Case Report

Refactory Lupus Panniculitis Treated Successfully with Rituximab: Two Cases

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Abstract

Lupus panniculitis is usually difficult to treat, and the patient is often put on multiple immunosuppressives with variable clinical response and relapses, notwithstanding the long-term side effects. We describe two cases of refractory lupus panniculitis which have been treated successfully with rituximab which is a chimeric anti-CD20 antibody. It reduces the number of circulating mature B-cells, thereby reducing the autoantibodies and the mediators of inflammation. Rituximab is a good alternative to patients who are not responsive to conventional treatment options for lupus panniculitis. There have been few side effects reported by the patients, but the clinical response and psychological well-being clearly outweigh them.

Keywords: India, lupus, panniculitis, refractory, rituximab

Résumé

La panniculite lupique est généralement difficile à traiter et le patient est souvent soumis à plusieurs immunosupresseurs avec une réponse clinique variable et les rechutes, malgré les effets secondaires à long terme. Nous décrivons deux cas de panniculite lupique réfractaire qui ont été traités rituximab qui est un anticorps anti-CD20 chimérique. Il réduit le nombre de cellules B matures en circulation, réduisant ainsi la les autoanticorps et les médiateurs de l’inflammation. Le rituximab est une bonne alternative aux patients qui ne répondent pas aux traitements conventionnels options de traitement pour la panniculite lupique. Les patients ont signalé peu d’effets secondaires, mais la réponse clinique et le bien-être psychologique les surpassent clairement.

Mots clés: Inde, lupus, panniculite, réfractaire, rituximab

Introduction

One of the rare manifestations of systemic lupus erythematosus (SLE) is panniculitis, presenting as subcutaneous tender erythematous nodules usually affecting the proximal extremities and shoulders, the buttocks, trunk, breast, face, and scalp.[1] The incidence of panniculitis among SLE patients is reported to be around 2%–5%.[2] Lupus panniculitis is often difficult to treat, and patients often require multiple immunosuppressive drugs with variable clinical response and relapses. Here, we report two cases of lupus panniculitis refractory to several drugs such as antimalarials, systemic steroids, and immunosuppressives which finally responded to rituximab, an anti-CD20 antibody.

Case Reports

Case 1

A 34-year-old female presented with painful nodules over the extensor aspect of the legs, oral ulcers, reduced vision in eyes, mood disturbances, and irritability for the past 3 years.

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In 2001, she developed low-grade continuous fever, alopecia, and hyperpigmentation on exposed areas of the body. On investigation, she was found to have Antinuclear antibody (ANA) positivity and was started on chloroquine with the provisional diagnosis of autoimmune disease. In 2003, she developed malar rash, pain, and swelling of small joints of the hands and feet with morning stiffness, oral ulcers, and a single episode of generalized seizure, following which she was diagnosed to have SLE. She was started on prednisolone along with chloroquine. In 2011, she had worsening of symptoms with polyarthralgia, oral ulcers, and diffuse skin rashes. She was started on mycophenolate 2 g/day. In January 2014, she developed painful palpable fluctuating red nodules in the extensor aspect of both the legs, largest measuring 3 cm × 5 cm, which turned violet followed by black. Skin biopsy revealed infiltration of subcutaneous fat with foamy macrophages and perivascular lymphocytic infiltrate consistent with lupus panniculitis [Figure 1]. Mycophenolate was stopped and she was started on intravenous pulse cyclophosphamide (500 mg/month) for 6 months, following which azathioprine was added, but the lesions persisted.

On investigations, her complete blood count, kidney function test, and liver function test were normal. Her anti-ds DNA was positive (196 U/mL, normal <20 U/mL). C3 and C4 levels were normal. She had nonnephrotic range proteinuria (24-h urine protein = 235 mg) with microscopic hematuria. She was given two doses of 1 g of rituximab 2 weeks apart for the lupus panniculitis. She had a remarkable response to rituximab and all her nodules disappeared. She was relieved of all the symptoms attributed to lupus. She was symptom-free for the past 24 months, and on maintenance, rituximab at a dose of 500 mg every 6 months along with deflazacort (6 mg/day) and hydroxychloroquine (HCQ).

**Case 2**

A 46-year-old female presented with the complaints of pain, thickening, and discoloration of the skin over the right leg for 1 year, which was insidious in onset, gradually progressive, starting from the ankle and ascending in nature involving lower 2/3rd of the leg. In 1994, she developed polyarthritis low-grade continuous fever, malar rash, itchy scaly lesions over the face and upper limbs, photosensitivity, and three episodes of generalized seizures. She was diagnosed as central nervous system lupus and was started on prednisolone (1 mg/kg/day) and HCQ. In 2011, she had relapse of SLE with fever, oral ulcers, malar rash, and alopecia. She also developed facial puffiness. Urine routine and microscopy revealed proteinuria (2 g/day) and microscopic hematuria; kidney biopsy revealed diffuse proliferative lupus nephritis (lupus nephritis Class IV). She responded to mycophenolate (2 g/day). On examination, there was no pallor, icterus, clubbing, cyanosis, lymphadenopathy, or pedal edema. On local examination, there was blackening over the lower part of the right leg up to the ankle joint. There was also tenderness over the same area. Systemic examination was within the normal limits. Her erythrocyte sedimentation rate was 94 mm in the 1st h and anti-ds DNA was 117 U/mL (normal <20 U/mL). Skin biopsy showed features consistent with lupus panniculitis [Figure 2]. Her serum C3 was mildly decreased (79 mg/dL). Urine microscopy revealed 10–12 red blood cells/high-power field. Serum urea and creatinine were normal. Thus, she was diagnosed as a case of lupus nephritis with panniculitis which was refractory to prednisolone, HCQ, and mycophenolate. She was given two doses of rituximab 1 g 2 weeks apart, following which her symptoms subsided. On follow-up at 24 months, there was no recurrence of panniculitis. She is continuing on the maintenance doses of mycophenolate (2 g/day), HCQ, prednisolone (5 mg/day), and rituximab (500 mg) infusion every 6 monthly.

**DISCUSSION**

The first-line treatment of lupus panniculitis is antimalarials (HCQ/chloroquine) followed by systemic steroids. Immunosuppressives such as methotrexate, mycophenolate, cyclophosphamide, and azathioprine are some of the other treatment modalities that have been tried but with variable outcome. Lupus panniculitis is particularly difficult to treat.
In the first case, she was a known case of SLE for the past 17 years and she had lupus nephritis as well. Initially, she was on antimalarials (chloroquine) and prednisolone followed by mycophenolate, cyclophosphamide, and azathioprine. In an endeavor to treat refractory panniculitis, rituximab was administered to which she responded [Figure 3]. In the second case, she had SLE for the past 24 years and was on HCQ and prednisolone. Later, she developed lupus nephritis and mycophenolate was added to her treatment. She developed panniculitis while being treated with steroids, HCQ, and mycophenolate. She was treated with rituximab to which she responded well and was found to be asymptomatic at follow-up after 2 years [Figure 4]. Thus, we describe two cases of refractory lupus panniculitis which have been treated with rituximab, which is a chimeric anti-CD20 antibody. It reduces the number of circulating mature B-cells which leads to the reduction of autoantibodies and the mediators of inflammation in the circulation. In a case report described by McArdle and Baker,[1] a case of refractory lupus panniculitis was treated with two infusions of rituximab at a dose of 1 g each, and the patient demonstrated remarkable clinical response. In a case series from Spain,[4] two cases of lupus panniculitis who were tried on several immunosuppressives received 375 mg/m²/week infusions of rituximab. One case showed significant disappearance of lesions after two infusions. The other case showed improvement after 1 month of therapy. In a study of 340 cases of SLE in Senegal by Diallo et al.,[5] lupus panniculitis was found in 16.9% of cases as the primary lesion in chronic lupus. In a prospective observational study conducted in South Africa by Jacyk and Bhana,[6] ten South African women were observed between 1990 and 2003. Subcutaneous nodules or plaques were found on the face in eight patients and at extrafacial sites only in one patient. One patient developed discoid lupus over subcutaneous nodules on the face. Of six patients on chloroquine, three patients showed marked improvement with chloroquine alone. The remaining three patients required oral corticosteroids. One patient was treated effectively with only systemic corticosteroids. Three patients did not comply with the treatment. In a case report by Ben Dhaou et al.,[7] a 40-year-old Tunisian woman was diagnosed with lupus panniculitis. She was treated with antimalarial and corticosteroid at a dose of 20 mg/day with the resolution of the nodules leaving depressed lipoatrophic areas.

To our knowledge, there have been no previous case reports on the use of rituximab in refractory lupus panniculitis from India. There have been few case reports in the world literature suggesting that rituximab has shown to be efficacious in the treatment of lupus panniculitis who have not responded to other immunosuppressives.

**Conclusion**

Rituximab is a good alternative to patients who are not responsive to conventional treatment options for lupus panniculitis. Individual case reports have justified its role in providing excellent clinical outcome and remission. However, its use as a first-line agent needs further studies.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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**Figure 3:** Histological findings of Case 1 (H and E, ×40) showing infiltration of subcutaneous fat by foamy macrophages and infiltration of dermal blood vessels by perivascular lymphocytes

**Figure 4:** Histological findings of Case 2 (H and E, ×40) consistent with inflammation of subcutaneous fat and perivascular lymphocytic infiltrate
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