Abstract Number: FRDEL-0009

PARVOVIRUS B19 DISEASE POST RENAL TRANSPLANT PRESENTING AS REFRACTORY ANEMIA – CASE SERIES OF 20 PATIENTS

Dr Ankur Mittal, Dr Umapati Hegde, Dr Sishir Gang, Dr Abhijit Konnur, Dr Hardik Patel
DEPARTMENT OF NEPHROLOGY
Muljibhai Patel Society for Research in Nephro-Urology and Muljibhai Patel Urological Hospital, Nadiad, Gujarat, INDIA
www.mpuh.org

INTRODUCTION

- Parvovirus B19 is a small, non-enveloped single-stranded DNA virus of the Erythrovirus genus and parvoviridae family. PVB19 infection has characteristic tropism to infect red blood cell and their precursor.
- Serological studies for PVB19 demonstrate antibodies against PVB19 in 60% - 90% of the patients.[1]
- In a post renal transplant patient, Due to failure to mount a neutralizing antibody response to the virus, patients present with features of pure red cell aplasia, these patients usually do not have arthritis or rash because of the absence of immune response to the virus.
- In a post-renal transplant recipient, parvovirus disease manifest as persistent or refractory anemia[2] usually present in the early post transplant period.
- Intrarenal persistence of the PVB19 virus may lead to chronic allograft nephropathy.[3]
- Organ-invasive PVB19 disease was considered definite, probable, or possible on the basis of the following criteria:

(1) Detection of PVB19 by PCR or other methodology in tissue specimens,
(2) Response to PVB19-directed therapy and
(3) Absence of other infectious or noninfectious processes that could explain the organ-specific finding

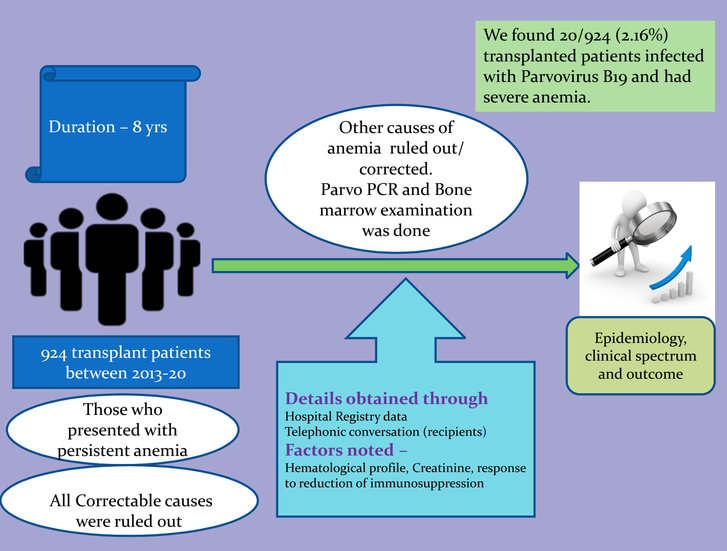
- A definite case of organ-invasive PVB19 disease had to satisfy all 3 criteria.
- A probable case had to satisfy 1 of the first 2 criteria in addition to the third criterion.
- All other cases reported as organ-invasive disease that did not satisfy the criteria for a definite or probable case were considered possible cases

AIMS AND OBJECTIVES

- To Study the Epidemiology, clinical spectrum and outcome of patients with post transplant PVB19 infection.
- To study the different modes of management of patient with post transplant PVB19 infection.

MATERIALS AND METHODS

Methodology: Retrospective observational study



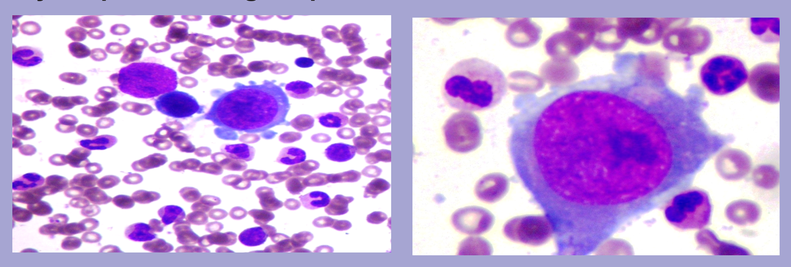
RESULTS

Table 1 : Baseline Characteristic

Baseline Characters	Findings
Total	20
Mean Age (In years)	31.4 ± 9.81
Gender ratio (Male: Female)	4:1
Induction Immunosuppression	12
Mean hemoglobin (mg/dl)	6.49 ± 1
Mean leukocyte count (cells/mm³)	6600
Mean Platelets count (lakhs/mm³)	3.22 Lacs
PCR positive	19
Mean Reticulocyte count (%)	0.5%
Normocytic Normochromic blood smear	85%

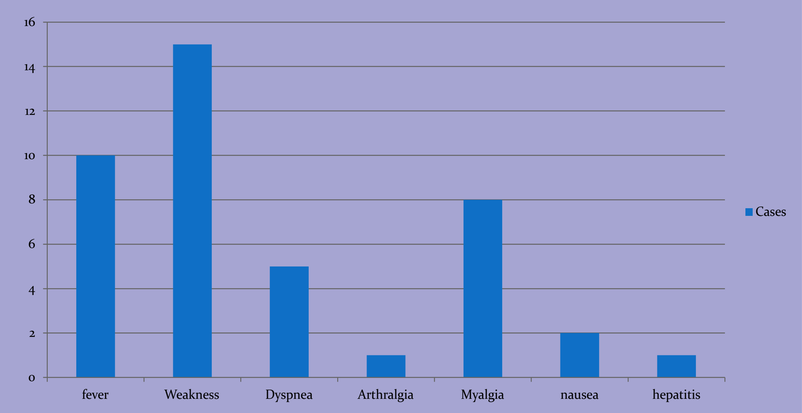
RESULTS

Parvovirus B19 PCR was positive in 19 out of 20 patients. Bone marrow examination was performed in 6 of the patients and all of them had hypo proliferative marrow of which 1 patient showed normal granulopoiesis and thrombopoiesis with suppressed erythropoiesis and giant pronormoblasts with viral inclusions.



Parvovirus PCR may be negative –
1) Low level of viremia
2) Ability to detect Genotype 2 and 3 is low
3) Inhibitory substances that may be present in the specimen.
4) Later in the course of the disease

Figure 1: Clinical presentation



18 out of 20 patients presented within the first year of transplant

The median time of onset of disease was 39 days after transplantation. In 75% (15/20) of patients, the onset was within 3 months after transplantation.

Figure 2: Time of Presentation

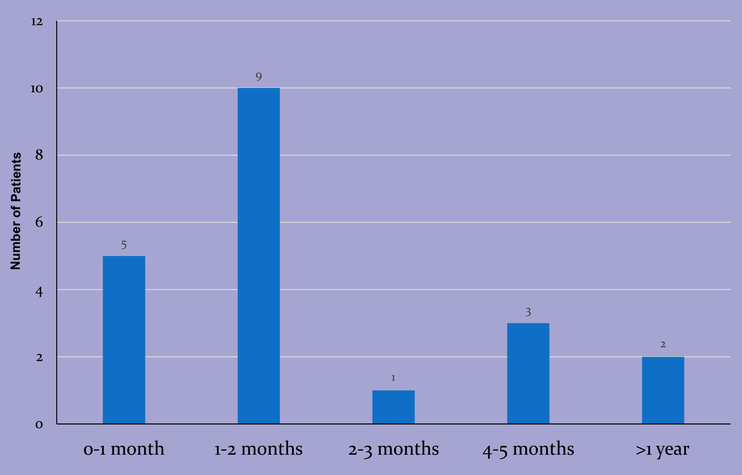


Figure 3: Hemoglobin trend with Parvovirus B19

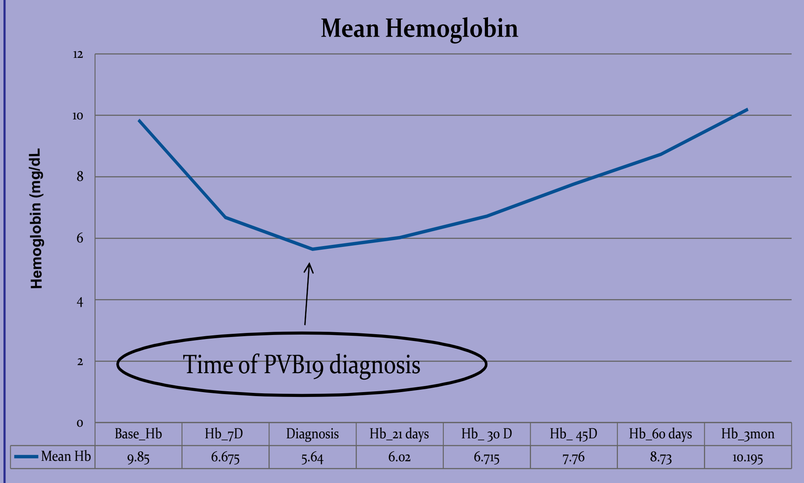
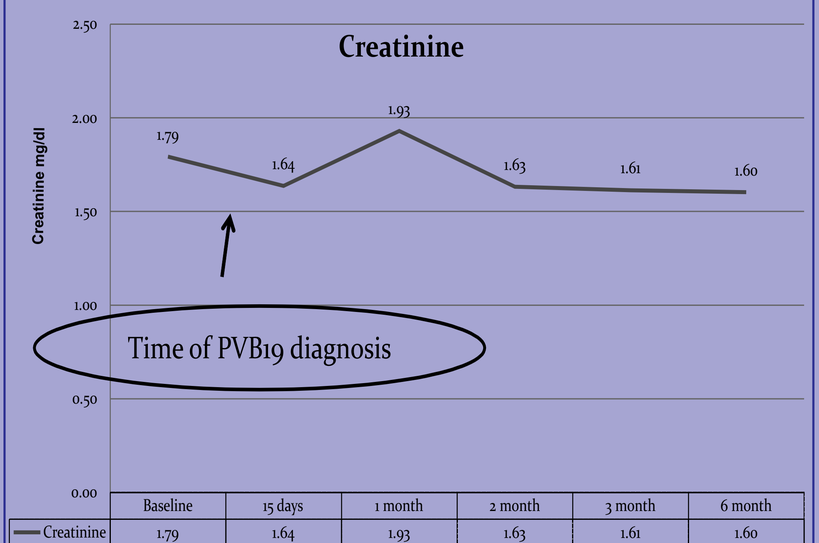


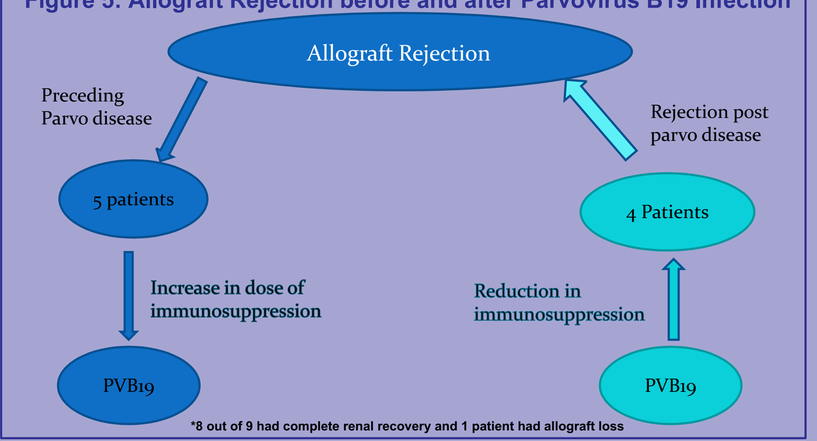
Figure 4 : Trend of Serum creatinine over the course of disease



ALLOGRAFT DYSFUNCTION AND ACUTE REJECTION

- Cavallo et al reported that 36% of patients with active infection had elevated serum creatinine.[8] Kidney biopsy revealed tubular cell damage, and parvovirus DNA was detected by PCR in biopsy. Direct viral infection of endothelial cells leading to sensitization of glomerular endothelium has been proposed for predisposition to ACR. Murer et al implicated graft dysfunction in B19 infection for thrombotic microangiopathy[9]
- We saw 50% patients with Parvovirus disease had graft dysfunction evidenced by 30% elevation in the creatinine from baseline.
  5 patients developed Parvo after ACR treatment
  4 patient developed ACR after reduction in he immunosuppression

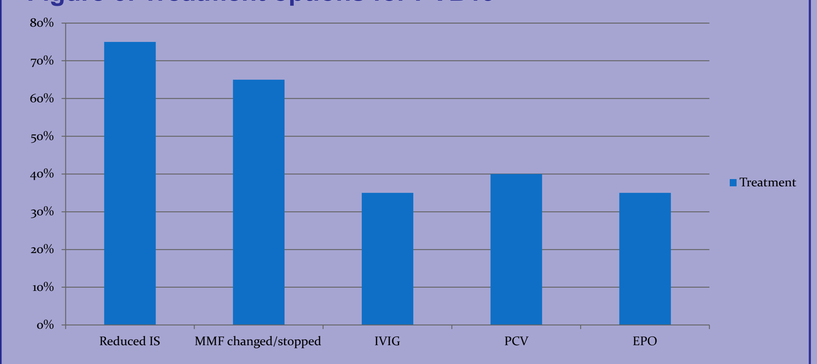
Figure 5: Allograft Rejection before and after Parvovirus B19 Infection



*8 out of 9 had complete renal recovery and 1 patient had allograft loss

TREATMENT

Figure 6: Treatment options for PVB19



COMPARISON WITH OTHER STUDIES

Table 2 : Comparison with a study by Eid Albert J et. al.

	Eid et al (1990-2005)	Our study(2013-2020)
No of Patients -n	53	20
Age (years)	36.7± 15.5	31.4 ± 9.81
Male ; Female	34 :19	16 ; 4
Time of disease after transplantation days	37 days	39 days
Mean Hb gm%	6.2	6.49
Leukopenia %	34	20
Low platelets %	19.1	10%
Positive PCR at the time of diagnosis n(%)	46(86.7%)	19(95%)
Treatment with IV Ig n(%)	46(86.7%%)	7 (35%)
Death due to Parvo	0	0

**Eid, Albert J., et al. "Parvovirus B19 infection after transplantation: A review of 98 cases" OUP Academic, Oxford University Press, 1 July 2006, academic.oup.com/cid/article/43/1/40/308979*

LIMITATIONS OF THE STUDY

- The limitation of this study was Parvovirus PCR was not checked in all KTRs. It was checked when the patient had severe anemia and other causes of anemia have been ruled out. Bone marrow examination was done in only indicated patients and was not performed in all patients with severe anemia. This study was a single center study; hence it becomes difficult to estimate the prevalence of parvovirus B19 infection in KTRs.

CONCLUSION

- Parvovirus B19 infection is rare but can present with serious complications in the early post-transplant period. A high index of suspicion is required when the patient develops refractory or prolonged anemia. DNA PCR or Bone marrow examination is needed for the diagnosis and reduction in immunosuppression, particularly the anti-proliferative agents are the mainstay of treatment.
- We suggest to check Parvo virus in those transplant patient with anemia and inappropriate reticulocyte response with or without:
  - Fever, arthralgia or rash
  - Organ-invasive disease such as hepatitis, myocarditis, pneumonitis, neurological disease or vasculitis
  - Pancytopenia

REFERENCES

- 1. Cohen BJ, Buckley MM. The prevalence of antibody to human parvovirus B19 in England and Wales. *J Med Microbiol*. 1988;25(2):151-153. doi:10.1099/00222615-25-2-151
- 2. Beckhoff A, Steffen I, Sandoz P, Hirsch HH, Schaub S. Relapsing severe anaemia due to primary parvovirus B19 infection after renal transplantation: a case report and review of the literature. *Nephrol Dial Transplant*. 2007;22(12):3660-3663. doi:10.1093/ndt/gfm531
- 3. Eid AJ, Brown RA, Patel R, Razonable RR. Parvovirus B19 infection after transplantation: a review of 98 cases. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2006;43(1):40-48. doi:10.1086/504812
- 4. Cavallo R, Merlino C, Re D, et al. B19 virus infection in renal transplant recipients. *J Clin Virol Off Publ Pan Am Soc Clin Virol*. 2003;26(3):361-368. doi:10.1016/s1386-6532(02)00104-x
- 5. Murer L, Zacchello G, Bianchi D, et al. Thrombotic Microangiopathy Associated with Parvovirus B 19 Infection after Renal Transplantation. *J Am Soc Nephrol*. 2000;11(6):1132-1137. doi:10.1681/ASN.V11611321