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LETTER TO THE EDITOR

# Rituximab Therapy in Chronic Childhood Immune Thrombocytopenic Purpura: Is it worth trying?

Gonca KESKINDEMIRCI[1], [MD], Muge GOKCE[1], [MD] [PhD], Deniz TUGCU[1], [MD] [PhD], Cengiz BAYRAM[1], [MD], Sevinc GENC[1], [MD], Gonul AYDOGAN[1], [MD]

1 Pediatric Hematology & Oncology Division, Department of Pediatrics, Kanuni Sultan Süleyman Research and Training Hospital, İstanbul

* *Corresponding Author: Muge Gokce, Associate Professor Pediatric Hematology & Oncology Division Kanuni Sultan Suleyman Research and Training Hospital, Altınşehir Halkalı, İstanbul TURKEY*

*e-mail: drgundogdu@yahoo.com*

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*To The Editor;*

Childhood immune thrombocytopenia – previously known as idiopathic thrombocytopenic purpura (ITP)–is defined as a platelet count $< 100 \times 10^9$/L, not explained by any other cause [1]. Approximately one-third of children will go on to have chronic ITP, and 5-10% will develop severe, refractory disease [2]. The recommended first-line therapy for symptomatic ITP is glucocorticoids and/or intravenous immunglobulin (IvIg) [3]. In cases refractory to theses therapies, rituximab (RTX) can be used as 2nd line drug for treatment [4]. It depletes B cells by binding to the CD20 antigen to remove the autoreactive B-cell clones [5]. Liang et al reported that the initial response rate of RTX was 68% in children and median time to response was 3 weeks with a median duration – response of 12.8 months [6].

We reviewed the data of eight children treated with RTX (375 mg/m$^2$/week for 4 consecutive weeks) (Table 1). All patients had been treated with steroid/IvIg before and all were either resistant to or dependent on 1st line treatments. Hepatitis B serology and serum immunglobulin (Ig) levels were evaluated before RTX was initiated in all patients. One patient developed an anaphylactic reaction during the first dose and was excluded from the evaluation. The median duration of RTX was 33 months (3–82 months). RTX was given due to severe epistaxis in 4 children and, menorrhagia in 2 children. Cushingoid side effect of steroids was the indication in the other 2 patients. Median platelet count before treatment was $5.8 \times 10^9$/L ($3 - 19 \times 10^9$/L). Of the seven patients who completed four courses of RTX treatment, three achieved a complete response (CR)($>100 \times 109$/L). Two achieved a CR in 3 months whereas the other did in 6 months. Partial response ($\geq 50 \times 10^9$/L) was not noted in any of our patients. A sustained response to RTX was observed in all 4 patients with a median follow-up of 13 months. No side effects such as infection or, thrombosis were observed.

Rituximab was found to be effective in 3 of our 7 patients (42.8%), this result is similar to previous studies [6]. It has been proposed that a previous response to steroids and history of secondary ITP predicts a better response to RTX [7]. Our patients who achieved CR with RTX were also responsive to steroids. A longer follow-up period is necessary due to the fact that late relapses are possible. In the case of a relaps repeated doses might be considered in previously RTX responsive patients.

Infection is a concern after administration of RTX because there have been reports in children of pneumonia, varicella, meningoencephalitis and reactivation of hepatitis B after treatment [7]. Immunglobulin production is sustained after RTX because plasma cells do not have CD20 on their surface and humoral immunity is thought to be spared [8]. However in case of repeated doses of RTX, serum Ig levels should be monitored closely and supplemental IvIg should be considered [8]. Hypogammaglobulinemia was not observed before or after RTX in our patients. No immunglobulin G level below 600 mg/dL was detected after treatment.

Childhood ITP is usually a self-limiting and benign condition. However; in the case of severe bleeding

**Table 1.** The characteristics of patients

| No | Sex | Age at diagnosis (mo) | Duration of RTX (mo) | Platelet Count before RTX (109/L) | Steroid/Ivlg response | RTX response | Follow-up (mo) |
|---|---|---|---|---|---|---|---|
| **1** | M | 89 | 4 | $8 \times 10^9$ | –/– | – | 16 |
| **2** | M | 23 | 21 | $19 \times 10^9$ | –/+ | – | 7 |
| **3** | M | 132 | 12 | $18 \times 10^9$ | –/– | Anaphylaxis | |
| **4** | M | 73 | 7 | $4 \times 10^9$ | +/+ | + | 33 |
| **5** | F | 126 | 45 | $5 \times 10^9$ | +/– | + | 13 |
| **6** | F | 54 | 82 | $3 \times 10^9$ | –/+ | – | 10 |
| **7** | F | 63 | 60 | $15 \times 10^9$ | +/+ | + | 10 |
| **8** | F | 177 | 3 | $5.8 \times 10^9$ | –/– | – | 11 |

M: Male, F: female, mo: Months, RTX: rituximab

at presentation or for those who develop prolonged symptomatic disease, we – as hematologists–have a tendency to try 2nd line drugs such as RTX. Its side effects, evidence of sustained response, the patient's preference and quality of life should be taken into consideration before decision of treatment is made. In the light of the current literature and the results of the present case series, we recommend RTX as a 2nd line treatment option in selected patients for ITP.

## Conflict of Interest Statement

The authors of this paper have no conflict of interest, including specific financial interests, relationships relevant to the subject matter or materials included.

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