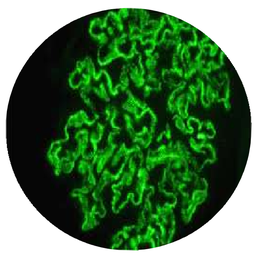
Use of Rituximab as induction therapy in anti-glomerular-basement-membrane disease



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Introduction and Objectives: Anti-glomerular-basement-membrane (anti-GBM) disease is characterized by severe kidney and lung involvement. Although its prognosis has improved with treatment combining cyclophosphamide, plasma exchange (PE) and corticosteroids. However, patients with severe renal involvement have poor renal outcome and cyclophosphamide causes significant complications. Anti-GBM antibodies have a direct pathogenic effect and therapeutics that aim to decrease their production, such as Rituximab, an anti-CD20 monoclonal antibody, could be a good alternative to improve renal prognosis.

Methods: We retrospectively collected data from five patients referred to our university hospital from 2013 to 2016 for anti-GBM disease. They received an induction therapy of Rituximab instead of cyclophosphamide, given as 4 weekly pulses of 375 mg/m^2 in addition to PE and corticosteroids. Plasma exchange was performed daily until circulating anti-GBM antibodies became undetectable.

Results: At diagnosis, all patients had severe disease manifestations. Four patients required dialysis within 7 days after diagnosis and remained dialysis dependent with a mean follow-up of 15 months. Three patients had pulmonary involvement and recovered even though mechanical ventilation was required. Anti-GBM antibodies became rapidly undetectable in all patients. Only one infection and two hematologic complications were observed and these occurred with in the same patient.

Patient Gender, age	Initial clinical presentation	Creatinine at diagnosis (µmol/L)	Initial dialysis within 7 days after diagnosis	Crescents on kidney biopsy	Initial anti-GBM titer (IIF)	Number of plasma exchange sessions	Corticosteroids	Rituximab	Outcome	Complications	Follow up duration (months)	Evolution
Patient 1 M, 73	General weakness, dyspnea, AKI	706	yes	20%	10	9	120mg x3 + 1mg/kg	375mg/m^2 x4	ESRD	no	39	Transplantation
Patient 2 F, 63	AKI with diarrhea, dyspnea and desaturation, hemoptysis	800	yes	90%	80	23	1mg/kg	375mg/m^2 x4	Pulmonary recovery ESRD	no	23	Hemodialysis
Patient 3 F, 72	Hemoptysis, respiratory distress with mechanical ventilation, AKI in intensive care	47	no	NC	> 5	10	1mg/kg	375mg/m^2 x4	Pulmonary recovery	Candida colonization	4	Creatinine 48 µmol/L
Patient 4 F, 75	Rapidly progressing glomerulonephritis, hematuria	273	yes	NC	> 640	21	500mg x 4 + 1mg/kg	375mg/m^2 x4	ESRD	Esophageal candidiasis + temporary thrombocytopenia + leucopenia at 6 months	9	Peritoneal dialysis
Patient 5 F, 18	Hemoptysis, AKI	605	yes	100%	200	20	500mg x 3 + 1mg/kg	375mg/m^2 x4	Pulmonary recovery ESRD	no	14	Transplantation

Patients characteristics and treatment summary
ESRD : end stage renal disease ; F : female ; M : male ; AKI : acute kidney injury ; IIF: indirect immunofluorescence; ANCA: anti-neutrophil-cytoplasmic antibody; anti-GBM: anti glomerular-basement-membrane antibody

Conclusion: Rituximab was effective as previously shown with cyclophosphamide to induce complete resolution of pulmonary hemorrhage. It is associated with a good biological response and without major life threatening major side effects and death. However, for dialysis dependent patients at presentation, renal outcome did not seem to be significantly improved.

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