NEUTROPENIA DURING OCRELIZUMAB AND OFATUMUMAB TREATMENT IN MULTIPLE SCLEROSIS: A CASE SERIES

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Background

Neutropenia is a recognized but rare complication of anti-CD20 monoclonal antibody therapy in multiple sclerosis (MS), typically described as a late-onset adverse event. However, early-onset cases have also been reported, raising concerns about the timing, severity, and management of this condition in real-world settings.

Objectives

We describe three cases of neutropenia in patients with relapsing-remitting multiple sclerosis (RRMS) treated with anti-CD20 therapies—Ocrelizumab and Ofatumumab—focusing on timing of onset, clinical course, and therapeutic management.

Patients and Methods

We retrospectively identified, in a single-center setting, three adult female patients with RRMS who developed neutropenia during treatment with Ocrelizumab or Ofatumumab. Clinical records, complete blood counts , and bone marrow evaluations were reviewed. Each case was assessed for timing of neutropenia onset, clinical presentation, hematological findings, treatment response, and therapy continuation.

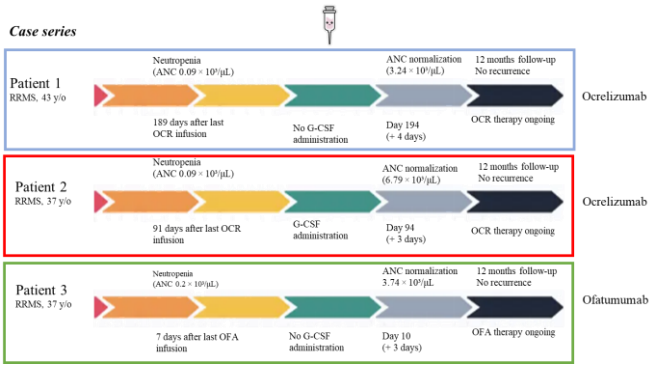
Results

Two patients developed late-onset neutropenia following Ocrelizumab infusion.

Patient 1 presented with severe neutropenia (ANC $0.09 \times 10^3/\mu L$) 189 days after the last dose, with spontaneous normalization ($3.24 \times 10^3/\mu L$) within 4 days.

Patient 2 developed severe neutropenia (ANC $0.45 \times 10^3/\mu L$) 91 days after infusion, resolving after administration of G-CSF (ANC $6.79 \times 10^3/\mu L$). In both cases, Ocrelizumab was safely resumed, and no recurrence of neutropenia was observed after one year of follow-up.

Patient 3, treatment-naïve, developed early-onset severe neutropenia (ANC 0.4 and $0.2 \times 10^3/\mu L$ on consecutive days) seven days after the first Ofatumumab dose. Hematologic recovery occurred spontaneously (ANC $3.74 \times 10^3/\mu L$), and therapy was successfully resumed. None of the patients experienced neutropenia-related infections. Consultation with the hematology department included a bone marrow analysis, which revealed no signs of malignancy and normal cellularity with left-shifted, maturing granulopoiesis up to the promyelocyte stage.



Conclusions

These cases highlight neutropenia as a rare but clinically significant adverse effect of anti-CD20 therapy in MS.

While late-onset neutropenia is well-documented, this report includes an early-onset case associated with Ofatumumab in a treatment-naïve patient, supporting the hypothesis of a class effect among anti-CD20 agents.

The pathogenesis remains unclear but is likely multifactorial, involving immune dysregulation, impaired granulopoiesis, and enhanced neutrophil apoptosis. All patients achieved hematologic recovery and were able to resume therapy, suggesting that, with close monitoring, permanent treatment discontinuation may not be necessary.

These findings underscore the importance of vigilant hematological surveillance and individualized patient counselling in managing anti-CD20-related neutropenia.