Journal of Autoimmunity 43 (2013) 55–59

Contents lists available at SciVerse ScienceDirect

Journal of Autoimmunity

journal homepage: www.elsevier.com/locate/jautimm

B-cell depletion therapy and pregnancy outcome in severe, refractory systemic autoimmune diseases

Shirish R. Sangle, Pamela M.K. Lutalo, Rachel J. Davies, Munther A. Khamashta, David P. D'Cruz*

Graham Hughes Research Laboratory, The Rayne Institute, St Thomas' Hospital, Guy's, St Thomas' Hospital and King's College Medical School, London SE1 7EH, UK

ARTICLE INFO

Article history:
Received 1 February 2013
Received in revised form
26 February 2013
Accepted 5 March 2013

Keywords:
Autoimmune diseases
B cells
Systemic lupus erythematosus
Systemic vasculitis

ABSTRACT

Objective: To study the pregnancy outcome following Rituximab treatment before conception in patients with refractory autoimmune rheumatic diseases.
Methodology: Five women with systemic lupus erythematosus (SLE) and 1 woman with ANCA positive vasculitis fulfilling the respective ACR classification criteria were studied retrospectively when they became pregnant following rituximab treatment for refractory disease. Rituximab was given as a 1 g infusion together with 500 mg Methylprednisolone, on day 1 and day 15 after written informed consent.
Results: The median age was 34 (range 32–39) years and median disease duration was 10 (range 5–16) years. All the patients achieved complete B-cell depletion $<$ 1 cell/μL at 1 month and $<$5 cells/μL at 6 months with prolonged B-cell depletion. Four women had successful pregnancies with median gestational age of 38 (range 31–40) weeks; median weight of the new born was 3.25 (range1.17–3.3) kg with no documented adverse neonatal events. One patient with lupus nephritis (LN) had a premature delivery and increasing proteinuria in the third trimester. One other patient with LN had a premature delivery and the new born had oesophageal atresia.
Conclusion: We report a child with oesophageal atresia born to a mother with lupus nephritis who had received Rituximab 12 months prior to conception, while four other pregnancies in women with SLE resulted in morphologically normal children. We also describe the first report, to our knowledge, of a successful pregnancy outcome in a woman with granulomatosis with polyangiitis treated with rituximab.
© 2013 Published by Elsevier Ltd.

1. Introduction

Pregnancy in severe autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE) and systemic vasculitis is often associated with significant morbidity. Maternal and foetal outcomes are unfavourable if the disease is not in remission prior to conception and pre-pregnancy counselling is critical to improving outcome for mother and foetus. Complications include spontaneous miscarriages, still-births, pre-term delivery, low-birth weight, congenital abnormalities and maternal disease flare [1].

B cell depletion therapy is widely used in the management of refractory SLE and ANCA associated vasculitis such as granulomatosis with polyangiitis (GPA). However, there is very little published literature on pregnancy outcomes following B cell depletion therapy in patients with SLE and GPA. We report pregnancy outcomes in 6 women with severe, refractory autoimmune disease which required treatment with B-cell depletion therapy rituximab to achieve disease control prior to conception.

1.1. Patients and methods

Five women with systemic lupus erythematosus (SLE) and 1 woman with GPA, (formerly known as Wegener's granulomatosis), who fulfilled the respective ACR classification criteria for SLE and GPA, were studied retrospectively [2,3]. They had all received rituximab for their severe, refractory disease and were regularly assessed in dedicated clinics at the Louise Coote Lupus Unit, St Thomas' Hospital London. Data was collected on clinical and laboratory markers of disease activity, lymphocyte subsets and immunoglobulin levels. All patients were closely monitored during their pregnancies.

Four women had SLE complicated by aggressive WHO class IV + V lupus nephritis, 1 had SLE and immune thrombocytopenia (ITP) and 1 had cANCA positive GPA with an intra orbital mass with previous vasculitis and nephritis. All patients had previously failed to respond to three or more immunosuppressive therapies

* Corresponding author. Tel.: +44 207 188 3569; fax: +44 207 188 3574.
E-mail address: david.d'cruz@kcl.ac.uk (D.P. D'Cruz).

0896-8411/$ – see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.jaut.2013.03.001

including azathioprine, mycophenolate mofetil, methotrexate and cyclophosphamide (Table 1).

1.2. Rituximab protocol

Rituximab was given as a 1 g intravenous infusion together with 500 mg methylprednisolone, on day 1 and day 15 after written informed consent. All immunosuppressive drugs, except hydroxychloroquine and oral corticosteroids were stopped 2 weeks before the first infusion. B-cell depletion was monitored by circulating $CD19^+$ lymphocyte cell counts on flow cytometry (range 1–5 cells/μL) and patients were considered to have achieved B-cell depletion if absolute $CD19^+$ B lymphocyte counts were <5 cells/μL. Patients were counselled to avoid pregnancy following rituximab therapy especially in the context of very active disease.

2. Results

Five women were Caucasian and 1 was Afro Caribbean in origin, with a median age of 34 (range 32–39) years and median disease duration of 10 (range 5–16) years. All the patients achieved complete B-cell depletion < 1 cell/μL at 1 month, B-cell depletion < 5 cells/μL at 6 months and prolonged B-cell depletion as measured by interval lymphocyte subsets up to 24 months after rituximab therapy (Fig. 1). Patient 5 (Table 1) conceived an unplanned pregnancy while not using adequate contraception 8 months after her rituximab therapy. All the other patients had planned pregnancies following careful pre-pregnancy counselling about the risks and benefits including advice about the lack of knowledge of the effects of rituximab on pregnancy and the neonate. All were advised to wait until at least 6 and preferably 12

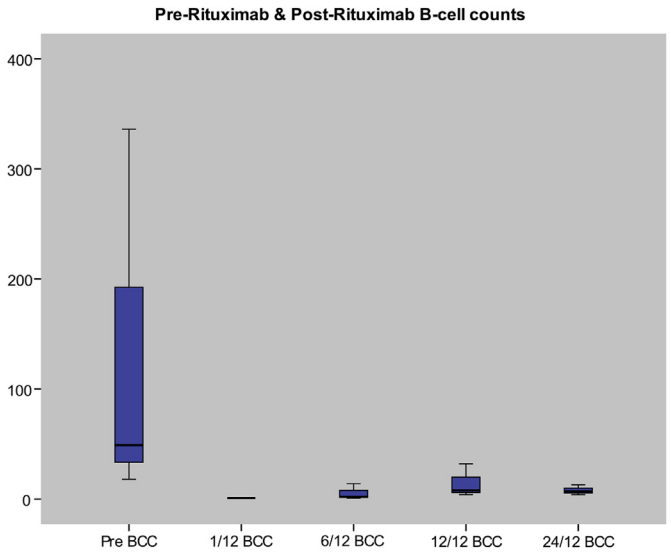

Fig. 1. *X* axis: Pre BCC: B lymphocyte count before rituximab therapy, 1/12 BCC, 6/12 BCC, 12/BCC, 24/12 BCC: B cell counts 1, 6, 12 and 24 months after rituximab. *Y* axis: B lymphocyte values (Normal B-cell count 100–500 cells/μL).

Table 1
Drug therapy and characteristics of patients before Rituximab.

	Patients' age	Disease and disease duration (years)	Autoantibody profile	Previous medication	Time of exposure to BCDT before conception (months)	Complications during pregnancy	Delivery	Birth weight (kg)	Neonatal health
1	38 yr C	GPA 5 years	cANCA	Steroids HCQ MTX AZA MMF CyC IVIG	10	Nasal septal perforation	40 weeks C/S	2.9	Healthy neonate
2	39 yr C	SLE LN (IV + V)	ANA dsDNA Ro La	Steroids HCQ AZA MMF CyC IVIG	18	Proteinuria >3 g/day at 21/40 gestation	31 weeks C/S	1.17	Pre-term Low-birth weight neonate
3	34 yr C	SLE LN (IV + V)	ANA dsDNA	Steroids HCQ AZA MMF	10	–	38 weeks NVD	3.25	Healthy neonate
4	32 yr C	SLE ITP	ANA dsDNA	Steroids HCQ AZA IVIG PEX	22	–	40 weeks C/S	3.2	Healthy neonate
5	32 yr AC	SLE LN (IV) APS	ANA dsDNA Sm RNP LA aCL	Steroids HCQ AZA CyC	8	Cutaneous lupus rash	38 weeks NVD	3.3	Healthy neonate
6	32 C	SLE LN (V)	ANA, dsDNA, Ro	Steroids HCQ MMF, AZA, Ramipril Alendronic acid	12	Premature delivery at 32 weeks,	32 weeks	2.3	New born with oesophageal atresia

AC, Afro Caribbean; aCL, anticardiolipin antibody; AZA, Azathioprine; BCDT, B-cell depletion therapy; BW (kg), birth weight in kilograms; C, Caucasian; C/S, Caesarean section; CyC, Cyclophosphamide; dsDNA, anti-double-stranded DNA antibody; GPA, granulomatosis with polyangiitis; HC, Hydroxychloroquine; ITP, Immune thrombocytopenia; IVIG, Intravenous immunoglobulin; La, anti-La antibody; LA, Lupus Anticoagulant; LN, Lupus Nepritis; MMF, Mycophenolate Mofetil; MTX, Methotrexate; NVD, normal vaginal delivery; PEX, plasma exchange NVD; RNP, anti-RNP antibody; Ro, anti-Ro antibody.

Download English Version:

https://daneshyari.com/en/article/3367805

Download Persian Version:

https://daneshyari.com/article/3367805

Daneshyari.com