Case Report

Adult-Onset Anti-NXP2 Dermatomyositis and MGUS triggered by COVID-19 vaccination: A clinical pharmacist's report

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Abstract

Background

A 35-year-old previously healthy male developed progressively worsening proximal muscle weakness and pain shortly after receiving the Covishield COVID-19 vaccine, initially presenting with low back and bilateral thigh pain followed by rapid progression to quadriparesis and significant functional impairment. Laboratory evaluation revealed markedly elevated creatine phosphokinase, anti–NXP2 antibody positivity, and MRI findings consistent with inflammatory myositis with subcutaneous involvement. Despite comprehensive autoimmune and malignancy screening being largely negative, serum immunofixation identified a monoclonal IgM lambda gammopathy of uncertain significance. The patient was treated with intravenous immunoglobulin, corticosteroids, and supportive care, resulting in significant clinical and biochemical improvement. Three years later, he experienced a relapse with proximal weakness and characteristic skin changes, which responded well to high-dose steroids and rituximab. This case illustrates severe adult-onset anti–NXP2 antibody-positive dermatomyositis temporally associated with COVID-19 vaccination and complicated by monoclonal gammopathy, highlighting the need for vigilant long-term monitoring for relapse and malignancy, and the importance of timely immunosuppressive therapy to achieve favorable outcomes.

Keywords: Anti–NXP2 antibody; Dermatomyositis; COVID-19 vaccines; Rituximab

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1. Introduction

Idiopathic inflammatory myopathies (IIMs) represent a diverse spectrum of autoimmune diseases that primarily involve skeletal muscle inflammation, producing progressive weakness, and may also affect other organ systems, including the skin, lungs, and heart. Dermatomyositis (DM) is a classic form of IIM, distinguished by symmetrical proximal muscle weakness in combination with pathognomonic cutaneous features such as a violaceous periorbital rash and Gottron's papules [1].

Recent advances in serological profiling have highlighted the diagnostic and prognostic value of myositis-specific autoantibodies (MSAs), which delineate distinct clinical phenotypes within dermatomyositis. One such antibody, directed against nuclear matrix protein 2 (NXP2), is relatively rare in adults, occurring in approximately 1–17% of patients across published series [2,3]. In juvenile populations, anti-NXP2 positivity has been strongly linked to more severe disease courses with calcinosis, marked muscle involvement, and extensive subcutaneous edema [4]. Adult patients with NXP2 antibodies often

display an aggressive clinical phenotype, frequently manifesting severe proximal muscle weakness, pronounced myalgia, generalized edema, and accelerated functional decline. Importantly, this subset also carries a comparatively higher risk of malignancy, underscoring the need for vigilant neoplastic surveillance alongside immunosuppressive therapy [2,5].

Since the introduction of COVID-19 vaccines, a number of reports have emerged describing autoimmune complications temporally associated with immunization, including inflammatory myopathies [6–9]. Overall, vaccination has proven to be highly safe, but isolated immune-mediated events such as Guillain–Barré syndrome, thrombocytopenia, vasculitis, and myositis have been documented ([10,11]. The pathophysiological basis of such rare events remains uncertain, with proposed mechanisms including molecular mimicry between viral antigens and self-tissues, immune adjuvant–related activation, and nonspecific T-cell stimulation. While a causal link has not been firmly established, vaccination may, in select individuals, act as a trigger that unmasks underlying autoimmune susceptibility [7,10].

In adults with dermatomyositis, the incidental finding of a monoclonal gammopathy adds another dimension of clinical concern. Monoclonal gammopathy of uncertain significance (MGUS) becomes more common with advancing age, but its occurrence in younger patients is uncommon and may suggest a predisposition toward malignancy or immune dysregulation (12,13). In the context of myositis, the coexistence of monoclonal gammopathy, although rare, has been occasionally reported and justifies careful longitudinal surveillance for both functional outcomes and potential hematological evolution [14].

Here we describe a case of severe adult-onset anti–NXP2 antibody-positive dermatomyositis with subcutaneous involvement temporally linked to Covishield COVID-19 vaccination and complicated by monoclonal IgM lambda gammopathy, highlighting diagnostic challenges, therapeutic considerations, and the need for longitudinal monitoring.

2. Case Presentation

A 35-year-old previously healthy male remained well until the last week of April 2022, when he developed moderate, non-radiating low back pain, which over the next few days extended to both thighs. He experienced difficulty climbing stairs but had no trouble gripping slippers or lifting his feet. The pain persisted throughout the day. He was admitted locally and received injectable medications for five days, following which his weakness improved, although mild pain persisted. By the third week of May, thigh pain worsened and was accompanied by pain in both arms. He gradually became unable to perform overhead activities and developed progressive weakness of his lower limbs, requiring support to get up from a seated position and climb stairs. Over the next five days, he needed assistance to turn in bed and sit up. By 25 May, he was unable to stand even with support and was bedridden. There was a history of intermittent low-grade fever at the height of the pain and generalised swelling of the limbs. He denied any history of diabetes, hypertension, tuberculosis, jaundice, epilepsy, or hypothyroidism. On detailed enquiry, it was noted that the onset of these symptoms occurred shortly after receiving a Covishield COVID-19 vaccine.

On 30 May 2022, he presented to an outside hospital with rapidly progressive, painful proximal-distal quadriparesis. Laboratory evaluation revealed mild anaemia, a reticulocyte counts of 8.8% suggesting haemolysis, a CPK of 46,000 U/L, and elevated LDH, ferritin, CRP, ESR, SGOT, and SGPT, with low serum calcium. Direct and indirect Coombs

tests were negative. Urine analysis was normal with no myoglobinuria. HIV, HBsAg, and HCV were negative, and autoimmune screening (ANA, ANCA, rheumatoid factor, and paraneoplastic antibody panel) results were also negative. The myositis antibody panel demonstrated strong anti–NXP2 positivity. MRI of the muscles revealed extensive inflammatory changes, fascial oedema, panniculitis, and scattered necrosis, consistent with NXP2-associated inflammatory myositis with subcutaneous involvement. Pulmonary function testing showed a restrictive pattern, and autonomic function testing demonstrated mild cardiac autonomic dysfunction with a negative tilt-table test. Nerve conduction studies were normal. The malignancy workup, including a peripheral smear, urine for Bence-Jones protein, and urine immunofixation electrophoresis, was negative. However, serum immunofixation revealed a polyclonal gamma elevation, likely due to post-IVIG or infection, along with a monoclonal IgM lambda protein. Ultrasound of the abdomen was unremarkable except for mild left perinephritic fat stranding suggestive of possible early pyelonephritis.

He was treated with IVIG at a dose of 2 g/kg over six days, oral corticosteroids, two units of packed red blood cells, intravenous fluids, DVT prophylaxis, and potassium and calcium supplementation with general supportive care. During hospitalisation, he developed Methicillin-Susceptible Staphylococcus aureus MSSA sepsis, which was treated successfully with 10 days of intravenous piperacillin–tazobactam and amikacin, and later de-escalated to oral therapy according to sensitivity. At discharge, his lower limb and neck muscle strength had improved significantly, with mild improvement in upper limbs; he was free of pain, and CPK had decreased to 641 U/L. PET-MR/CT was deferred until resolution of muscle inflammation. He was counselled regarding prognosis, risk of relapse, and the importance of malignancy surveillance, and was advised to follow up for monitoring of the IgM lambda gammopathy.

He remained stable for the next three years but was admitted on 19 July 2025 with a 20-day history of back pain, bilateral thigh pain, and difficulty climbing stairs and rising from a seated position. Examination revealed a periorbital rash with mild periorbital puffiness and proximal lower limb weakness. Anti–NXP2 antibody was positive, and dermatomyositis was considered. This episode was part of his relapse course, with the original onset having occurred after the Covishield vaccination. He was treated with high-dose intravenous methylprednisolone 1 g daily for four days, followed by a tapering dose of oral steroids, and received rituximab 1 g in accordance with his ongoing immunotherapy regimen. Supportive measures included a proton pump inhibitor, calcium, and vitamin D supplementation. He improved markedly, with resolution of weakness and skin rash, and was discharged afebrile, haemodynamically stable, and with full strength (5/5) in both lower limbs. Discharge medications included Tab. Pantoprazole 40 mg once daily, Tab. Dical-D 500 mg twice daily, Tab. Cilnidipine 10 mg once daily, and Tab. Prednisolone 40 mg once daily with a planned taper.

This case highlights an adult-onset anti–NXP2 antibody-positive dermatomyositis with severe initial presentation, temporally associated with Covishield vaccination, complicated by monoclonal gammopathy of uncertain significance. The patient demonstrated a good therapeutic response to IVIG, corticosteroids, and rituximab, but required ongoing follow-up for relapse surveillance, functional recovery, and malignancy screening.

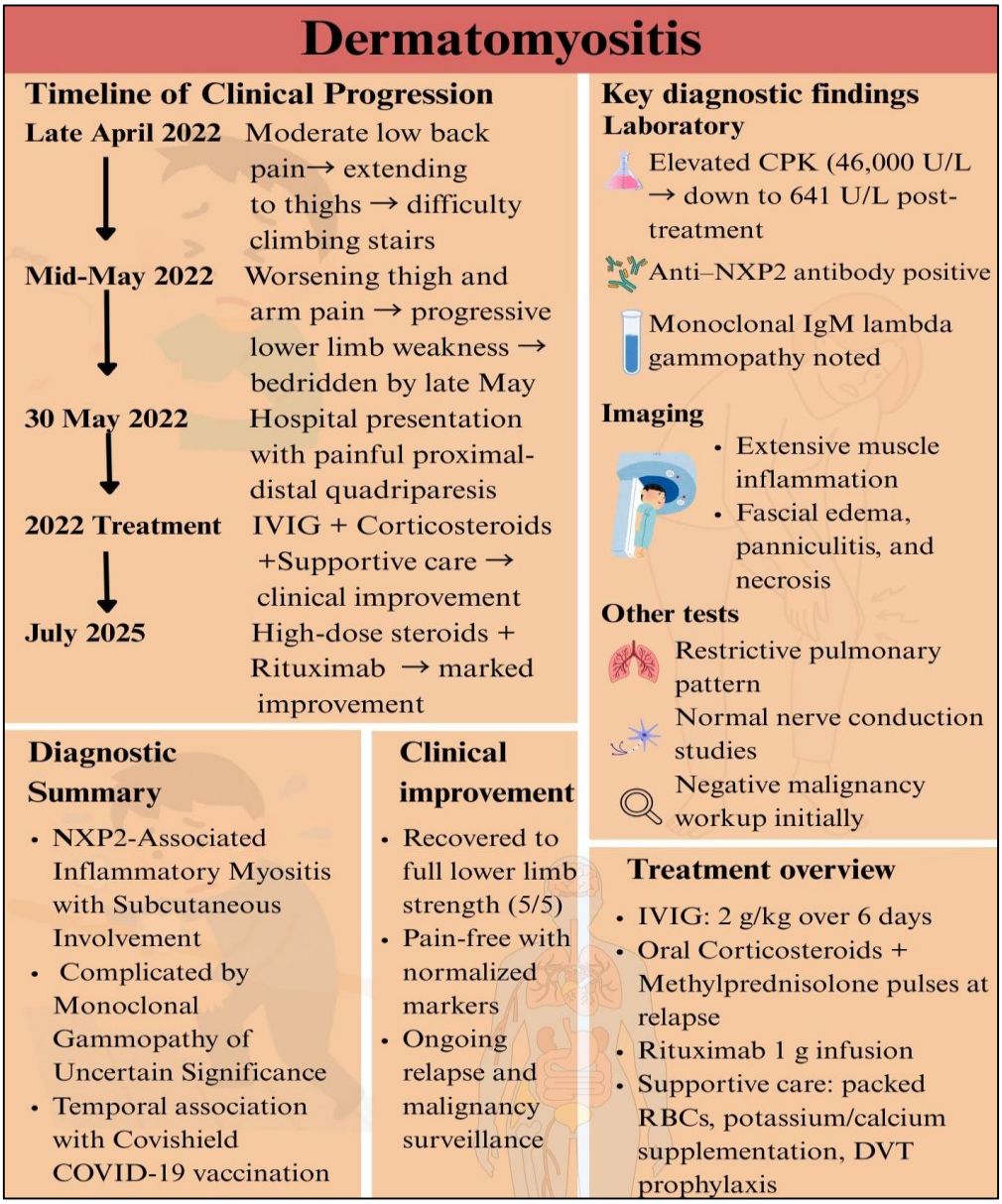

Fig (1): Overview of Dermatomyositis in a 35-year-old Male

3. Discussion

This case highlights an uncommon and severe manifestation of adult-onset dermatomyositis associated with anti–NXP2 antibodies, complicated by the presence of monoclonal gammopathy of uncertain significance (MGUS), and occurring soon after COVID-19 vaccination. The patient's extensive muscle inflammation and subcutaneous involvement align with the aggressive clinical profile typically seen in NXP2-related myositis, a form that is recognized for its serious disease course and elevated risk of cancer in adults. While this condition is well documented in pediatric populations, adult cases are less frequently reported, underscoring the importance of awareness for prompt diagnosis and treatment.

The onset of symptoms shortly after Covishield vaccination prompts consideration of vaccines as possible immune triggers. Although a definitive causal relationship cannot be established, this report contributes to the limited but growing evidence of rare auto-

immune muscle disorders arising post–COVID-19 vaccination. Hypotheses include molecular mimicry and immune system stimulation, with vaccination potentially acting as an immunologic "second hit" that unmasks latent autoimmunity rather than being a direct cause. Given the millions of vaccine doses administered with only rare autoimmune side effects, these events remain exceptional, yet clinicians should remain vigilant for early detection and management.

The unexpected finding of a monoclonal IgM lambda gammopathy adds diagnostic complexity. MGUS is generally found in older adults, and its occurrence in younger individuals with inflammatory myopathies is unusual but not unprecedented. This association might indicate an underlying immune system dysregulation or serve as an early sign of hematological malignancy, necessitating periodic monitoring. Considering the increased cancer risk linked with adult anti-NXP2 dermatomyositis, comprehensive malignancy screening and continued surveillance are essential.

From a therapeutic standpoint, this patient's positive response to intravenous immunoglobulin, corticosteroids, and rituximab highlights the value of aggressive immunosuppression in controlling severe and rapidly progressing dermatomyositis. The relapse after three years reflects the chronic and potentially recurrent nature of the disease, emphasizing the importance of sustained immunomodulatory treatment and follow-up care.

4. Conclusion

This case underscores the rare but significant presentation of adult-onset anti–NXP2 antibody-positive dermatomyositis with severe muscle and subcutaneous involvement, temporally linked to COVID-19 vaccination. The coexistence of monoclonal gammopathy of uncertain significance adds a challenging dimension, highlighting the need for thorough malignancy screening and long-term monitoring. Prompt recognition and aggressive immunosuppressive therapy, including intravenous immunoglobulin and rituximab, can lead to substantial improvement even in severe cases. Given the potential for relapse and the multifaceted nature of this condition, multidisciplinary care and vigilant follow-up are essential to optimize patient outcomes and manage disease recurrence or complications effectively.

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