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Treatment Strategies and Outcome of Parvovirus B19 Infection in Kidney Transplant Recipients: A Case Series and Literature Review of 128 Patients

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ABSTRACT

Background: There is no specific antiviral treatment for parvovirus B19 (PVB19) infection. **Objective:** The objective of this study was to study the treatment and outcome of PVB19 infection in kidney transplant recipients (KTR) at our institution, and cases published in the medical literature. **Methods:** We conducted a retrospective review of PVB19 infection in KTR at an academic medical center over a 16-year period and summarized the data on its treatment and outcome in 120 KTR in the medical literature. **Results:** In our cohort of eight patients, the median time to the onset of PVB19 disease was 7.2 weeks after transplantation. All patients had severe aregenerative anemia (mean hemoglobin (Hb) of 6.2 ± 1.0 g/dl); all were treated with a reduction in their immunosuppressive regimen and the administration of single-dose intravenous immunoglobulin (IVIG) (mean total dosage of 0.87 ± 0.38 g/kg). The median time to anemia improvement (Hb >10 g/dl) was 3-week post-treatment. No recurrences were documented during follow-up (median 25 months). Among 128 patients (including our cohort of 8 and 120 reported in literature), therapeutic strategies included: 43% IVIG alone, 39% IVIG and reduced immunosuppression, 9% reduction of immunosuppression, and 9% conservative therapy. Clinical relapses were observed in 35% of 71 reported cases. **Conclusions:** In KTR, decreasing immunosuppression and the administration of low-dose immunoglobulin seem to be not worse than the standard dose in PVB19 infection. (REV INVEST CLIN. 2019;71:265-74)

Key words: Human parvovirus B19. Kidney transplantation. Conservative treatment. Intravenous immunoglobulin. Treatment outcome.

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INTRODUCTION

Transplant recipients are susceptible to many primary viral infections and to the reactivation of persistent viruses. In the 1st year post-transplantation, approximately 10% of kidney transplant recipients (KTR) have measurable Parvovirus B19 (PVB19) DNAemia in plasma samples without clinical manifestations. However, the incidence of symptomatic infection is very low[1]. Management of PVB19 infection is primarily symptomatic since there is no specific antiviral drug available for its treatment. In 1989, Kurtzman, et al.[2] reported the first successful treatment of PVB19 human infection with intravenous immunoglobulin (IVIG), and it later became the treatment of choice. Unfortunately, the optimal dosing and duration of IVIG therapy in PVB19 infection have not been established; furthermore, some patients have been reported to have long-lasting resolution of the infection without IVIG therapy[3,4]. The American Society of Transplantation recommends a reduction of immunosuppression at the time of diagnosis and 400 mg/kg/day of IVIG for 5 consecutive days[5]. However, there is no consensus in clinical practice on the ideal treatment of PVB19 infection. Based on these findings, the purpose of this study was to describe the treatment and outcome of PVB19 infection in KTR at our institution and summarize the data obtained in 120 cases published in the medical literature.

PATIENTS AND METHODS

Study population

We conducted a retrospective review of all cases of PVB19 infection among KTR at the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán,* a third-level academic hospital in Mexico City, from January 2000 to September 2016. We collected all pertinent information on their demographic characteristics, immunosuppressive (IS) regimens, clinical features, laboratory tests, bone marrow findings, adjustments in IS regimen, dose of IVIG therapy, and outcome (in terms of relapse, graft function, and mortality).

Definitions

PVB19 infection was defined according to the following criteria: (1) aregenerative severe anemia (reticulocyte production index < 2, hemoglobin (Hb) < 10 g/dl) after transplantation, in the absence of hematologic disturbances or active bleeding and (2) qualitative or quantitative positive polymerase chain reaction (PCR) or a positive serologic assay (immunoglobulin M [IgM] antibodies) and/or positive immunohistochemistry in bone marrow biopsy with pure red cell aplasia (PRCA). Anemia improvement was defined as an Hb value > 10 g/dl.

Induction and maintenance immunosuppression

At our center, we use induction therapy according to the patient's immunologic risk. In high-risk KTR (e.g., positive pre-transplant donor-specific antibodies, highly sensitized, deceased donor transplantation, or second renal transplantation), we administer rabbit antithymocyte globulin (total dose 4.5 mg/kg) plus methylprednisolone, and basiliximab (20 mg, at days 0 and 4) plus methylprednisolone in low-risk KTR. Maintenance IS includes triple-drug therapy with tacrolimus, mycophenolate mofetil, and prednisone.

Review of literature

We analyzed the medical literature for cases of PVB19 infection in KTR treated with IVIG by searching for articles published in PubMed and Medline databases from January 1989 to December 2017, with the following Medical Subject Headings terms: "human PVB19" and "kidney transplantation" (KT). The data on published cases were carefully collected according to a pre-established protocol.

Statistical analysis

We used descriptive statistics according to variable distribution. Categorical variables were compared using χ^2 or Fisher's exact test when appropriate. A two-tailed $p < 0.05$ was considered statistically significant. All analyses were performed using the GraphPad Prism 5 software for Windows (Version 5.01).

RESULTS

Summary of cases at our institution

Demographic data

A total of 795 patients who had received KT between January 2000 and September 2016 were analyzed.

Table 1. Demographic, clinical characteristics, and outcome of eight patients with PVB19 infection after KT in our institution

Variable	Patient							
	1	2	3	4	5	6	7	8
Age, years	19	38	43	22	40	21	19	19
Sex	M	F	F	F	F	M	M	F
Year of KT	2004	2011	2012	2014	2014	2015	2015	2011
Type of KT	LD	LD	LD	LD	LD	DD	LD	DD
Type of IS induction	Daclizumab + MPD	ATG + MPD	MPD	Basiliximab + MPD	ATG + MPD	ATG + MPD	Basiliximab + MPD	ATG + MPD
TAC trough levels from KT to infection, median (range) ng/mL	8.4 (6.4-11.3)	11.2 (3.5-14.1)	15 (6.0-25.1)	7.4 (6.4-9.5)	6.9 (3.9-11.3)	15.2 (3.3-19.8)	6.9 (2-30)	8.3 (5.1-16.5)
Onset of infection after KT, days	54	39	34	94	43	105	29	2´045
PVB19 IgG/IgM status at infection onset	−/+	+/−	−/+	NP/NP	NP/NP	NP/NP	+/−	NP/NP
PVB19, PCR result	NP	NP	>100,000,000	2,133,090	+	+	+	+
Bone marrow findings	NP	PRCA	NP	NP	PRCA	NP	NP	HBM + MEC
Lowest Hb level, g/dl	5.6	5.4	7	7.7	5.4	6.8	7.1	4.9
Leukopenia	Yes	No	Yes	Yes	No	No	Yes	Yes
Lowest WBC count, ×109/L	1.8	¬-	4	3.6	-¬	-¬	3.3	2.2
Symptoms	Fever	Dyspnea, weakness	Fever	Dyspnea, weakness	Dyspnea, weakness	Flu-like symptoms	Flu-like symptoms	Dyspnea, weakness
Treatment	IVIG and reduced IS	IVIG and reduced IS	IVIG and reduced IS	Reduced IS	IVIG and reduced IS	IVIG and reduced IS	IVIG and reduced IS	IVIG and reduced IS
IVIG total dose, g	80	24	30	-	84	48	48	50
IVIG dosage, g/kg/day	1.45	0.4	0.43	-	1.12	1.06	0.76	0.86
Days improvement anemia[a]	12	60	19	17	22	20	24	36
Recurrence of PVB19 infection	No	No	No	No	No	No	No	No
Graft dysfunction	No	No	No	No	No	No	No	Yes
Months of follow-up	155	22	62	43	22	5	28	16

[a]Anemia improvement was defined with hemoglobin >10g/dL. M: Male, F: Female, KT: Kidney transplantation, LD: Living donor, DD: Deceased donor, IS: Immunosuppression, ATG: Rabbit antithymocyte globulin, MPD: Methylprednisolone, TAC: Tacrolimus, + or −: Positive or negative, NP: Not performed, PRCA: Pure red cell aplasia, HBM: Hypocellular bone marrow, MEC: Megaloblastic erythroid cells, Hb: Hemoglobin, WBC: White blood cell, IVIG: Intravenous immunoglobulin, PVB19: Parvovirus B19.

Over a 16-year period, eight patients with PVB19 infection were identified. The clinical data, treatment, and outcome of our case series are described in Table 1. Patient mean age was 28.1 ± 10.3 years, 6 (75%) were living donor KTR, and 7 (88%) were receiving triple IS therapy with prednisone, tacrolimus, and mycophenolate mofetil. The median time to the onset of PVB19 infection was 7.2 weeks (range, 4.1-292 weeks) after transplantation. 7 (88%) patients developed the infection within the first 4 months after transplantation, and only one patient had late-onset (6 years after KT) infection after having received treatment for active humoral rejection (plasma exchange, IVIG, rituximab, and bortezomib). At the time of diagnosis, the median tacrolimus trough levels were 9.4 (range, 2-30) ng/mL.

Clinical features

All patients had hypoproliferative anemia (mean Hb value, 6.2 ± 1.0 g/dL) and 5 (62%) patients had leukopenia (median leukocyte count 3.3, 1.8-4 × 10^9/L). 6 (75%) patients required blood transfusion with a median of 2 (range 1-3) units of packed red blood cells per patient. No patient presented with skin, neurological, or cardiac involvement.

Diagnosis

PVB19 testing was performed when clinical diagnosis was considered. In six cases, the diagnosis was established by PCR (75%). Positive IgM antibodies and positive immunohistochemical staining in the bone marrow biopsy were found in one patient for each test, respectively. Only three patients had bone marrow examination; two had PRCA and one had a hypocellular bone marrow and megaloblastic erythroid cells.

Treatment

After diagnosis, the IS regimen was decreased in all patients: the antiproliferative drug (mycophenolate mofetil or azathioprine) was discontinued in 6 (75%) patients and in 2 (25%), the dosage was halved and tacrolimus was reduced to achieve trough levels of approximately 5 ng/mL. 7 (88%) patients received single-dose IVIG at a mean total dose of 0.87 ± 0.38 g/kg.

Outcome

After these interventions, Hb levels improved progressively in all subjects. The median time to anemia improvement was 3 weeks (range, 1.7-8.6 weeks) post-treatment (Fig. 1). The median follow-up period after treatment of PVB19 infection was 25 months (range, 5-155). No subjects relapsed, developed graft loss, or died during PVB19 infection. No adverse events relating to IVIG administration were observed during or after the infusion.

Review of literature

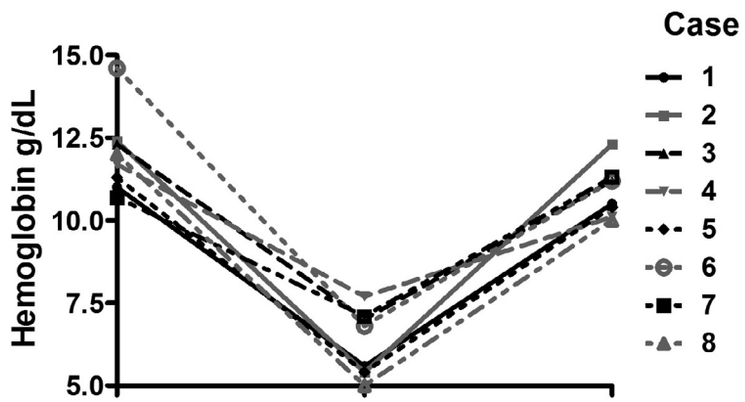
Table 2 lists the clinical data, treatment, and outcome of 128 cases of KTR with PVB19 infection, including our patients[3,4,6-53]. The median time to PVB19 infection was 2 months (interquartile range, 1-6) and the most common manifestation was anemia in 96 (75%) patients. 10 (8%) patients had thrombotic microangiopathy, 9 (7%) pancytopenia, 3 (2%) hepatitis, 2 (1.5%) encephalitis, 2 (1.5%) hemophagocytic syndrome, and 1 (0.8%) collapsing glomerulopathy. Among the 128 patients, the therapeutic strategies included: (1) IVIG only (n = 54, 43%), (2) IVIG and decreased IS (n = 50, 39%), (3) decreased IS only (n = 12, 9%), and (4) conservative therapy, with transfusion and/or erythropoietin, or no treatment (n =12, 9%).

Follow-up data on clinical relapses were available in 71 patients, 25 (35%) of whom relapsed. According to the therapeutic strategy, the recurrence rate was as follows: 18/44 (41%) for IVIG plus IS reduction, 6/16 (35%) for IVIG only, 1/6 (17%) for IS reduction, and 0/5 (0%) if there was no therapeutic intervention (p = 0.23).

DISCUSSION

We herein report the data obtained in a series of eight KTR with PVB19 infection in our center over a 16-year period, and the review of 120 additional cases obtained in literature. The patients' clinical characteristics were similar to other reports[3,11,25], in which severe aregenerative anemia was the most common manifestation in the early post-transplant period (median time to infection was 2 months in the medical literature) and a median time to Hb recovery of 3 weeks[3].

Figure 1. Evolution of parvovirus B19-induced anemia in our cohort.



Patient	Weeks after KT		Weeks after IVIG
1	1.6	7.8	1.7
2	0.8	6.1	8.6
3	2.6	8.1	1.3
4	4.0	9.0	-
5	1.4	6.1	3.1
6	5.1	20.7	7.7
7	1.6	3.7	3.4
8	286.6	291.7	4.6

KT: Kidney transplant. IVIG: Intravenous immunoglobulin.

There is no specific antiviral therapy available to treat PVB19 infection. The treatment options in KTR described in the medical literature include: IVIG only, IVIG and decreased immunosuppression, reduction of immunosuppression only, and conservative therapy, including transfusions, erythropoietin, and/or surveillance[25,54].

IVIG is an important source of anti-PVB19 antibodies; it provides passive immunity and has proven to be efficacious, although no controlled trials have compared the effectiveness of the different dose regimens. As described in Table 2, the reported dose of IVIG was highly variable. The American Society of Transplantation recommends 400 mg/kg/day of IVIG for 5 consecutive days and reduction of immunosuppression at the time of the PVB19 infection diagnosis[5]. In a review of the literature, Crabol, et al.[11] reported that at an initial IVIG dose of 2.3 ± 1.3 g/kg could be effective in eradicating the PRCA associated to PVB19 infection. However, this analysis included a heterogeneous population of immunosuppressed subjects; only 47% were solid organ transplant recipients, while the remainders were patients with HIV infection (30%), hematological (14%), and systemic autoimmune and/or inflammatory diseases (5%). In this series, IS was decreased in only 38% of patients (discontinuation of immunosuppressant in 32% and introduction of highly active antiretroviral therapy in 6%). In non-modifiable immunosuppression states, higher doses could be the only treatment option in PVB19 infection. However, IVIG administration is frequently associated with a concomitant decrease in IS[3,23,25]. There is controversy on whether low- versus high-dose IVIG regimens are preferable, due to cost-effectiveness and complications due to immune complex formation[34]. KTR is a potentially modifiable IS state, which could allow the use of lower doses of IVIG in association with reduction of IS.

There is no universal access to IVIG in the Mexican healthcare system. The out-of-pocket health expenditure (percentage of total health expenditure) is 44%, which is much higher than in the USA or

Table 2. Treatment and outcome of 128 cases of PVB19 infection in KTR

Reference	Number of cases	Response		Treatment	Clinical recurrence (episodes)
		Virologic	Clinical		
Current report	8	NS	Yes	RIS+1.45 g/kg	No
		NS	Yes	RIS+0.4 g/kg	No
		NS	Yes	RIS+0.43 g/kg	No
		NS	Yes	RIS	No
		NS	Yes	RIS+1.1 g/kg	No
		NS	Yes	RIS+1 g/kg	No
		NS	Yes	RIS+0.76 g/kg	No
		NS	Yes	RIS+0.86 g/kg	No
Baek, et al., 2017[6]	39	NS	Yes	RIS (4/39), 0.4 g/kg×5 days (29/39), no treatment (6/39)	NS
Malbora, et al., 2017[7]	1	Yes	Yes	RIS+0.4 g/kg×5 days	No
Parodis, et al., 2017[8]	1	Yes	Yes	RIS+0.5 g/kg×10 doses	No
Rivas-Delgado, et al., 2016[9]	1	No	Yes	RIS+0.4 g/kg×5 days	Yes (2)
Alves, et al., 2013[10]	1	NS	Yes	0.4 g/kg×5 days	NS
Crabol, et al., 2013[11]	3	Yes	Yes	RIS +3 g/kg×2 days	No
		Yes	Yes	RIS +4 g/kg×4 days	No
		No	Yes	RIS +2 g/kg×2 days	No
Gosset, et al., 2012[12]	2	Yes	Yes	RIS+2 g/kg×1 day×12 doses	Yes (9)
		No	No	RIS+2 g/kg×1 day×8 doses	Yes (7)
Tavera, et al., 2012[13]	1	NS	No	RIS+0.4 g/kg×5 days	NS
Labbadia, et al., 2012[14]	1	Yes	Yes	RIS+0.5 g/kg×4 days	No
Kurukulasuriya, et al., 2011[15]	1	NS	Yes	RIS+1 g/kg×5 days	No
Leon, et al., 2010[16]	1	Yes	Yes	RIS+0.4 g/kg×5 days	No
Shen, et al., 2010[17]	1	Yes	Yes	RIS+0.4 g/kg×5 days×5 cycles	Yes (1)
Ardalan, et al., 2008[18]	6	NS	Yes	RIS+0.5 g/kg×5 days	NS
		NS	Yes	RIS+0.5 g/kg×5 days	NS
		NS	Yes	RIS+0.5 g/kg×5 days	NS
		NS	Yes	0.5 g/kg×5 days	NS
		NS	No	Nephrectomy+0.2 g/kg×5 days	NS
		NS	Yes	RIS+0.5 g/kg×5 days	NS
Ardalan, et al., 2008[19]	1	NS	Yes	RIS +0.4 g/kg×5 days	No
Pinto, et al., 2008[20]	2	Yes	Yes	RIS+1 g/kg×2 days×2 cycles	Yes (1)
		Yes	Yes	1 g/kg×2 days	No
Beckhoff, et al., 2007[21]	1	No	Yes	RIS+150 g+125 g	Yes (1)
Arzouk, et al., 2006[22]	1	Yes	Yes	RIS +0.5 g/kg×2 days×4 months	No
Renoult, et al., 2006[23]	3	NS	Yes	RIS+(1 g/kg×9 days)/ 3 weeks×5 months	Yes (1)
		NS	No	RIS+0.4 g/kg×10 days×3	Yes (2)
		NS	Yes	RIS+0.4 g/kg and 2 g/kg	Yes (1)

(Continue)

Table 2. Treatment and outcome of 128 cases of PVB19 infection in KTR *(continued)*

Reference	Number of cases	Response		Treatment	Clinical recurrence (episodes)
		Virologic	Clinical		
Laurenz et al., 2006[24]	1	Yes	Yes	RIS	No
Eid et al., 2006[3]	6	NS	Yes	1 g/kg×2 days	Yes (NS)
		NS	Yes	RIS+1 g/kg×2 days	Yes (NS)
		NS	Yes	RIS+0.5 g/kg×2 days	No
		NS	Yes	RIS+0.4 g/kg×5 days	No
		NS	Yes	1 g/kg×2 days	Yes (NS)
		NS	Yes	1 g/kg×2 days	Yes (NS)
Egbuna et al., 2006[25]	3	Yes	Yes	0.5 g/kg×4 days	Yes (1)
		Yes	Yes	0.5 g/kg×4 days	NS
		Yes	Yes	0.5 g/kg×4 days	NS
Vales-Albertos et al., 2005[26]	1	NS	Yes	RIS	No
Bilge et al., 2005[27]	1	Yes	Yes	1 g/kg×2 days×6 months	No
Subtirelu et al., 2005[28]	1	NS	Yes	1 g/kg×2 days	NS
Ki et al., 2005[29]	2	Yes	Yes	0.5 g/kg×7 days	NS
Kumar et al., 2005[30]	1	No	Yes	RIS+0.4 g/kg×4 days× 2 cycles	Yes (1)
Gomez-Huertas et al., 2005[31]	1	Yes	Yes	RIS+0.4 g/kg×5 days	No
Rerolle et al., 2004[32]	1	NS	Yes	RIS+1 g/kg×2 days×2 cycles	Yes (1)
Garewal et al., 2004[33]	1	NS	Yes	RIS+0.4 g/kg×5 days	No
Liefeldt et al., 2002[34]	1	Yes	Yes	RIS+0.25 g/kg×3 days, 0.5 g/kg×5 days	Yes (1)
Yango et al., 2002[35]	1	NS	Yes	RIS+0.4 g/kg×10 days	NS
Choi et al., 2002[36]	1	No	Yes	RIS+0.4 g/kg×10 days	Yes (1)
Shan et al., 2001[37]	1	No	No	RIS+0.4 g/kg×7 days	Yes (1)
Lui et al., 2001[38]	3	NS	No	21 g/day×5 days×2 cycles	NS
		Yes	Yes	21 g/day×5 days×2 cycles	Yes (1)
		Yes	Yes	No treatment	No
Murer et al., 2000[39]	4	Yes	Yes	No treatment	No
Geetha et al., 2000[40]	1	Yes	Yes	RIS	No
So et al., 2000[41]	1	NS	Yes	0.5 g/kg×5 days	No
Lee et al., 2000[42]	1	No	Yes	RIS+0.4 g/kg×7days	No
Pamidi et al., 2000[43]	2	NS	Yes	50 g×5 days	No
		NS	Yes	RIS+25 g×5 days	No
Shimura et al., 2000[4]	3	NS	Yes	RIS	No
		NS	Yes	RIS	Yes (1)
		NS	Yes	RIS	NS
Wong et al., 1999[44]	1	Yes	Yes	RIS+0.4 g/kg×5 days	Yes (2)
Marchand et al., 1999[45]	1	NS	Yes	RIS+0.5 g/kg×2 days	No
Keung et al., 1999[46]	1	NS	Yes	No treatment	NS

(Continue)

Table 2. Treatment and outcome of 128 cases of PVB19 infection in KTR *(continued)*

Reference	Number of cases	Response		Treatment	Clinical recurrence (episodes)
		Virologic	Clinical		
Moudgil, et al., 1997[47]	3	NS	Yes	0.4 g/kg×10 days	Yes (1)
		NS	Yes	0.4 g/kg×10 days	No
		NS	Yes	RIS+1 g/kg×2 days and then every week for 3 months	Yes (1)
Mathias, et al., 1997[48]	1	NS	Yes	RIS+1 g/kg×2 days	No
Ahsan, et al., 1997[49]	1	Yes	Yes	RIS+0.4 g/kg×5 days	No
Bertoni, et al., 1997[50]	4	No	Yes	0.4 g/kg×15 days	No
Sturm, et al., 1996[51]	1	No	Yes	RIS+0.4 g/kg×4 days	Yes (1)
Uemura, et al.,1995[52]	1	No	Yes	35 g	NS
al-Khaldi, et al.,1994[53]	1	NS	Yes	No treatment	No

NS: Not specified, RIS: Reduction in immunosuppression, PVB19: Parvovirus B19, KTR: Kidney transplant recipient.

European Union (11 and 13.9%, respectively), placing us as well as other low-income countries at a disadvantage in terms of access to health services[55]. The standard cost of the recommended IVIG dose (e.g., 2 g/kg in an individual weighing 70 kg) is approximately 10,216.34 USD and this amount grossly exceeds the monthly income of a Mexican family, 804 USD. The low dose of IVIG used in our series was due to the inability of patients or the health system to afford higher doses, although the outcome did not seem worse than in other reported series.

Our patients received a single total dose of IVIG (mean 0.87 ± 0.42 g/kg) plus IS reduction, and none relapsed clinically. We cannot attribute the success rate and lack of recurrence to the dose of IVIG due to the associated IS reduction, an evident confounder. However, we believe that our cases may represent a model of reverse innovation, and its effectiveness could be generalized to low-income populations and be subsequently evaluated in high-income countries in multicenter controlled clinical trials[56]. Although IVIG is considered to be relatively safe, about 10-13% of patients develop side effects, mainly acute renal failure and pulmonary edema[3,11].

This study underscores the need for the temporary decrease in IS, if feasible, as part of the treatment to allow the immune system to mount a specific immune response against PVB19 infection. Some investigators have reported success with reduction of IS alone[4,24,26,40]. Our population was predominantly at low risk for rejection, which allowed us to decrease IS (discontinuation or halving of antiproliferative drugs) and use low doses of IVIG (mean dose of 0.87 ± 0.38 g/kg), with subsequent improvement in Hb and no relapses during follow-up. In contrast, Liefeldt, et al.[34] failed to eradicate viremia in a patient with decreased IS and low-dose IVIG (0.25 g/kg for 3 days), but he was successfully treated using higher doses of IVIG (0.5 g/kg for 5 days). Some authors reported spontaneous recovery in KTR[39,45,46,53,57], suggesting that a conservative approach with blood transfusions, recombinant erythropoietin, or surveillance may be an option in those with less severe infections.

Clinical PVB19 infection relapses can occur many months after completion of any of the above therapies and are usually heralded by the reappearance of anemia. Factors fostering relapse include failure to eradicate fully the virus, degradation of exogenous IVIG, reintroduction of IS, or failure to mount a humoral and/or cellular immune response[54]. In our analysis of the KTR population, overall recurrence was 35%, similar to that reported by Crabol, et al.[11], in a heterogeneous population with 34% of relapses in initial responders over a mean time period of 4 months and that required an additional course of IVIG to achieve a sustained response rate at 12 months, all a result of their non-modifiable states of immunosuppression.

In our analysis, the relapse rates according to the type of therapeutic strategy included 41% in the group of

IVIG plus IS reduction and 35% in the group treated only with IVIG. These outcomes may be biased due to the tendency to publish successful cases in which the administered therapeutic strategy was different from the standard approach (17% relapses in the group with IS reduction and no relapses in patients with no therapeutic intervention) and more intensive treatment in patients with more relevant clinical PVB19 manifestations.

Our study was limited by its retrospective design. Furthermore, the available information on PVB19 infection in KTR is predominantly presented as case reports. Another potential limitation is the lack of serial quantitative PCR assays during follow-up, to evaluate virological behavior and the eradication of viremia. However, the value of such a monitoring has not been studied, and the improvement in Hb levels with treatment and no recurrence of anemia over a median follow-up of 2 years suggests the absence of virus replication.

In KTR, reduction of immunosuppression and the administration of low-dose immunoglobulin seem to be not worse than the standard dose in PVB19 infection.

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