Treatment

OA Nephrology
Open Access

Critical review

The antiglomerular basement membrane disease: treatments and outcomes

K Hirayama[1,2]*, K Yamagata[3]

Abstract

Introduction

Antiglomerular basement membrane (anti-GBM) disease is a rare autoimmune disorder characterized by rapidly progressive glomerulonephritis (RPGN) with diffuse crescentic formation on renal biopsy, and it is a well-characterized cause of glomerulonephritis. Although the effectiveness of treatment using therapeutic plasma exchange combined with immunosuppressive agents to improve renal function has been reported, the prognosis for patients with this disease is poor. To improve the prognosis, it may be necessary to detect this disease in earlier stages and to treat it without delay. This critical review discusses the treatments and outcomes of anti-GBM disease.

Conclusion

Anti-GBM disease is rare, but the treatment has been reported to improve renal function. This disease needs to be detected in its early stages to tackle the life cycle of the disease.

Introduction

Antiglomerular basement membrane (anti-GBM) disease is a rare autoimmune disorder characterized by rapidly progressive glomerulonephritis (RPGN) with diffuse crescentic formation on renal biopsy, and it is a well-characterized cause of glomerulonephritis. Anti-GBM disease is defined as the presence of serum autoantibodies to the non-collagenous domain of the alpha 3 chain of type IV collagen or a linear binding of IgG to glomerular capillary walls as detected by direct immunofluorescence in patients with RPGN. Although effective treatments to improve renal function have been reported, the prognosis of patients with this disease is poor.

This critical review focuses on treatments and outcomes of anti-GBM disease in order to improve the prognosis of the disease.

Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964), and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Treatments

As the pathogenesis of anti-GBM disease became clear, treatment regimens were designed to remove the circulating pathogenic anti-GBM antibodies by therapeutic plasma exchange, attenuating the pathogenic antibody-mediated glomerular inflammatory responses by administration of corticosteroids and suppressing further production of these pathogenic antibodies by the use of immunosuppressive agents.

Therapeutic plasmapheresis

To remove the circulating pathogenic anti-GBM antibodies, therapeutic plasma exchange is recommended as the initial treatment. The effectiveness of therapeutic plasmapheresis for improving renal function has been reported. Several regimens were reported (Table 1)[1–9], and plasma exchange of 4 L of plasma for 5% human albumin was most commonly performed daily for 14 days or until the circulating anti-GBM antibodies were no longer detected[1]. In the presence of alveolar haemorrhage, 300–400 ml of fresh-frozen plasma was given at the end of each treatment.

To reduce the plasma replacement, anti-GBM antibody removal has been modified. Immunoadsorption to remove circulating IgG without the need for protein substitution during daily treatments may also be beneficial in Goodpasture's disease. Anecdotal case reports suggest that it may be an alternative to plasmapheresis in patients with severe renal failure[10]. A case report of Goodpasture's syndrome treated with double-filtration plasmapheresis combined with immunosuppression therapy[11] showed that the removal efficiency for the anti-GBM antibody was 24%–60% for each procedure.

Corticosteroids

To attenuate the pathogenic antibody-mediated glomerular inflammatory responses, corticosteroid is also a key element of this treatment. According to the most commonly used regimens, oral dosing of prednisolone at 1 mg/kg/day of ideal body weight (maximum 80 mg daily) continues for at least 2 weeks, after which the dose is reduced

* Corresponding author
Email: k-hira@naritasekijyuji.jp

[1] Department of Nephrology, Japanese Red Cross Narita Hospital, Narita, Chiba
[2] Department of Nephrology, Tokyo Medical University Ibaraki Medical Center, Ami, Ibaraki, Japan
[3] Department of Nephrology, University of Tsukuba, Tsukuba, Ibaraki, Japan

FOR CITATION PURPOSES: *Hirayama K, Yamagata K.* The antiglomerular basement membrane disease: treatments and outcomes. OA Nephrology 2013 Apr 01;1(1):1.

Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

OA Nephrology
Open Access

Table 1 Reported regimens of plasmapheresis in anti-GBM disease

Authors	Years	*N*	Regimes of Plasmapheresis				Survival Rates(%)	
			Methods	Fluids	Volume	Sessions and Periods	Patients	Renal
Lockwood et al.[1]	1975	7	PLEX	5% Alb (+ FFP)	4.0 l	Daily for 2 weeks*	86	43
Briggs et al.[2]	1979	4	PLEX	5% Alb (+ FFP)	4.0 l	Daily for 2 weeks	100	50
Simpson et al.[3]	1982	8	PLEX	CDP	3.0 l	Ten times for 2 weeks	100	63
Peters et al.[4]	1982	41	PLEX	5% Alb (+ FFP)	4.0 l	Daily for 2 weeks*	85	16
Johnson et al.[5]	1982	8	PLEX	FFP + saline	4.0 l	Every 3 days*	100	75
Merkel et al.[6]	1994	25	PLEX	NA	NA	Daily for 10 days*	88	32
Stegmayr et al.[7]	1999	3	PLEX	5% Alb	0.8×PV	> three times for 5 days	67	0
		3	IA	None	2.5×PV	> three times for 5 days	67	0
Levy et al.[8]	2001	71	PLEX	5% Alb (+ FFP)	50 ml/kg (maximum 4 l)	Daily for 2 weeks*	97	41
Lazor et al.[9]	2007	24	PLEX	NA	NA	Alternate day 10 times	100	42

*Until anti-GBM antibody is undetectable.
N, number of patients; PLEX, plasma exchange; IA, immunoabsorption; Alb, albumin; FFP, frozen fractionated protein; CDP, cryoprecipitate-depleted plasma; PV, estimated plasma volume; NA, not available.

every second week to 30 mg by the eighth week. The dosages of prednisolone are then tapered to 2.5–5.0 mg/week and maintained at 7.5–10 mg/kg/day. Oral corticosteroids are generally continued for at least 6 months. Intravenous administration of methylprednisolone 10 mg/kg (500–1000 mg) once daily for 1–3 days has been advocated for patients with severe alveolar haemorrhage or very rapid deterioration of renal function[5].

Immunosuppressive agents

To further suppress the production of pathogenic anti-GBM antibodies, a combination of immunosuppressive agents is usually given. Among these immunosuppressive agents, cyclophosphamide is usually administered. According to the most commonly used regimens, the oral dose is 2–3 mg/kg/day (this is rounded down to the nearest 50 mg; reduced to 2 mg/kg/day in patients over 55 years) for 3 months. This administration is stopped if white blood cell counts fall below 4,000/μl. In such cases, the agent is restarted at a lower dose once the white blood cell counts return above 4,000/μl. Intravenous cyclophosphamide is not usually administered, but it may be useful for a refractory case of the standard therapy[12].

Although azathioprine is sometimes used as maintenance therapy, it does not provide adequate immunosuppression to modify the disease alone.

Therapeutic options for refractory diseases

There is very little research on the treatment of refractory anti-GBM disease. Cyclosporine is controversial; at 6 mg/kg/day it was effective for an anti-GBM disease patient treated with corticosteroid, cyclophosphamide and plasma exchange[13], whereas in other cases it was not useful[14]. Small numbers of case reports of successful outcomes with mycophenolic acid or mycophenolatemofetil in patients unresponsive to or intolerant of standard therapy have been published[15–17]. Rituximab, a chimeric monoclonal anti-CD20 antibody, was effective for a case of relapsed anti-GBM disease that was resistant to standard treatment[18]. In that case, rituximab (375 mg/m^2) was administered once a week for 6 consecutive weeks; the symptoms completely resolved and anti-GBM antibody titres were decreased from 51 U/ml to the undetectable range. However, these treatments cannot yet be recommended as a first-line therapy because randomized controlled trials have not been carried out.

Prognosis

Most patients without treatment died shortly after diagnosis of anti-GBM disease; the survival rate at 12 months was 4% and the renal survival rate was 2%[19]. Although mortality has improved by the introduction of intense immunosuppression, renal survival remains very poor because of the delayed diagnosis of anti-GBM disease or delayed initiation of induction therapies.

Outcomes

The prognosis for patients with anti-GBM disease is poor; the survival rate at 6–12 months was 67–94%, but the renal survival rate was 15%–58% (Table 2)[2,3,5,6,8,9,19–29].

FOR CITATION PURPOSES: *Hirayama K, Yamagata K.* The antiglomerular basement membrane disease: treatments and outcomes. OA Nephrology 2013 Apr 01;1(1):1.

Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

OA Nephrology
Open Access

Table 2 Investigation of treatments for anti-GBM disease

Authors	Year	*N*	Age, mean (median)	AH (%)	s-Cr Levels (mg/dl)	Treatments		Survival Rate (%)	
						Immunosup-pressant	PLEX (%)	Patients	Renal
Benoit et al.[19]	1963	52	NA	100	NA	None	0	4	2
Proskey et al.[20]	1970	56	(26.8)	100	NA	Various	0	77	23
Wilson et al.[21]	1973	53	28.5	60	NA	Various	0	53	13
Beirne et al.[22]	1977	29	NA	54	NA	Various	0	42	17
Briggs et al.[2]	1979	7	21.0	0	6.4 ± 3.1	None or OCS+CYC	0	86	0
		7	21.0	100	3.1 ± 2.9	Various	0	71	29
		4	21.0	100	9.5 ± 13.8	Various	100	100	50
Peters et al.[4]	1982	24	NA	80	> 6.8	Various	46	79	4
		17	NA		< 6.8			94	88
Simpson et al.[3]	1982	8	28.1	100	8.0 ± 6.7	None	0	63	25
		4	22.3	100	4.1 ± 4.0	OCS+AZA	0	100	50
		8	22.1	100	3.9 ± 3.1	OCS+CYC	100	100	63
Johnson et al.[5]	1985	9	22.9	78	5.3 ± 1.6	OCS+CYC	0	89	22
		8	24.8	100	4.3 ± 1.6		100	100	75
Savage et al.[23]	1986	108	47.8	52	NA	Various	42	78	22
Williams et al.[24]	1988	10	57.2	30	11.8 ± 4.6	Various	60	90	10
Herody et al.[25]	1993	29	35.2	50	NA	OCS+CYC+AZA	0	93	41
Merkel et al.[6]	1994	35	34.7	57	11.4 ± 5.6	OCS+CYC	71	89	29
Daly et al.[26]	1996	40	[18–76]	67	5.1 ± 6.8	Various	58	98	20
Levy et al.[8]	2001	19	(40) [17–76]	62	< 5.7	OCS+CYC	100	100	95
		13			> 5.7			85	69
		39			ESRD			67	5
Li et al.[27]	2004	10	58.6	40	7.0 ± 6.4	Various	80	70	15
Cui et al.[28]	2005	23	38	42	< 6.8	Various	45	NA	61
		46			> 6.8			NA	2
Lazor et al.[9]	2007	10	(23) [17–65]	100	< 1.4	OCS+CYC	54	NA	0
		12		100	AKI		100	NA	83
Hirayama et al.[29]	2008	33	52.6	0	9.1 ± 5.0	Various	55	79	21
		10	49.4	100	8.5 ± 5.1		30	70	20
		12	48.3	25	< 6.0	Various	50	75	42
		29	52.1	24	> 6.0		48	79	14
		21	56.1	14	8.6 ± 5.3	Various	0	86	24
		22	46.8	36	9.4 ± 4.8		100	68	14

N, number of patients; AH, alveolar haemorrhage; s-Cr, serum creatinine; ESRD, end-stage renal disease; AKI, acute kidney injury; OCS, oral corticosteroids; CYC, cyclophosphamide; AZA, azathioprine; PLEX, plasma exchange; NA, not available.

FOR CITATION PURPOSES: *Hirayama K, Yamagata K.* The antiglomerular basement membrane disease: treatments and outcomes. OA Nephrology 2013 Apr 01;1(1):1.

Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

OA Nephrology
Open Access

Renal function improves in 15%–75% of patients with anti-GBM disease through the combination of plasma exchange with corticosteroids and immunosuppressive agents; whereas, the renal survival rates of anti-GBM disease patients treated with immunosuppressive agents alone ranged from 2% to 22%. Improvement of renal function is usually evident within days of the start of plasma exchange. However, it should be emphasized that this regimen has never been properly assessed by a prospective randomized controlled trial because of the rarity and acuteness of the condition. The only reported randomized controlled trial was very small and used lower doses of both plasma exchange and cyclophosphamide than those that are generally used in practice.

Although the effectiveness of treatment using therapeutic plasma exchange combined with immunosuppressive agents to improve renal function has been reported, only half of patients with anti-GBM disease had been treated with plasma exchange in Japan[29]. Therefore, there was no significant difference in the renal survival rates between anti-GBM antibody disease patients treated with or without plasma exchange (P = 0.683 by the log-rank Mantel–Cox test). Moreover, there was no significant difference in mortality between anti-GBM antibody disease patients treated with or without plasma exchange (P = 0.109).

Predictors of survival

The best predictors of renal survival are serum creatinine (s-Cr) levels at the initiation of treatment and the mean percentage of crescent formations. Renal function improves coincidentally with the introduction of plasma exchange in about 80–95% of patients with s-Cr levels less than or equal to 5.7–6.8 mg/dl (500–600 μmol/l), but rarely in those with higher s-Cr levels or those who require dialysis. Unfortunately, most patients with anti-GBM disease had renal failure at the time of diagnosis, and the mean percentage of crescent formation was high in anti-GBM disease patients. Therefore, in most patients with anti-GBM disease, the diagnosis may have been made too late to improve renal function by combination therapy. In the recent cohortstudy[30], the combination therapy of plasmapheresis and corticosteroids with cyclophosphamide had an overall beneficial effect on both patient survival (HR for patient mortality, 0.31; P = 0.001) and renal survival (HR for renal failure, 0.60; P = 0.032), particularly patient survival for those with alveolar haemorrhage (HR for patient mortality, 0.29; P = 0.004) and renal survival for those with anti-GBM diseases with initial s-Cr levels over 6.8 mg/dl (HR for renal failure, 0.52; P = 0.014).

Relapse/recurrence

Relapses of anti-GBM disease are rarely observed, in contrast to most other autoimmune kidney diseases. The anti-GBM antibodies seem to disappear spontaneously after 12–18 months[31]. However, several reports demonstrated recurring cases with anti-GBM disease[31–34]. In the Japanese survey[29], relapse or recurrence was also rare in patients with anti-GBM disease (13.9%) in comparison with patients with ANCA-associated vasculitis, such as granulomatosis with polyangiitis (29.4%) and microscopic polyangiitis (29.3%). Therefore, remission induction therapy is more important in anti-GBM disease. The mean time to recurrence is estimated to be 4.3 years (range, 1–10 years) and that late recurrence may occur with a frequency of 2–14%. During relapses, circulating anti-GBM antibodies often reappear. The combination of plasmapheresis and immunosuppressive agents as re-remission induction therapy is also successful in relapsing cases[31].

Conclusion

Anti-GBM disease is a rare but well-characterized glomerulonephritis. Although the effectiveness of treatment using therapeutic plasma exchange combined with immunosuppressive agents to improve renal function has been reported, the prognosis of patients with this disease is poor. To improve the prognosis, it may be necessary to detect this disease in its earlier stages and to treat it without delay.

Acknowledgement

The authors acknowledge the participants in this Japanese nationwide survey and the members of the RPGN Clinical Guidelines Committee of Japan. The Japanese nationwide RPGN survey was supported by a grant-in-aid from the Research Fund for the Special Study Group on Progressive Glomerular Disease, the Ministry of Health, Labor and Welfare, Japan.

Abbreviations list

Anti-GBM, antiglomerular basement membrane; RPGN, rapidly progressive glomerulonephritis

References

1. Lockwood CM, Rees AJ, Pearson TA, Evans DJ, Peters DK, Wilson CB. Immunosuppression and plasma-exchange in the treatment of Goodpasture's syndrome. Lancet. 1976 Apr;1(7962):711–5.
2. Briggs WA, Johnson JP, Teichman S, Yeager HC, Wilson CB. Antiglomerular basement membrane antibody-mediated glomerulonephritis and Goodpasture's syndrome. Medicine (Baltimore). 1979 Sep; 58(5):348–61.
3. Simpson IJ, Doak PB, Williams LC, Blacklock HA, Hill RS, Teague CA, et al. Plasma exchange in Goodpasture's syndrome. Am J Nephrol. 1982;2(6):301–11.
4. Peters DK, Rees AJ, Lockwood CM, Pusey CD. Treatment and prognosis in antibasemeent membrane antibody-mediated nephritis. Transplant Proc. 1982 Sep; 14(3):513–21.
5. Johnson JP, Moore J Jr., Austin HA 3rd, Balow JE, Antonovych TT, Wilson CB. Therapy of anti-glomerular basement membrane antibody disease: analysis of

FOR CITATION PURPOSES: *Hirayama K, Yamagata K.* The antiglomerular basement membrane disease: treatments and outcomes. OA Nephrology 2013 Apr 01;1(1):1.

Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

OA Nephrology
Open Access

prognostic significance of clinical, pathologic and treatment factors. Medicine (Baltimore). 1985 Jul;64(4):219–27.
6. Merkel F, Pullig O, Marx M, Netzer KO, Weber M. Course and prognosis of anti-basement membrane antibody (anti-BM-Ab)-mediated disease: Report of 35 cases. Nephrol Dial Transplant. 1994; 9(4):372–6.
7. Stegmayr BG, Almroth G, Berlin G, Fehrman I, Kurkus J, Norda R, et al. Plasma exchange or immunoadsorption in patients with rapidly progressive crescentic glomerulonephritis. A Swedish multicenter study. Int J Artif Organs. 1999 Feb;22(2):81–7.
8. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-term outcome of anti-glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. Ann Intern Med. 2001 Jun; 134(11):1033–42.
9. Lazor R, Bigay-Gamé L, Cottin V, Cadranel J, Decaux O, Fellrath JM, et al. Alveolar hemorrhage in anti-basement membrane antibody disease: a series of 28 cases. Medicine (Baltimore). 2007 May; 86(3):181–93.
10. Laczika K, Knapp S, Derfler K, Soleiman A, Horl WH, Druml W. Immunoadsorption in Goodpasture's syndrome. Am J Kidney Dis. 2000 Aug;36(2):392–5.
11. Nagasu H, Abe M, Kuwabara A, Kawai T, Nishi Y, Okuda N, et al. A case report of efficiency of double filtration plasmapheresis in treatment of Goodpasture's syndrome. Ther Apher Dial. 2009 Aug;13(4):373–7.
12. Baumgartner I, Gmür J, Fontana A, Widmer U, Walter E. Recovery from life threatening pulmonary hemorrhage in Goodpasture's syndrome after plasmapheresis and subsequent pulse dose cyclophosphamide. Clin Nephrol. 1995 Jan; 43(1):68–70.
13. Quérin S, Schürch W, Beaulieu R. Ciclosporin in Goodpasture's syndrome. Nephron. 1992;60(3):355–59.
14. Pepys EO, Rees AJ, Pepys MB. Enumeration of lymphocyte populations in whole peripheral blood of patients with antibody-mediated nephritis during treatment with cyclosporin A. Immunol Lett. 1982 Apr;4(4):211–14.
15. García-Cantón C, Toledo A, Palomar R, Fernandez F, Lopez J, Moreno A, et al. Goodpasture's syndrome treated with mycophenolatemofetil. Nephrol Dial Transplant. 2000;15(6):920–2.
16. Kiykim AA, Horoz M, Gok E. Successful treatment of resistant antiglomerular basement membrane antibody positivity with mycophenolic acid. Intern Med. 2010; 49(6):577–80.
17. Malho A, Santos V, Cabrita A, Silva AP, Pinto I, Bernardo I, et al. Severe relapsing Goodpasture's disease successfully treated with mycophenolatemofetil. Int J Nephrol. 2010;16:383548.
18. Arzoo K, Sadeghi S, Liebman HA. Treatment of refractory antibody mediated autoimmune disorders with an anti-CD20 monoclonal antibody (rituximab). Ann Rheum Dis. 2002 Oct;61(10):922–4.
19. Benoit FL, Rulon DB, Theil GB, Doolan PD, Watten RH. Goodpasture's syndrome: A clinicopathologic entity. Am J Med. 1963 Sep;58:424–44.
20. Proskey AJ, Weatherbee L, Easterling RE, Greene JA Jr., Weller JM. Goodpasture's syndrome. A report of five cases and review of the literature. Am J Med. 1970 Feb;48(2):162–73.
21. Wilson CB, Dixon FJ. Anti-glomerular basement membrane antibody-induced glomerulonephritis. Kidney Int. 1973 Feb;3(2):74–89.
22. Beirne GJ, Wagnild JP, Zimmerman SW, Macken PD, Burkholder PM. Idiopathic crescentic glomerulonephritis. Medicine (Baltimore). 1977 Sep;56(5): 349–81.
23. Savage COS, Pusey CD, Bowman C, Rees AJ, Lockwood CM. Antiglomerular basement membrane antibody mediated disease in the British Isles 1980-4. Br Med J (Clin Res Ed). 1986 Feb; 292(6516):301–4.
24. Williams PS, Davenport A, McDicken I, Ashby D, Goldsmith HJ, Bone JM. Increased incidence of anti-glomerular basement membrane antibody (anti-GBM) nephritis in the Mersey Region, September 1984-October 1985. Q J Med. 1988 Sep;68(257):727–33.
25. Herody M, Bobrie G, Gouarin C, Grünfeld JP, Noel LH. Anti-GBM disease: Predictive value of clinical, histological and serological data. Clin Nephrol. 1993 Nov;40(5):249–55.
26. Daly C, Conlon PJ, Medwar W, Walshe JJ. Characteristics and outcome of anti-glomerular basement membrane disease: a single-center experience. Ren Fail. 1996 Jan;18(1):105–12.
27. Li FK, Tse KC, Lam MF, Yip TP, Lui SL, Chan GS, et al. Incidence and outcome of antiglomerular basement membrane disease in Chinese. Nephrology (Carlton). 2004 Apr;9(2):100–4.
28. Cui Z, Zhao MH, Xin G, Wang HY. Characteristics and prognosis of Chinese patients with anti-glomerular basement membrane disease. Nephron Clin Pract. 2005;99(2):49–55.
29. Hirayama K, Yamagata K, Kobayashi M, Koyama A. Anti-glomerular basement membrane antibody disease in Japan: part of the nationwide rapidly progressive glomerulonephritis survey in Japan. Clin Exp Nephrol. 2008 Oct;12(5): 339–47.
30. Cui Z, Zhao J, Jia XY, Zhu SN, Jin QZ, Cheng XY, Zhao MH. Anti-glomerular basement membrane disease: outcomes of different therapeutic regimens in a large single-center Chinese cohort study. Medicine (Baltimore). 2011 Sep;90(5): 303–11.
31. Levy JB, Lachmann RH, Pusey CD. Recurrent Goodpasture's disease. Am J Kidney Dis 1996 Apr;27(4):573–8.
32. Adler S, Bruns FJ, Fraley DS, Segel DP. Rapid progressive glomerulonephritis: relapse after prolonged remission. Arch Intern Med. 1981 Jun;141(7):852–4.
33. Hind CRK, Bowman C, Winearles CG, Lockwood CM. Recurrence of circulating anti-glomerular basement membrane antibody three years after immunosuppressive treatment and plasma exchange. Clin Nephrol. 1984 Apr;21(4):244–6.
34. Klasa RJ, Abboud RT, Ballon HS, Grossman L. Goodpasture's syndrome: recurrence after a five-year remission. Case report and review of the literature. Am J Med. 1988 Apr;84(4):751–5.

FOR CITATION PURPOSES: *Hirayama K, Yamagata K.* The antiglomerular basement membrane disease: treatments and outcomes. OA Nephrology 2013 Apr 01;1(1):1.

Competing interests: none declared. Conflict of interests: none declared.
All authors contributed to conception and design, manuscript preparation, read and approved the final manuscript.
All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.