Early addition of rituximab in the management of myositis associated with systemic lupus erythematosus

Mervat E. Behiry, Ahmed Shaker, Kyrillus Shohdy, Fadi Nagy

Department of Internal Medicine, Faculty of Medicine, Cairo University, Giza, Egypt

Correspondence to Ahmed Shaker, BSc, Department of Internal Medicine, Faculty of Medicine, Cairo University, Giza, 12613, Egypt. Tel: +20 102 618 1641; fax: 02-37484078; e-mail: ahmedshaker0000@yahoo.com

Received 6 October 2018
Accepted 7 August 2019
Published: 18 August 2020

The Egyptian Journal of Internal Medicine
2019, 31:981–982

Targeting B-cell in systemic lupus erythematosus (SLE) seems to be a promising approach. Although rituximab failed to show efficacy in refractory SLE in clinical trial setting, real-world experience still shows some efficacy in certain situations. A 20-year-old woman was diagnosed with SLE with coexistent myositis. The patient's muscular condition did not improve on corticosteroids, addition of rituximab could achieve complete response. Introducing rituximab early for the nonrenal manifestations of SLE merits further investigation.

Keywords:
myositis, rituximab, systemic lupus erythematosus

Egypt J Intern Med 31:981–982

1110-7782

Introduction

Systemic lupus erythematosus (SLE) is an auto-inflammatory disorder with a myriad of systemic affections and manifestations. B-cells play an important role in the pathogenesis of SLE. This pushes investigation of anti-B-cell antibody therapies such as rituximab (anti-CD20) in the refractory cases of SLE. Several case series and off-label experiences showed promising efficacy of rituximab. However, the three prospective clinical trials of rituximab in patients with refractory SLE failed to meet their primary endpoints. Currently there is only one drug, belimumab, that targets B-cells that holds approval from US FDA in such setting based on three positive clinical trials [1]. This heterogenous results suggest the potential role of rituximab for a selected population of SLE patients.

Case presentation

A 20-year-old woman presented to our clinic with fever of 1-month duration that was associated with arthralgia involving both the knees, ankles, elbows, and wrists. She also had malar rash and symmetric weakness of both extremities. She reported dyspnea on mild exertion. She denied hair loss, Raynaud's phenomenon, or any other musculoskeletal manifestations. Physical examination showed proximal muscle wasting of both upper and lower limbs. Lab workup showed microcytic hypochromic anemia with leukopenia, Erythrocyte sidemination rate (ESR) of 123, and C-reactive protein (CRP) of 120 mg/l (normal<5). Lactate dehydrogenase (LDH) was elevated to 462 U/l (NL<247) with a creatine phosphokinase value of 282 (NL: 60–170). Her serology was positive for Anti nuclear antibodies (ANA) and anti-dsDNA. C3 and C4 were consumed. electromyography (EMG) showed excessive spontaneous activity, polyphasic potentials of short duration and low amplitude confirming diffuse myositis of the proximal and distal muscles of both upper and lower limbs. Screening for renal and other system affections was unremarkable. Diagnosis of SLE was made and the patients started corticosteroids and showed improvement of fever and hematologic indices. In view of persistent severe muscle weakness, she received rituximab 1 g every 2 weeks. After two doses, her muscular condition was completely improved. Muscle enzymes and EMG were normal. Then she was kept on the standard treatment.

Discussion

Several studies either retrospective or prospective randomized trials have investigated the efficacy and safety of rituximab for refractory SLE patients. Not all SLE manifestations respond the same to rituximab. Proliferative nephritis and central nervous system (CNS) affection were among the most common responding disease activities. Muscular affection is a pertinent feature of SLE and is highly variable across studies (range: 2.6–16%) [2]. It is important in this regard to differentiate between myalgia, which is a common symptom, and true myositis; the latter has to satisfy the following criteria: (a) persistent muscle weakness in the proximal or distal extremities, (b) increased levels of creatine phosphokinase, and (c) abnormal EMG. Overlap syndrome should be carefully excluded. One cross-sectional study [3] on 1701 lupus patients could identify 44 (2.6%) patients with SLE-associated myositis.

Table 1 Studies reporting response of myositis-associated systemic lupus erythematosus to rituximab

References	Type of study	Total patients/with muscular affection	Regimen of rituximab	Outcome
Tanaka *et al.* [5]	Open-label phase I/II trial	15/2	500 mg/week ×4 doses or 1 g/2 weeks ×2 doses	One patient showed transient improvement (24 weeks) on his BILAG score
Ramos-Casals *et al.* [4]	Off-label case series	107/3	375 mg/m^2/week (×4) or 1 g/15 days (×2)	One patient improved
Hui *et al.* [6]	Case report	One with small muscle myositis	500 mg/2 weeks ×2	Excellent clinical improvement
Bang *et al.* [7]	Retrospective study	39/3	Various regimens	Two partial clinical response at 6 months

BILAG, British Isles Lupus Assessment Group.

Myositis in those SLE patients tend to present with weakness rather diffuse pain without dysphagia or respiratory muscles affection. In studies of rituximab in refractory SLE, few reports of SLE-associated myositis were included. For instance, one case series of 107 SLE patients, only one patient of the three with muscular affection achieved organ-specific response [4]. Data on muscular affection response is sparse due to the infrequency of such events and poor characterization of such manifestation (Table 1). It is of utmost importance to distinguish true inflammatory myositis from other muscle-related conditions in SLE. Myositis-associated SLE in our patient was diagnosed based on clinical examination and EMG. EMG is still the most accurate practical way to diagnose true myositis from myalgia and fatigue [8]. Biopsy is not required in most occasions. Introducing rituximab in early phase may contribute to the marked response in our case. Proper selection and tailoring options might improve the response rate of SLE patients with nonrenal manifestations to the commonly available anti-B-cell therapies such as rituximab.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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