SHORT COMMUNICATON

Management of pemphigus during COVID-19 pandemic era: An experience of single centre

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Abstract

The management of pemphigus vulgaris disease was challenging during the coronavirus diseases-2019 pandemic. The current study was planned to determine whether or not rituximab increases the risk and severity of coronavirus diseases-2019 infection in pemphigus vulgaris patients. The retrospective study was conducted at the Lady Reading Hospital, Peshawar, Pakistan, and comprised data from the dermatology unit of 34 diagnosed cases of pemphigus vulgaris who received rituximab treatment from March 2020 to March 2022. The mean age of the patients was 36.58±12.44 years. Majority of patients 28(82.3%) received rituximab as a second-line therapy, while 6(17.64%) were given it as a first-line therapy. Only 1(2.9%) patient developed mild covid pneumonia, and did not need in-patient care or faced oxygen dependence. There was a significant weak association between coronavirus diseases-2019 positivity with age (p=0.000). Rituximab therapy could be given to pemphigus patients during the pandemic, but only when necessary.

Keywords: COVID-19, Pemphigus, Severe acute respiratory syndrome coronavirus therapy, Rituximab.

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Introduction

Pemphigus, an autoimmune bullous disease (AIBD) of the skin, affects 0.76 to 16.1 per million population worldwide.[1] The two main subtypes of pemphigus are pemphigus vulgaris (PV) and pemphigus foliaceus (PF), contributing to 75% and 20% of patients, respectively.[2] Rituximab (RTX), which is a chimeric, humanised anti-cluster of differentiation-20 (CD20) monoclonal antibody, targets desmoglein (Dsg)-specific immunoglobulin G (IgG)-positive B lymphocytes in PV, resulting in its clinical effects.[3] CD20 antigen is expressed on circulating B lymphocytes in their early and late stages, but this expression stops when they differentiate into plasma cells. It plays a role in the regulation of calcium release from the B cell receptor.[4] According to the European Academy of Dermatology and Venereology (EADV) guidelines, RTX is considered a first-line therapy option for mild and moderate to severe pemphigus.[5] Cases of reactivation of hepatitis B virus (HBV), hepatitis C virus (HCV), tuberculosis (TB), and, rarely, opportunistic infections, such as cytomegalovirus infection and pneumocystis pneumonia (PCP), have been reported in patients treated with RTX.[6] The risk of delayed complications of this therapy, mainly infections, increase with the concurrent use of corticosteroid.

The upsurge of coronavirus disease-2019 (COVID-19) infection turned out to be a dreadful pandemic that caused millions of deaths over the span of a few months. With the COVID-19 pandemic, there were several concerns regarding the risk of infection and the management of pre-existing AIBD, and complications of both the disease and the drugs. Patients treated with corticosteroids and other immunosuppressive agents, including RTX, were at a high risk of contracting severe covid pneumonia. Cases of pemphigus patients treated with RTX during 1 year were found to have more serious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection compared to healthy individuals, but an acute flare-up of PV after COVID-19 infection and vaccination was very rare.[7,8] The current study was planned to determine whether or not RTX increased the risk and severity of COVID-19 infection in PV patients.

Methods and Results

The retrospective study was conducted at the Lady Reading Hospital, Peshawar, Pakistan, and comprised data from the dermatology unit of 34 diagnosed PV cases who received RTX treatment from March 2020 to March 2022. The patients who had been lost to follow-up, who died or who were unable to provide accurate answers to study questions were excluded. The use of concomitant therapy was not an exclusion criterion, and patients with all types of adjuvant drugs were included. Data was retrieved after approval from the institutional ethics review committee. Data included gender, age, total RTX cycles, any adjuvant therapy, and remission period.

Data was analysed using SPSS 26. Data was expressed as frequencies and percentages, or as mean±standard

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Table-1: Age-wise distribution of the sample.

Age in groups	n (%)
9-20 years	1 (2.9)
21-30 years	11 (32.4)
31-40 years	11 (32.4)
41-50 years	6 (17.6)
51-60 years	4 (11.8)
61-70 years	1 (2.9)

Table-2: Treatment options and the number of rituximab (RTX) cycles.

Cycle	n (%)
First Line Therapy	28 (82.3)
Second Line Therapy	6 (17.6)
First Cycle	28 (82.3)
Second Cycle	6 (17.6)

deviation, as appropriate. Post-stratification chi-square test was used, with $p<0.05$ being statistically significant.

Of the 34 patients, 20(58%) were males and 14(%) were females, The overall mean age was 36.58±12.44 years, and 22(64.7%) patients were aged 21-40 years (Table 1). The majority of patients 28(82.3%) received RTX as a second-line therapy, while 6(17.64%) were given it as a first-line therapy. A total of 28(82.3%) patients received only one RTX, while 6(17.64%) received a second RTX cycle (Table 2).

Only 1(2.9%) patient had mild covid pneumonia, and the diagnosis was confirmed with positive polymerase chain reaction (PCR) test. This infected patient was a young male aged 27 years, and had no comorbidities other than PV over the preceding 3 years. Initially, he was on systemic corticosteroids and azathioprine with dose adjustments according to disease severity and body weight, but due to frequent relapses, he was administered RTX as per the protocol. He was given initial dose of 1g 2 weeks apart, after which disease control was achieved in the following few months. After 6 months, he was given a second cycle of 500mg RTX infusion. He was in clinical remission and was off-therapy by the time he contracted SARS-CoV-2 infection, which occurred almost 4 months after the second dose. He had mild symptoms, and no in-patient care or oxygen dependence was seen in the patient.

In the study, there was a weak association between COVID-19 positivity and age group (p=0.000; Phi Cramer's value 1.00), while no significant association was found for COVID-19 positivity with gender (p=0.197; Phi Cramer's value 0.221), and the number of treatment cycles (p=0.618; Phi Cramer's value 0.89).

Discussion

The COVID-19 pandemic had devastating effects not only on the physical health of the subjects, but also on their mental health. The viral infection resulted in non-pulmonological manifestations of the disease, including dermatosis as well as a flare-up of the already existing dermatological conditions. The patients who were on long-term use of corticosteroids and other immunosuppressant therapy for the management of different inflammatory and autoimmune diseases of the skin, including AIBD, were at a high risk of being affected by the pandemic. The risk of contracting the infection by the novel virus was a matter of concern despite the prophylactic vaccination and alteration in the pre-existing management plan. Only 0.2-1.2% of patients affected by COVID-19 infection in China were found to have cutaneous involvement, mainly erythematous rash and urticaria, which was as high as 20% in Italy.[9]

RTX, a monoclonal anti-CD-20 antibody, is associated with higher rates of infection and mortality due to opportunistic infections. A cross-sectional study in Iran found a 2.6-fold increase in the risk of COVID-19 infection in patients treated with B-cell depleting agents for multiple sclerosis, but the disease course was mild to moderate with limited need for intensive care.[10] Previous studies proposed tapering of corticosteroids, and either temporary discontinuation of RTX from the therapeutic regimen of patients with pemphigus, or reduction in its doses in the COVID-19 pandemic.[2]

In the current study, only 1 patient who had received RTX as a therapeutic regimen of PV had a mild COVID-19 infection. Previous studies found that RTX therapy was associated with a poor prognosis of COVID-19 infection in hospitalised patients treated with RTX for systemic rheumatic disease.[11]

A weak association between COVID-19 positivity with age group was seen in the current sample. The study did not find any significant association between COVID-19 positivity and the number of treatment courses, which was in line with earlier findings.[12]

The current study has limitations as it did not segregate the sample on the basis of co-morbidities, which may act as a confounding variable. The small sample size is another limitation. Larger studies are needed to validate the findings.

Conclusion

RTX therapy was found to be associated with a poor prognosis of COVID-19 infection, so its administration should only be advocated when necessary. There was a weak association between COVID-19 positivity and age. Co-morbidities and prolonged duration of the disease may be the confounding factors that might have contributed to this association.

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Author Contribution:
SMN: Concept, design, data interpretation and final approval.
FS: Critical analysis.
AS: Data analysis and interpretation.