REVISTA BRASILEIRA DE REUMATOLOGIA

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Brief communication

Rituximab use in young adults diagnosed with juvenile idiopathic arthritis unresponsive to conventional treatment: report of 6 cases

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ARTICLE INFO

Article history:
Received 10 July 2014
Accepted 24 December 2014
Available online 20 July 2015

Keywords:
Juvenile idiopathic arthritis
Children
Rituximab
Refractoriness

ABSTRACT

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood. Without an effective therapy, patients may progress quickly to functional disability. Recently, depletion of B cells emerged as a new approach for the treatment of autoimmune diseases, including JIA.

We describe six cases of JIA patients followed at a referral center for Rheumatology and Pediatric Rheumatology, submitted to treatment with rituximab (RTX) after refractoriness to three anti-TNF agents.

Patients received RTX cycles with two infusions every six months. Response to treatment was assessed by DAS28, HAQ/CHAQ, and an overall assessment by the doctor and the patient.

Of our six patients, four were girls (mean age at onset of disease: 6.1 years; mean disease evolution time: 15.1 years; mean age upon receiving RTX: 21.6 years). Four patients belonged to polyarticular subtype (1 rheumatoid factor [RF]-negative, 3 FR-positive), a patient with systemic JIA subtype with a polyarticular course and arthritis related to enthesitis. Of our six patients, five responded to treatment; and during the course of 12 months, the clinical response was maintained, although not sustained. However, discontinuation by infusion reactions caused the withdrawal of RTX in two patients.

The use of RTX in JIA is restricted to cases refractory to other biological agents and, even considering that this study was held in a small number of advanced patients, RTX proved to be an effective therapeutic option.

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http://dx.doi.org/10.1016/j.rbre.2015.05.002

Uso de rituximabe em adultos jovens com diagnóstico de artrite idiopática juvenil refratária ao tratamento convencional: relato de 6 casos

Palavras-chave:
Artrite idiopática juvenil
Crianças
Rituximabe
Refratariedade

RESUMO

A artrite idiopática juvenil (AIJ) é a doença reumática mais frequente na infância. Sem terapia efetiva, os pacientes podem evoluir rapidamente para incapacidade funcional. Recentemente, a depleção dos linfócitos B surgiu como nova abordagem para o tratamento de doenças autoimunes, incluindo a AIJ.

Descrevemos seis casos de pacientes com AIJ, acompanhados em um centro de referência em Reumatologia e Reumatologia Pediátrica, submetidos ao tratamento com rituximabe (RTX) após refratariedade a três anti-TNF.

Os pacientes receberam ciclos de RTX com duas infusões a cada seis meses. A resposta ao tratamento foi avaliada pelo DAS28, HAQ/CHAQ, avaliação global do médico e do paciente.

Dos seis pacientes, quatro eram meninas (média de idade de início da doença: 6,1 anos; média de tempo de evolução de doença: 15,1 anos; média de idade ao receber RTX: 21,6 anos). Quatro pacientes pertenciam ao subtipo poliarticular (1 fator reumatoide (FR) negativo, 3 FR positivo), um paciente com AIJ subtipo sistêmico com evolução poliarticular e um com artrite relacionada à entesite. Dos seis pacientes, cinco responderam ao tratamento e durante a evolução de 12 meses, a resposta clínica foi mantida, embora não sustentada. No entanto, a descontinuação por reações infusionais motivaram a suspensão do RTX em dois pacientes.

O uso do RTX em AIJ é restrito aos casos refratários a outros biológicos e, mesmo tendo sido realizada em um número pequeno de pacientes e de forma tardia, mostrou ser uma opção terapêutica eficaz.

Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood and without appropriate treatment it can quickly result in functional disability.[1]

Recently, B lymphocyte depletion emerged as a new therapeutic approach for JIA and SLE.[2–7] Rituximab (RTX) is a chimeric monoclonal antibody directed against the CD20 pre-B cells and mature B cells with efficacy and safety in adult patients with rheumatoid arthritis (RA) with an inadequate response to disease-modifying drugs (DMARDs) and anti-TNF-alpha inhibitors.[8–12]

The objective of this study was to describe six patients with JIA followed in a Pediatric Rheumatology Unit between 1993 and 2014 who underwent treatment with RTX.

Methods

Six patients diagnosed with JIA according to the ILAR (International League of Associations of Rheumatology) criteria[13] received RTX cycles with two intravenous infusions of 1 g each on days 1 and 15, every six months.

The clinical response was measured by DAS28 (Disease Activity Score in 28 joints),[14] erythrocyte sedimentation rate (ESR), Health Assessment Questionnaire (HAQ)[15] or the Child Health Assessment Questionnaire (CHAQ)[16] and evaluation of visual analog scale (VAS) of the patient and the physician.

The assessments were performed before and every six months of treatment. According to EULAR (European League Against Rheumatism) criteria, the patients were classified as good responders if improvement in DAS28 was greater than 1.2, moderate responders if between 0.6 and 1.2, and non-responders if less than 0.6, in two consecutive measurements. Clinical remission was defined as a DAS28 less than 2.6.[17]

Primary failure was defined as a reduction lower than 0.6 of DAS28 after 12 weeks and secondary failure, such as loss of efficacy over 24 weeks in patients who had responded in the first 12 weeks.[17] Adverse events were recorded.

Case report

The mean onset age of the disease was 6.1 years and mean disease duration was 15.1 years. The mean age at start of RTX was 21.6 years (18–26 years) (Table 1). Uveitis was not observed in any patient.

Table 1 – Clinical data of 6 patients treated with rituximab.

	Age at diagnosis	Age at rituximab	JIA subtype
DAB	5	19	Polyarticular RF +
DC	5	24	Systemic
DSS	7	21	Enthesitis-related arthritis
FAGS	7	26	Polyarticular RF−
MILP	4	20	Polyarticular RF+
ELS	9	18	Polyarticular RF+