Journal of the
Bahrain Medical Society

Altamimi et al., J Bahrain Med Soc. 2022;34(4):44-48

CASE REPORT

Rituximab Therapy in Polymyositis-associated Severe Dysphagia: A Case Report

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Received date: December 10, 2021; **Accepted date:** March 20, 2022; **Published date:** December 31, 2022

Abstract

Polymyositis is one of the inflammatory myopathies. It is a chronic autoimmune disease that usually involves the proximal muscles. It is caused by an inflammatory infiltrate of the skeletal muscle. Notably, dysphagia occurs in one-third of the patients. Traditional treatment with steroids and immune modulators has been reported to have varied outcomes and recurrent symptomatic flares. The dysphagia which occurs in such myopathies may be one of the recurrent and severe symptoms of myopathies, often associated with considerable mortality and morbidity. Dysphagia, an often-noted clinical presentation of polymyositis (PM) /dermatomyositis (DM) can be the initial sign of idiopathic inflammatory myopathies. It can cause considerable morbidity in patients such as reduced pharyngeal contractility, hypomotility of the esophagus, cricopharyngeal dysfunction, and decreased laryngeal elevation. Here is a case of severe dysphagia in a patient with muscle and skin involvement in PM. Steroids are the first line of treatment for patients with myositis and the same was adopted initially for the current case. Rituximab was used after unsuccessful attempts with other recommended first-line treatments. Reversal of dysphagia and overall improvement were achieved with the use of rituximab and intravenous immunoglobulins. The patient demonstrated significant improvement in swallowing, with reasonable improvement, following which the percutaneous endoscopic gastrostomy (PEG) tube was removed. After 15 months, the patient showed 100% resolution of all symptoms and was advised to stop all medications. Therefore, we suggest that this combination may be considered in cases with dysphagia flares in DM, where traditional treatment options have shown no benefit.

Keywords: Deglutition Disorders, Dysphagia, Muscular Diseases, Myopathy, Polymyositis, Rituximab

Introduction

Dermatomyositis (DM), inclusion body myositis (IBM), and polymyositis (PM) are three main subgroups of idiopathic inflammatory myopathies (IIM).[1] The symptoms of dysphagia or difficulty in swallowing may be seen due to inflammation of the striated skeletal muscles in the upper oropharynx.[1] A recent study estimated a prevalence of 2.3–4.0 for

IIM per 100,000 persons per year with a mean age of 51.2 (± 16.9) years. A female predominance has been reported in the case of IIM, with more than two-thirds of patients suffering from associated comorbidities (interstitial lung disease).[2] The main clinical feature of PM is subacute proximal myopathy presented as muscle weakness.[3] PM is a diagnostic challenge and mimics many other myopathies. On the other hand, DM is clinically identified by characteristic cutaneous findings accompanying the classic presentation.[3]

Dysphonia (altered speech or hoarseness of voice) and dysphagia are documented as early manifestations of autoimmune inflammatory myopathies of which dysphagia can result in mortality and morbidity.[4,5] Investigations such as serological markers, evaluation of swallowing patterns, and screening scans apart from clinical presentation are needed to diagnose these conditions.[1,2] Glucocorticoids (GC) are still the first line of treatment along with immune modulators, while intravenous immunoglobulins (IVIG) and non-pharmacotherapy (exercises) are also known to show improvement in some cases.[5,6] The use of Rituximab in cases of refractory inflammatory myopathies was documented in several trials and a case report [overlapped systemic sclerosis (SSC)-myositis].[7,8] In this case, rituximab and IVIG was used for severe dysphagia requiring PEG feeding in a case of polymyositis.

Case Presentation

A 29-year-old male patient, reported to the Rheumatology Clinic, University Hospital Waterford, with complaints of flu-like symptoms over two weeks. The chief complaint was pain in the muscles of the lower limbs for a few weeks. The limb pain was described to have worsened over the past few days and was associated with lower back pain as well. The patient also gave a history of swelling of the left arm extending from the middle portion of the arm towards (and around) the elbow joint over the past 4-5 days. He additionally complained of fatigue associated with weight loss (around 10 kg) but no fever, sweats, orchills. Signs such as muscle pain, proximal muscle weakness (in all four limbs), struggling to stand up from a sitting position, and lifting of proximal upper limbs were also noted. Reduced handgrip strength, (bilaterally over last 3 to 4 weeks), occurrence of a new rash around the nose and erythema. A maculopapular rash on the abdomen that resolved in a few days was also noted from previous sources. The patient gave a history of eczema and psoriasis but denied a history of photosensitivity, skin rash, joint pain or swelling, mouth ulcers, and dry eyes or mouth. There was no evidence of documented Raynaud's syndrome. There was no family history of connective tissue disorders or inflammatory arthritis. However, a positive family history of esophageal and pancreatic cancer was noted. The patient's drug history revealed that he was using seretide (salmeterol and fluticasone) inhalers and proton pump inhibitors for bronchial asthma and gastritis respectively.

On examination, the patient was conscious, oriented, and afebrile. He showed a malar rash across the nose, diffuse erythematous papules on his forehead, dry scalp, and psoriatic patches on the lower limbs. The skin over the abdomen did not show any erythema or rash. The left-arm showed a 3x4 cm diffused swelling, extending from the center of the arm to the wrist. The swelling showed a local rise in temperature, elicited tenderness along the muscles, but no erythema. There was tenderness and swelling on the left elbow with a reduced range of movements (ROM). There was tenderness of the right upper limb muscles, but not over the joints. The proximal muscles of both upper and lower limbs demonstrated weakness with reduced hand grip. He was unable to stand from a sitting position without aid. There was no distal muscle weakness and no tenderness or swelling of the lower limbs.

Serology showed raised creatinine phosphokinase (CPK) of 21304 IU/L initially, which later reduced to 17880 IU/L, and then to 14810 IU/L. The C reactive protein (CRP) level was 17, and the serum lactate dehydrogenase (LDH) level was 1117 U/L. The liver function tests revealed a serum albumin level of 30 g/L, hepatic enzymology showed a value of 18 U/L and 452 U/L for the serum alanine aminotransferase (ALT), and serum aminotransferase (AST) respectively while C3 and C4 were within normal limits. The antinuclear antibody (ANA), antineutrophil cytoplasmic

antibodies (ANCA), and lupus autoantibodies have been requested but these results were not available at the time the clinical diagnosis was made. Considering the clinical presentation and serological profile of the patient, the diagnostic impression was inferred to be either dermatomyositis (DM) or polymyositis (PM). A dermatology consultation revealed nail fold capillary abnormalities, nail pitting, and purpuric purple discoloration of the eyelids, with a provisional diagnosis of 'cutaneous manifestations of dermatomyositis.

Further, doppler ultrasonography of the left upper limb showed no signs of deep vein thrombosis (DVT). A computed tomography scan (CT) of the thorax-abdomen-pelvis ruled out malignancies.

The patient was started on pulsed steroid therapy of 500 mg intravenous (IV) for 3 days followed by a maintenance dose of prednisolone 60 mg orally which was meant to be tapered,followed by methotrexate 15 mg orally once a week with folic acid supplements. Improvement of pain in the limbs was noted but weakness and associated reduced ROM persisted.

The patient was discharged as he showed improvement and indicated a satisfactory response to treatment with tapering of prednisolone dose to 55 mg over the following week. However, the patient reported back in 3 days with extreme difficulty in swallowing and hoarseness of voice. Although he was on prednisolone 55 mg, he was unable to tolerate oral intake of food and was deemed at risk of aspiration. Therefore a nasogastric tube (NGT) was inserted. His electromyography (EMG) initially requested showed acute inflammatory necrotizing myopathy, more evident in the upper limb than the lower limb. Muscle biopsy of the quadriceps showed striated muscle with no pathologic diagnosis.

At this stage, the team decided to administer rituximab 1 g given in 2 doses (on day 1 and on day 14). The patient was administered denosumab 60 mg while simultaneously tapering prednisolone. The patient remained symptomatic of dysphagia and hoarseness of voice, so we asked for ear nose throat specialist (ENT) and speech therapist consult. They conducted a fiberoptic endoscopic evaluation of swallowing (FEES) and advised percutaneous endoscopic gastrostomy (PEG) to avoid complications such as aspiration. Accordingly, the team started the patient on an intravenous immunoglobulins (IVIG) regime of 2 g/kg divided into three consecutive doses for three days (40 gm, 40 gm and 35 gm) and scheduled for a PEG insertion a week later.

The patient demonstrated significant improvement in swallowing, but his speech remained weak with hoarseness even after 3 months of treatment. In the following 6-month review, the patient showed reasonable improvement and the PEG tube was removed. The patient maintained stable weight at the time of the last appointment and was given a regular follow up.

Discussion

The present case had both muscle and skin involvement. Dysphagia noted in IIM is due to inflammation of this skeletal muscle belt.[1] The clinical signs of PM are subacute proximal myopathy that cause muscle weakness over weeks to months and is frequently misdiagnosed, owing to the lack of a unique clinical phenotype and often arrived at as a diagnosis of exclusion.[3,4] This excludes those who have a rash, a family history of neuromuscular disease, and exposure to myotoxic drugs (e.g., statins, and zidovudine).[3] PM mimics many other myopathies and may also be diagnosed incorrectly in cases of DM, or as an overlap syndrome associated with a connective tissue disease (CTD). DM on the other hand is clinically identified by a characteristic rash accompanying subacute muscle weakness. The skin manifestations of DM include a violaceous eruption (Gottron's papules) on the knuckles, facial rash, a characteristic periorbital heliotrope (blue–purple edema), or an atypical body rash which may evolve into a scaly discoloration. Also, dilated capillary loops at the base of the fingernails, irregular and thickened cuticles, and cracked palmar fingertips ("mechanic's hands") are characteristic of DM.[3] The self-limiting skin rash, dilated capillary loops, malar rash, and eyelid discoloration/ edema was noted in the case presented here.

Dysphagia, an often-noted clinical presentation of PM/DM can be the initial sign of IIM and can cause considerable morbidity in patients such as reduced pharyngeal contractility, hypomotility

of esophagus, cricopharyngeal dysfunction, and decreased laryngeal elevation. The prime consequence of these is impaired deglutition which can lead to life-threatening aspiration pneumonia.[4] The risk of such aspiration was anticipated and NGT insertion was carried out in this case. The American College of Rheumatology/European League against Rheumatism (ACR/EULAR) diagnostic criteria recommend assessments with a flexible endoscopic evaluation of swallowing (FEES) or video fluoroscopy (VFSS) for evaluation of swallowing in these sets of patients.[1] The FEES was aptly adopted in the current scenario. The laboratory findings included elevated creatine phosphokinase (CPK), autoantibodies in serum, and inflammatory infiltrates in muscle biopsy for diagnosis of PM.[2] This CPK enzyme served as a diagnostic and prognostic marker (the reduction in values post-treatment) in the current case. Standard immunomodulatory therapy can improve swallowing function and dysphagia and, therefore, must be included as one of the therapeutic targets.[1]

Steroids are the first line of treatment for patients with myositis and the same was adopted initially for the current case. GCs with another immunosuppressive agent are adopted by most clinicians to reduce the risk of GC-related side effects. However, a combination of drugs, adjuvant exercise therapies, and the use of newer drugs (such as rituximab) were in clinical trials due to the lack of effectiveness of one single approach.[5] The use of IVIG (immunoglobulins) after lack of response to conventional treatments (high-dose glucocorticoids with methotrexate and/or azathioprine) for dysphagia is also known in clinical practice. A study in 2021 showed that 2 g/kg IVIG for three doses, one month apart was effective for IIM-associated refractory dysphagia. Our case was presented prior to this study but it supports our choice even though we used single-dose regimen.[6] The use of rituximab in cases of refractory inflammatory myopathy (i.e., long-standing PM or DM) who responded poorly to prednisone combined with several immunosuppressants is well documented.[7] Intravenous rituximab 1,000 mg (two doses 14 days apart) not only improved muscle strength, but also decreased the need for steroids and methotrexate in the above case. A recent case report documented findings with systemic sclerosis (SSC)-myositis overlap syndrome, presenting with severe dysphagia requiring PEG feeding, similar to ours. An improvement was reported in this case with overlap syndrome with the use of high dose corticosteroids, azathioprine, two courses of IVIG and rituximab. This patient maintained her weight and normal function, 20 months following hospital discharge.[8] This is in line with the current case where similar course of medical management led to improvement over 15 months. Favorable rituximab-based response in patients with refractory idiopathic inflammatory myopathies was shown in a recent study but with a minimal response in young individuals.[9] Furthermore, an Asian study has endorsed rituximab to be an effective (response rate 86%) and safe therapeutic option (low adverse effects or infections) for refractory IIM in the absence of response to other conventional treatment modalities.[10]

Conclusion

Dysphagia may be one of the serious symptoms in patients with inflammatory myopathies mandating prompt PEG /intubation to prevent associated mortality and morbidity. Reversal of dysphagia and overall improvement were achieved with the use of rituximab and IVIG in the case presented. Therefore, we suggest that this combination may be considered in cases with dysphagia flares in DM where traditional treatment options have shown no benefit. The use of a single loading dose of IVIG was sufficient in our case.

Competing interests

The authors declare no competing financial interests.

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