting involvement of the pharyngeal and neck flexor muscles. Based on this classic clinical presentation and laboratory findings of markedly elevated muscle enzymes, a clinical diagnosis of polymyositis was made. He was commenced on a prolonged course of high-dose oral corticosteroids, which was slowly tapered over a 10-month period, in conjunction with azathioprine as a steroid-sparing agent. His response to therapy was excellent, with a complete resolution of all myopathic symptoms. At that time, definitive investigations, including electromyography (EMG) and a muscle biopsy, were recommended to confirm the diagnosis, but these were deferred by the patient. It was also during this initial workup that he was first discovered to be anti-HCV antibody positive; however, no further virological assessment or antiviral treatment was pursued at that time.

The patient, now 48 years old, presented to our hospital with a three-month history of recurrent, progressively worsening muscle weakness. The symptoms had accelerated dramatically over the two weeks prior to admission, rendering him nearly bedbound. He reported an inability to stand from a seated position without assistance and could only minimally lift his legs against gravity while in bed. He also complained of a constant, deep, aching myalgia localized to his thighs, shoulders, and calves. He denied any skin rash, joint pain, or significant weight loss. Four days prior to admission, he developed a mild, productive cough but remained afebrile and denied dyspnea or pleuritic chest pain. His medical history was negative for recent trauma, vaccinations, or the initiation of new medications, including statins. His family history was notable for a first cousin with systemic lupus erythematosus. Regarding his HCV risk factors, he denied any history of intravenous drug use but recalled receiving a blood transfusion in the early 1990s, prior to the routine implementation of HCV screening for blood products (Table 1).

On admission, the patient was alert, oriented, and in mild distress due to his weakness. He was afebrile with a temperature of 37.1°C, a blood pressure of 134/82 mmHg, a heart rate of 88 beats per minute, a respiratory rate of 16 breaths per minute, and an oxygen saturation of 98% on ambient air. The physical examination revealed no cutaneous abnormalities; specifically, there was no evidence of a heliotrope rash, Gottron's papules, shawl sign, or digital ulcers. His cardiopulmonary and abdominal examinations were unremarkable. The neurological examination was the most striking aspect of the presentation. Cranial nerve function was intact. His mental status was normal. The hallmark finding was a profound, symmetric, and predominantly proximal pattern of muscle weakness.

Table 1. Summary of Anamnesis & Clinical Findings on Admission

Comprehensive Patient Evaluation at Presentation

Patient History & Anamnesis	
Chief Complaint	Progressively worsening muscle weakness and myalgia over 3 months, debilitating for 2 weeks.
History of Present Illness	• Inability to stand from a seated position or lift legs off the bed. • Deep, aching myalgia in thighs, shoulders, and calves. • Mild productive cough for 4 days, afebrile. • History of a similar, severe episode 3 years prior, diagnosed clinically as polymyositis and resolved with immunosuppression.
Past Medical History	Hypertension; Chronic Hepatitis C (untreated)
HCV Risk Factors	Blood transfusion received in the early 1990s. Denies IV drug use.
Review of Systems & Vital Signs	
Key Systems Review	• **Musculoskeletal:** Positive for severe proximal weakness and myalgia. • **Constitutional:** Negative for fever, chills, significant weight loss. • **Dermatological:** Negative for rash, skin lesions. • **Neurological:** Negative for sensory deficits, paresthesias.
Vital Signs	Temp: 37.1°C; BP: 134/82 mmHg; HR: 88 bpm; RR: 16/min; SpO2: 98% on RA
Physical Examination Findings	
General Appearance	Alert and oriented, in mild distress due to profound weakness.
Skin	No rashes (Heliotrope, Gottron's papules), digital ulcers, or other relevant findings.
Neurological: Sensation & Reflexes	• Sensation to all modalities intact in all extremities. • Deep Tendon Reflexes: Diminished globally (1+ at knees and ankles).
Neurological: Manual Muscle Testing (MRC Scale 0-5)	Muscle Group — MRC Score Neck Flexors — 3/5 Deltoids (Bilateral) — 3/5 Iliopsoas (Bilateral) — 2/5 Quadriceps (Bilateral) — 2/5 Wrist/Finger Ext/Flex — 5/5
Key Clinical Finding	Profound, Symmetrical, Proximal Muscle Weakness This is the hallmark finding, strongly suggesting an inflammatory myopathy.

Manual Muscle Testing (MMT), graded on the Medical Research Council (MRC) 0-5 scale, revealed the following: (1) Neck Flexors: 3/5; (2) Upper Extremities: Deltoids 3/5 bilaterally, Biceps 4/5 bilaterally, Triceps 4/5 bilaterally, Wrist Flexors/Extensors 5/5, Finger Flexors/Extensors 5/5. He had difficulty combing his hair and lifting his arms above his head; (3) Lower Extremities: Iliopsoas 2/5 bilaterally, Quadriceps 2/5 bilaterally, Hamstrings 2/5 bilaterally, Tibialis Anterior 3/5 bilaterally, Gastrocnemius 3/5 bilaterally. He was unable to lift his legs off the bed against gravity; (4) Functional Assessment: He was unable to rise from a chair or from a squatting position. He required assistance to turn over in bed. Deep tendon reflexes were diminished globally, recorded as 1+ at the knees and ankles. Sensation to light touch, pinprick, vibration, and proprioception was intact throughout all four limbs. There were no cerebellar signs.

Initial laboratory investigations were significant for a marked systemic inflammatory response and profound muscle injury. Key findings are summarized in Table 2. Hematological analysis showed marked leukocytosis (17.76 x 10^9/L) with a neutrophilic predominance and thrombocytosis (450 x 10^9/L), consistent with an acute inflammatory state. Inflammatory markers were significantly elevated, with an Erythrocyte Sedimentation Rate (ESR) of 40 mm/hr and a C-Reactive Protein (CRP) of 25.0 mg/L. The most striking biochemical abnormalities were the profoundly elevated muscle enzymes, which confirmed severe myonecrosis. The Creatine Kinase (CK) level was 8,572 U/L (Reference Range: 30-200 U/L), and the aldolase level was similarly elevated at 25.4 U/L (Reference Range: <7.6 U/L). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were also elevated at 280 U/L and 155 U/L, respectively, a pattern more indicative of muscle rather than primary liver injury, given the CK: aminotransferase ratio. An extensive immunological workup was performed. The Antinuclear Antibody (ANA) was positive at a 1:320 titer with a speckled pattern. However, a comprehensive myositis-specific and myositis-associated antibody (MSA/MAA) panel was negative. This included antibodies against Jo-1, PL-7, PL-12, EJ, OJ (anti-synthetase antibodies), SRP (signal recognition particle), Mi-2, TIF1-γ, MDA5, NXP2, and SAE. Complement levels (C3, C4) were within normal limits. Virological studies were pivotal. A reactive anti-HCV antibody was confirmed, and the quantitative HCV RNA viral load was significantly elevated at 2.8 x 10^6 IU/mL. HCV genotyping identified Genotype 1b. Serologies for Hepatitis B virus and HIV were negative.

Based on the compelling clinical presentation of severe, symmetric proximal muscle weakness, the relapsing-remitting course mirroring a previous episode that responded to immunosuppression, and the robust biochemical evidence of myonecrosis and inflammation, a working diagnosis of an Acute Exacerbation of Presumed Polymyositis, strongly associated with chronic Hepatitis C Virus infection, was made. Definitive diagnostic studies, including MRI of the thighs to assess for muscle edema and to guide a muscle biopsy, as well as EMG/NCS to confirm myopathic changes, were again strongly recommended to the patient. However, after extensive discussion, the patient once more deferred these investigations, expressing a desire to proceed with the treatment that had been effective for him previously.

Given the severity and rapidity of his functional decline, empirical immunosuppressive therapy was deemed medically necessary and was initiated promptly. He was started on high-dose intravenous methylprednisolone (1 gram daily for three days), followed by a transition to high-dose oral prednisone (1 mg/kg/day). Concurrently, azathioprine was re-initiated as a steroid-sparing agent after confirming normal thiopurine methyltransferase (TPMT) enzyme activity. Throughout this period, his liver function tests were monitored closely.

Table 2. Summary of Key Laboratory Findings

Biochemical, Hematological, and Virological Data on Admission

PARAMETER	ADMISSION VALUE	FOLLOW-UP (DAY 5)	REFERENCE RANGE
Muscle Enzymes & Myonecrosis Markers			
Creatine Kinase (CK)	**8,572 U/L ↑↑↑**	**4,250 U/L** ↓ 50.4% Decrease	30 - 200 U/L
Significance: Extremely elevated, confirming severe, acute muscle damage (myonecrosis). The rapid decrease supports a positive response to immunosuppressive therapy.			
Aldolase	**25.4 U/L ↑↑**	**15.1 U/L** ↓ 40.6% Decrease	< 7.6 U/L
Inflammatory Markers			
Erythrocyte Sed. Rate (ESR)	**40 mm/hr ↑**	**25 mm/hr** ↓ Improving	< 15 mm/hr
C-Reactive Protein (CRP)	**25.0 mg/L ↑**	8.0 mg/L ↓ Near Normal	< 5.0 mg/L
Hematology			
White Blood Cell Count	**17.76 × 10^9/L**	11.50 × 10^9/L ↓ Trending to Normal	4.0 - 11.0 x 10^9/L
Platelet Count	**450 × 10^9/L**	380 × 10^9/L ↓ Normalizing	150 - 400 × 10^9/L
Immunology & Virology			
Antinuclear Antibody (ANA)	**1:320 (Speckled Pattern)**	Not Repeated	Negative
Myositis Specific Panel	Negative	Not Applicable	Negative
HCV RNA Viral Load	**2.8 × 10^6 IU/mL**	Not Repeated	Not Detected
Significance: A high viral load confirms active, chronic Hepatitis C infection, strongly implicating it as the persistent immunological trigger for the myositis.			
HCV Genotype	**Genotype 1b**	Not Applicable	N/A

Table 3. Diagnosis, Treatment, and Outcome

A Summary of the Clinical Pathway and Patient Response

Diagnosis	
Presumptive Diagnosis	ACUTE EXACERBATION OF POLYMYOSITIS, strongly associated with Chronic HCV.
Key Supporting Evidence	• **Clinical:** Severe, symmetric, proximal muscle weakness with a relapsing course. • **Biochemical:** Markedly elevated Creatine Kinase (8,572 U/L). • **Virological:** High HCV viral load (2.8×10^6 IU/mL) of a high-risk genotype (1b). • **Historical:** Previous episode with excellent response to immunosuppression.
Diagnostic Limitations	⚠ PATIENT DEFERRAL Gold-standard tests (EMG, Muscle Biopsy) were deferred, making the diagnosis presumptive, not definitive.
Treatment Plan	
Therapeutic Strategy	**1. Acute Immunosuppression (Inpatient)** Goal: Rapidly suppress inflammation to prevent muscle damage. • High-Dose IV Methylprednisolone (1 gram/day for 3 days). • Transition to high-dose Oral Prednisone (1 mg/kg/day). **2. Steroid-Sparing Maintenance** Goal: Enable long-term steroid tapering and reduce side effects. AZATHIOPRINE re-initiated after TPMT testing. **3. Long-Term Viral Eradication** Goal: Remove the presumed immunological trigger to prevent relapse. Referral to Hepatology for Direct-Acting Antiviral (DAA) therapy.
Outcome & Patient Response	
Clinical Response (by Day 5)	✓ SIGNIFICANT IMPROVEMENT • Complete resolution of myalgias. • Objective strength improvement: MMT of hip/quadriceps increased from 2/5 to 3/5.
Biochemical Response (by Day 5)	✓ EXCELLENT RESPONSE Creatine Kinase (CK) level decreased by **50.4%** (from 8,572 U/L to 4,250 U/L).
Disposition	Discharged to an acute rehabilitation facility for intensive physical therapy and continued recovery.

The patient's response to treatment was both rapid and remarkable. By the fifth day of hospitalization, his myalgias had completely resolved, and his muscle strength began to show objective improvement. His MMT score for the iliopsoas and quadriceps muscles improved from 2/5 to 3/5. This clinical improvement was mirrored by a significant downtrend in his biochemical markers; his CK level decreased from

8,572 U/L to 4,250 U/L. He was discharged to an acute rehabilitation facility to continue intensive physical therapy on a slow tapering schedule of prednisone and maintenance azathioprine. A formal consultation and referral were made to a hepatologist to arrange for the initiation of direct-acting antiviral (DAA) therapy for his chronic HCV infection upon stabilization of his myositis.

3. Discussion

This case of severe, recurrent myopathy in a patient with untreated, high-titer chronic Hepatitis C presents a microcosm of the diagnostic and therapeutic complexities that define the intersection of rheumatology and infectious disease. The decision to initiate potent immunosuppression in the absence of definitive histopathological confirmation, yet in the presence of a clear viral trigger, encapsulates a common but high-stakes clinical dilemma.[11] The following discussion will deconstruct the clinical reasoning behind the presumptive diagnosis, explore the central role of the muscle biopsy in distinguishing key differential diagnoses, delve into the presumed immunopathology of both PM and the role of HCV as a trigger, and analyze the risk-benefit calculus that guided the pragmatic management strategy employed.

In the absence of the definitive gold-standard test—a muscle biopsy—the diagnosis of polymyositis remains presumptive. However, the constellation of findings in this case provided a strong, evidence-based foundation for this working diagnosis. The clinical phenotype of a subacute, severe, symmetric, and predominantly proximal muscle weakness, with a relapsing course responsive to steroids, is the quintessential presentation of PM.[12] The lack of any characteristic skin rash strongly argued against dermatomyositis, while the patient's age (48 years) and the acute, relapsing nature of his illness made sporadic inclusion body myositis, a more insidious and relentlessly progressive disease of older adults, less likely.

The laboratory findings provided crucial, albeit non-specific, supportive evidence. The markedly elevated CK level confirmed significant active muscle injury, and the negative comprehensive MSA panel helped to refine the differential diagnosis. Specifically, the absence of anti-SRP antibodies made IMNM a less probable, though not entirely excluded, diagnosis. The decision to treat for PM was therefore an exercise in clinical judgment, based on a high degree of suspicion in a patient with a rapidly debilitating condition for which effective treatment was available.[13]

However, the pivotal role of the muscle biopsy cannot be overstated, as it is the only tool that can definitively differentiate PM from its most important mimics (Figure 1). A more detailed exploration of what a biopsy could have revealed is essential to fully appreciate the diagnostic uncertainty. (1) Polymyositis (PM): The classic histopathological finding in PM is endomysial inflammation, characterized by an infiltration of CD8+ cytotoxic T-lymphocytes that are seen to surround and actively invade non-necrotic myofibers that aberrantly express MHC-I on their surface.[14] This finding provides direct evidence of the cell-mediated cytotoxicity central to PM's pathogenesis; (2) Immune-Mediated Necrotizing Myopathy (IMNM): This is arguably the most critical differential to exclude, especially given the patient's profoundly high CK level. While the anti-SRP antibody was negative, a substantial portion of IMNM cases are seronegative. Histologically, IMNM is defined by widespread myofiber necrosis and regeneration with a notable paucity of lymphocytic inflammatory infiltrates.[15] A biopsy showing this pattern would have fundamentally altered the therapeutic approach, potentially favoring agents like rituximab or intravenous immunoglobulin (IVIg) over azathioprine; (3) Dermatomyositis (DM) Sine Dermatitis: While clinically less likely due to the absence of a rash, an underlying DM process cannot be completely excluded without a biopsy. The characteristic pathology in DM is distinctly different from PM, featuring perimysial and perivascular inflammation composed of CD4+ T-cells and B-cells, often accompanied by perifascicular atrophy; (4) Inclusion Body Myositis (IBM): Although clinically atypical for this patient, IBM can share the

feature of endomysial inflammation with PM.[16] However, the pathognomonic findings in IBM are the presence of rimmed vacuoles within myofibers and intracellular protein aggregates (amyloid and p62), which are absent in classic PM.[17] Thus, the deferral of the muscle biopsy, while a patient-led decision, left the diagnosis resting on strong but circumstantial evidence. This reality powerfully reinforces the manuscript's central theme: clinicians must often act decisively based on a presumptive diagnosis, while simultaneously acknowledging the inherent limitations of that approach.

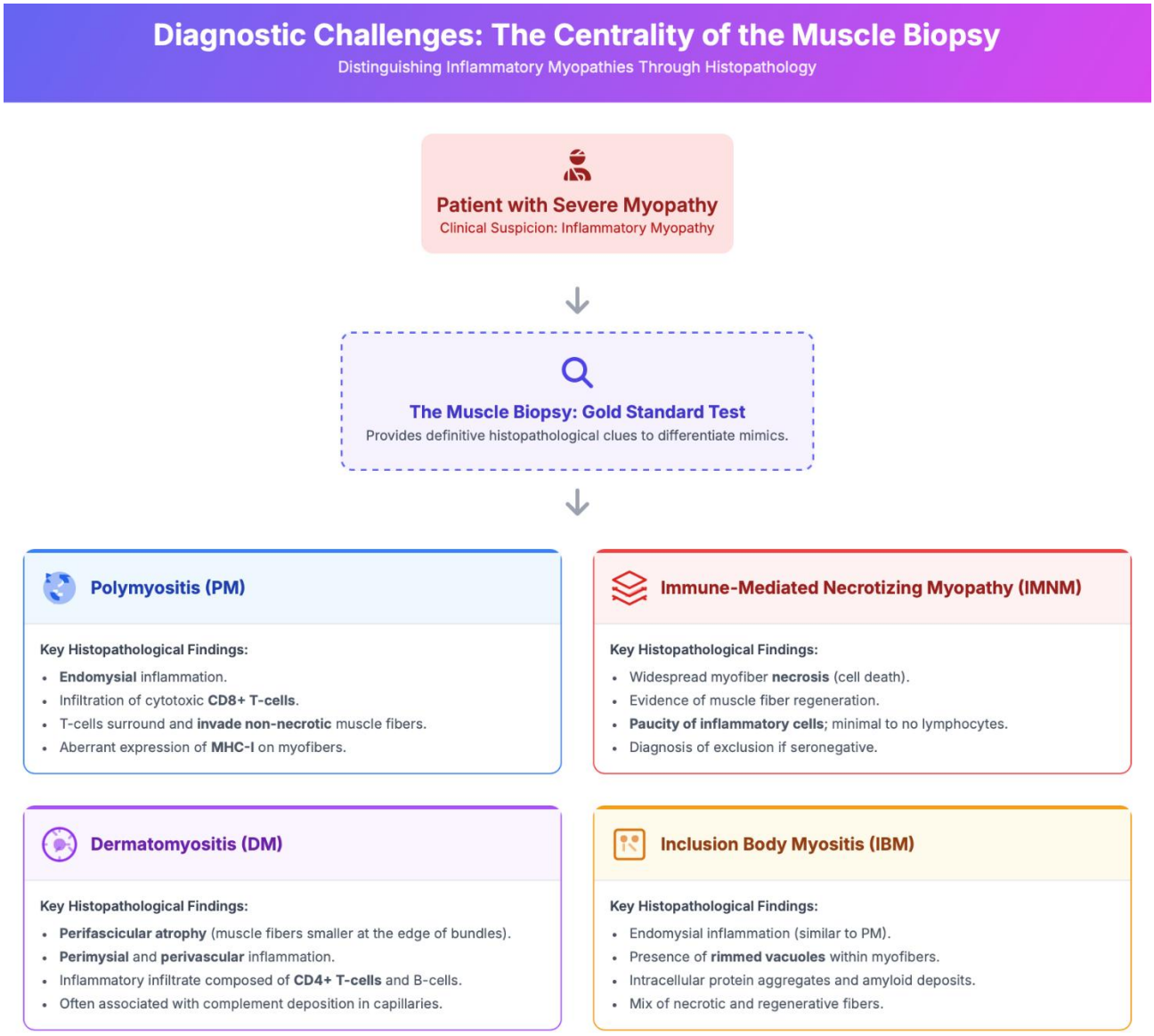

Figure 1. Diagnostic challenges: the centrality of the muscle biopsy in a field of mimics.

While not confirmed histopathologically in this patient, the weakness in presumed PM is driven by a well-elucidated immunopathological process. The cascade begins with the aberrant expression of MHC Class I molecules on the myocyte surface, a phenomenon likely induced by pro-inflammatory cytokines, particularly Interferon-gamma (IFN-γ).[18] In the setting of a chronic HCV infection, the host is in a state of continuous immune activation, providing a plausible and persistent source for such cytokines.

Once MHC-I is upregulated, muscle fibers begin presenting endogenous peptides to the immune system. In a genetically susceptible individual, these self-peptides are misidentified as foreign by cytotoxic CD8+ T-lymphocytes, leading to their activation, clonal expansion, and infiltration into the muscle endomysium. These activated T-cells then bind directly to the MHC-I-expressing myofibers and release cytotoxic granules containing perforin, which creates pores in the sarcolemma, and granzymes, which enter the cell and trigger apoptosis. This highly targeted, cell-by-cell destruction results in the profound weakness and muscle damage seen clinically. It is this presumed cytotoxic T-cell-mediated process that the immunosuppressive therapy with corticosteroids and azathioprine was intended to disrupt.[19]

The presence of a high-titer, active HCV infection is central to this case, strongly suggesting the virus acted as the persistent immunological trigger for both the initial onset and the subsequent relapse of the myopathy. Several mechanisms are plausible for this breach of self-tolerance: (1) Molecular Mimicry: Sequence homology may exist between certain HCV proteins and host muscle autoantigens. An immune response initially mounted against the virus could then cross-react with these self-antigens on muscle fibers, initiating an autoimmune attack; (2) Bystander Activation: The chronic inflammatory milieu created by the HCV infection, rich in cytokines and co-stimulatory molecules, may lead to the non-specific activation of pre-existing, dormant autoreactive T-cells that would otherwise remain quiescent; (3) General Immune Dysregulation: As a lymphotropic virus, HCV can directly infect and modulate the function of immune cells, leading to broad immune dysregulation. This can manifest as polyclonal B-cell activation—evidenced by the patient's positive ANA—and a general failure of the mechanisms that maintain self-tolerance.

The management of this patient epitomizes the challenge of balancing therapeutic urgency with diagnostic uncertainty and competing risks. The severity of the patient's weakness was a medical emergency, threatening his long-term mobility and independence. Delaying treatment pending definitive diagnostics was not a viable option given the rapid functional decline. The empirical use of high-dose corticosteroids and a steroid-sparing agent was a pragmatic decision aimed at rapidly suppressing the presumed T-cell-mediated inflammation to prevent further muscle damage and disability.[20] The patient's dramatic and positive response to this regimen provides strong retrospective support for the working diagnosis of a steroid-responsive inflammatory myopathy.

However, this decision was not without significant risk. Initiating potent immunosuppression in a patient with an HCV viral load of nearly 3 million IU/mL required a careful risk-benefit calculation. Potent immunosuppressants, particularly corticosteroids, can potentially suppress the host's antiviral immune response, leading to an increase in HCV replication. This could theoretically accelerate the progression of liver fibrosis or even trigger a flare of hepatitis, although the latter is less common with HCV than with Hepatitis B.

In this case, the clinical judgment was that the immediate, certain, and severe threat of permanent disability from the myositis outweighed the theoretical and manageable risk of an HCV flare. This calculation was heavily influenced by two factors: (1) the plan to monitor liver function tests closely throughout treatment, and (2) the availability of highly effective and well-tolerated direct-acting antiviral (DAA) therapies that could be initiated once the acute myositis was controlled. The planned sequential approach—stabilizing the life-threatening myositis with immunosuppression first, followed by viral eradication—was a prudent strategy. It allowed for clear monitoring of the response to immunosuppression without the confounding factor of concurrent DAA initiation and its potential side effects.

Ultimately, the most critical long-term strategy for this patient is the eradication of his Hepatitis C

infection. Curing the HCV with DAAs is intended to remove the primary antigenic stimulus that is presumed to be driving the recurrent autoimmune response. Successful viral eradication has been shown in other cases to lead to the remission of HCV-associated autoimmune phenomena, potentially allowing for the eventual withdrawal of long-term immunosuppressive therapy. The importance of patient counseling in this context is paramount, explaining the necessity of this dual approach and the rationale for pursuing definitive diagnostic tests to guide future therapy, should another relapse occur.

4. Conclusion

This case of severe, recurrent myopathy, presumptively diagnosed as polymyositis in a patient with chronic Hepatitis C, illustrates a critical and complex challenge in modern clinical medicine. It powerfully underscores the reality that while a definitive diagnosis via muscle biopsy remains the undisputed gold standard, clinicians must often initiate urgent, potentially life-altering treatment based on strong clinical acumen, a synthesis of supportive laboratory data, and a deep understanding of the likely underlying pathophysiology. The patient's robust positive response to empirical immunosuppression validated the working diagnosis and successfully stabilized the acute, debilitating flare, preserving muscle function.

However, this case argues emphatically that in the context of a known chronic viral trigger like HCV, addressing only the downstream autoimmune response is an incomplete strategy. A durable remission and prevention of future relapses necessitate a dual therapeutic paradigm. This involves not only the acute control of inflammation through immunomodulation but also the eventual eradication of the underlying viral trigger. This report serves as a pragmatic and detailed example of navigating profound diagnostic uncertainty while pursuing a logical, patient-centered, and forward-looking management plan aimed at both controlling debilitating symptoms and, ultimately, eliminating the root cause of the disease. The successful management of such cases hinges on a sophisticated risk-benefit analysis, a sequential therapeutic plan, and clear patient communication.

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