REVISTA NEUROCIÊNCIAS

4-Year Multiple Sclerosis Disease remission after a single cycle of Alemtuzumab: a case report

Remissão da Esclerose Múltipla por 4 anos após um ciclo único de Alemtuzumabe: relato de caso

Remisión de la enfermedad de esclerosis múltiple a los 4 años después de un solo ciclo de Alemtuzumab: reporte de un caso

Francisco de Assis Aquino Gondim[1], Antonio Miguel Furtado Leitão[2], Eduardo Ferreira Soares[3], Gabriela Mie Ejima Basso[4]

1.MD, PhD, FAAN, Department of Internal Medicine, Universidade Federal do Ceará. Fortaleza-CE, Brazil. Orcid: https://orcid.org/0000-0002-8957-5796
2.MD, MSc, Department of Morphology, Universidade Federal do Ceará. Fortaleza-CE, Brazil. Orcid: https://orcid.org/0000-0003-4590-812X
3.Medical Student, Universidade Federal do Ceará. Fortaleza-CE, Brazil. Orcid: https://orcid.org/0000-0001-9655-9914
4.Medical Student, Universidade Federal do Ceará. Fortaleza-CE, Brazil. Orcid: https://orcid.org/0000-0002-5622-4957

Resumo

Introdução. O Alemtuzumabe é um anticorpo monoclonal humanizado contra o antígeno CD52. É uma droga altamente eficaz para o tratamento da esclerose múltipla (EM) remitente recorrente. O protocolo de tratamento consiste em 2 ciclos de tratamento: 12mg/dia i.v. em infusões por 5 dias consecutivos e após um ano, infusões de 12mg/dia durante 3 dias. Até onde sabemos, há uma única série de casos na literatura detalhando a remissão da EM após um único ciclo de Alemtuzumabe. Aqui, relatamos uma experiência semelhante. **Relato de caso.** Uma mulher de 48 anos com fraqueza flutuante na perna direita há três anos e dor em queimação no pé direito foi diagnosticada com EM. Ela foi inicialmente tratada com Betaferon©. Sua condição progrediu e em menos de um ano, foi trocada para glatirâmer e, após novas recaídas de EM, para fingolimode. A doença progrediu para a Escala Expandida do Estado de Incapacidade (EDSS) de 7,0. Ela começou a tomar Alemtuzumabe (ciclo de cinco dias de 12mg i.v. em 6/2018). Um segundo ciclo de Alemtuzumabe não foi administrado porque ela não seguiu as diretrizes de monitoramento. Ela não desenvolveu sinais de atividade da doença após quatro anos. **Conclusão.** É possível que a remissão da EM seja alcançada com um único ciclo de Alemtuzumabe.

Unitermos. Esclerose Múltipla; Alemtuzumabe; Tratamento Modificador da Doença; Relato de Caso

Abstract

Introduction. Alemtuzumab is a humanized monoclonal antibody against the CD52 antigen. It is a highly efficacious drug for the treatment of relapsing remitting multiple sclerosis (MS). The treatment protocol consists in 2 treatment cycles: 12mg/day i.v. infusions for 5 consecutive days and after one-year 12mg/day infusions for 3 days. To our knowledge, there is a single case series in the literature detailing MS remission after a single cycle of Alemtuzumab. Here, we report a similar experience. **Case report**. A 48-year-old woman with fluctuating right leg weakness for three years and burning pain in the right foot was diagnosed with MS. She was started on Betaferon©. Her condition progressed and in less than one year, she was switched to glatiramer and after new MS relapses to fingolimod. Disease progressed to Expanded Disability Status Scale (EDSS) of 7.0. She was started on Alemtuzumab (five-day course of 12mg i.v. on 6/2018). A second Alemtuzumab cycle was not given since she failed to follow monitoring guidelines. She had no signs of disease

activity after four years. **Conclusions**. It is possible that MS remission may be achieved with a single cycle of Alemtuzumab.
Keywords. Multiple Sclerosis; Alemtuzumab; Disease Modifying Treatment; Case Report

Resumen

Introducción. Alemtuzumab es un anticuerpo monoclonal humanizado contra el antígeno CD52. Es un fármaco muy eficaz para el tratamiento de la esclerosis múltiple (EM) remitente recidivante. El protocolo de tratamiento consta de 2 ciclos de tratamiento: 12mg/día i.v. infusiones durante 5 días consecutivos y después de un año 12mg/día infusiones durante 3 días. Hasta donde sabemos, hay una serie de casos únicos en la literatura que detalla la remisión de la EM después de un solo ciclo de Alemtuzumab. Aquí, reportamos una experiencia similar. **Reporte de Caso.** Una mujer de 48 años con debilidad fluctuante en la pierna derecha durante tres años y dolor ardiente en el pie derecho fue diagnosticada con EM. Comenzó con Betaferon©. Su condición progresó y en menos de un año, se cambió a glatiramer y después de una nueva EM recayó a fingolimod. La enfermedad progresó a la Escala de Estado de Discapacidad Expandida (EDSS) de 7.0. Comenzó con Alemtuzumab (curso de cinco días de 12mg i.v. el 6/2018). No se administró un segundo ciclo de Alemtuzumab porque no siguió las pautas de seguimiento. No tenía signos de actividad de la enfermedad después de cuatro años. **Conclusión.** Es posible que la remisión de la EM se logre con un solo ciclo de Alemtuzumab.
Palabras clave. Esclerosis Múltiple; Alemtuzumab; Tratamiento Modificador de la Enfermedad; Reporte de Caso

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Corresponding address: Antonio Miguel Furtado Leitão. Department of Morphology, Universidade Federal do Ceará. Rua Delmiro de Farias s/n. CEP 60430-170. Fortaleza-CE, Brazil. Telephone +55(85)3366-8471. E-mail: miguelleitao1955@gmail.com

INTRODUCTION

Alemtuzumab is a humanized CD52 (Cluster of differentiation 52) monoclonal antibody approved for the treatment of multiple sclerosis (MS) in Europe since 2013. The treatment protocol for Alemtuzumab occurs in 2 treatment cycles. The first cycle consists in 12mg/day i.v. infusions for 5 consecutive days. After one year, the second cycle is administered: 12mg/day i.v. infusions for 3 days[1]. Although highly efficacious, it is associated with a 30-40% induction of additional auto-immune conditions[1,2]. Although Alemtuzumab can induce remyelination and reversal of old neurological deficits[3], it can occasionally lead to less predictable side effects, including *alopecia universalis*,

which can be sustained or permanent[1,2]. Therefore, it requires monthly laboratory testing for a prolonged period (60 months) to monitor side effects.

Kocsik *et al*[4] described their experience with the Alemtuzumab treatment in 29 patients. In their series, five patients had signs of MS activity, 4/5 in the first year after the first cycle of Alemtuzumab, that led to the second treatment. Among the 24 patients without relapses in the first year, eight received a second dose at one year and 16 did not receive a second dose. Since 96% of the patients who did not relapse after the first cycle remained disease-free regardless of the second dose, the authors postulated that Alemtuzumab could induce remission after one cycle. Here, like Kocsik *et al*[4], we report a patient who reached disease remission for four years after a single cycle of Alemtuzumab and no additional immunotherapy. Part of this study has been published in abstract form elsewhere[5].

METHOD

This is a retrospective case report study based on data collection from medical records and literature review. Written informed consent was obtained from the patient and the study is part of a 10-year cohort study approved by the Institutional Review Board from the Hospital Universitário Walter Cantídio, Fortaleza, Ceará, Brazil to evaluate the clinical course and treatments of patients with Multiple Sclerosis and Neuromyelitis Optica (Study identification CAAE: 73722017.3.0000.504).

Case report

A 48-year-old woman, smoker for 35 years, previously healthy with no family history of MS, complained of fluctuating right leg weakness for three years and burning pain in the right foot and popliteal fossa for two years. She was diagnosed with MS at age 50 and started on Betaferon©. Her condition progressed and in less than one year, she was switched to glatiramer (Copaxone©). In the same period, Natalizumab was prescribed for three months but discontinued for unclear reasons. After new MS relapses in less than a year, fingolimod (Gylenia©) was started. While taking fingolimod, she experienced a major disease worsening, becoming paraplegic due to multiple new spinal cord lesions.

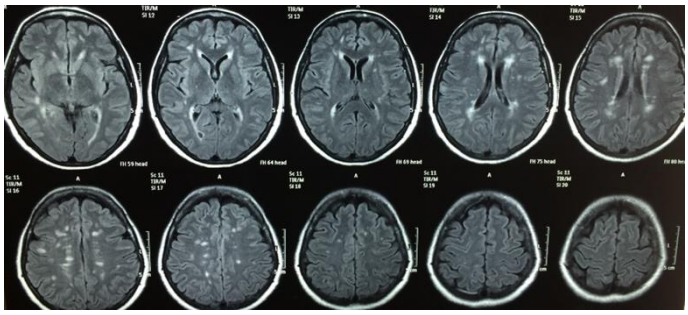
Her neurological exam revealed Expanded Disability Status Scale (EDSS) of 7.0 with paraparesis and minor weakness of the left upper extremity and a thoracic sensory level. Alemtuzumab was then prescribed, and while waiting for taking it, she had two additional relapses, that were treated with i.v. methylprednisolone and prednisone taper. She was then admitted to a five-day course of 12 mg i.v. Alemtuzumab in 6/2018.

She had no side effects from Alemtuzumab, but since she had lost several follow-ups and had not complied with the guidelines for monthly cell blood count (CBCs), renal, hepatic, and thyroid testing after 11 months, we decided not to pursue the second cycle of Alemtuzumab. She remained in remission (at least NEDA-3 status and although

no formal atrophy measurement was available, no atrophy was visually seen, therefore pointing towards NEDA-4 status, Figure 1) $2^1/_2$ years after the single Alemtuzumab cycle, without any need for treatment of relapses or new prophylactic agents. Subsequent blood tests and urine analysis did not reveal any side effect from Alemtuzumab after four years. Magnetic resonance imaging (MRI) was repeated only twice. Three years after Alemtuzumab treatment there was no imaging evidence of disease progression. Due to the Covid pandemics, she decided not to repeat MRI testing. She currently denies any clinical relapse and had no clinical evidence of disease progression. MRI of the cervical spine from 10.13.22 did not disclose any evidence of disease activity.

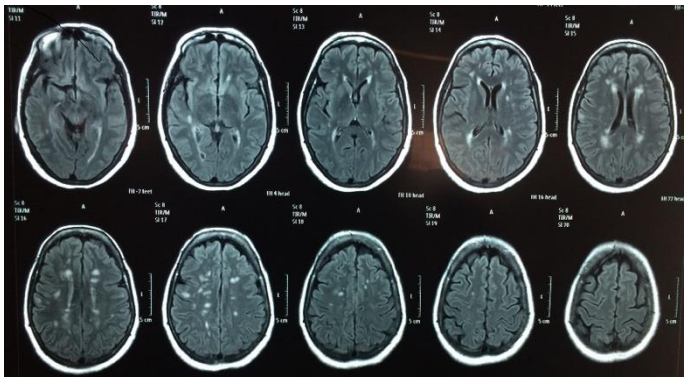
Figure 1.

A



A. Brain MRI, supratentorial Flair sequences reveal the presence of multiple periventricular and juxtacortical white matter lesions consistent with the diagnosis of Multiple Sclerosis, prior to Alemtuzumab treatment.

B



B. Brain MRI, supratentorial Flair sequences almost 2 years after a single Alemtuzumab cycle reveals similar pattern of multiple periventricular and juxtacortical white matter lesions, therefore documenting that disease did not progress.

DISCUSSION

Traditionally, MS has been treated with escalation of disease modifying therapies based on the aggressiveness of the condition[6]. However, treatment with high efficacy therapies has challenged those previous views[6]. Early treatment with high efficacy medications for the treatment of MS can prevent progression to secondarily progressive MS[7]. There is evidence that Alemtuzumab can provide partial lesion remyelination and may have neuroprotective effects in addition to the possibility of complete disease remission or at least excellent disease control[3]. Our patient had severe neurological deficits and reached the secondarily progressive MS stage, but she still exhibited signs of active inflammatory disease prior to Alemtuzumab treatment. After one single Alemtuzumab cycle, disease remission was achieved. Although certainly not appropriate or recommended by the primary neurologists, this status

was reached even after not adhering to safe follow-up laboratory monitoring guidelines recommended by the Brazilian government agencies. This reason for not providing the second course of Alemtuzumab after one year is different from the original report of Kocsik *et al*[4]. However, this issue is also very relevant for MS caregivers who experience the same challenges in providing adequate adherence to standard clinical guidelines. Further studies are important to evaluate the possible beneficial effects of one cycle of Alemtuzumab for MS control, including in Brazil, where new federal guidelines for the management of MS are under discussion[8].

CONCLUSIONS

In summary, to our knowledge, the present findings are the second available evidence (there is a single prior study) that a single 5-day course of Alemtuzumab can induce sustained MS remission.

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