

**Table 1.** Characteristics by outcome (AHRF vs. improvement) groups

Variable	Artemisinin-based combination-treated patients		P
	Death n = 12	Survivor n = 34	
Age [years, mean (SD)]	35.9 (10.2)	31.4 (11.4)	0.2
Male	75%	79.4%	0.5
Artemisinin-based combination with			
Lumefantrine	58.3%	38.2%	0.3
Amodiaquine	25%	39.4%	0.5
Mefloquine	0%	17.6%	0.3
Piperaquine/triméthoprim	16.6%	14.7%	1
Artemisinin treatment duration [day, mean (SD)]	2.9 (0.3)	2.8 (0.5)	0.46
Delay between drug starting and AHRF [day, mean (SD)]	3.5 (4.0)	2.3 (1.5)	0.6
Concomitant prescribed drugs			
Quinine	66.6%	70.6%	0.5
Paracetamol	25%	41.2%	0.5
Antibiotic	50%	47.1%	1
Coma on admission	41.7%	0%	0.0006
Fever [°C, mean (SD)]	37.9 (1.0)	37.6 (0.9)	1
Jaundice at any time (%)	9 (75)	18 (53)	0.3
Oliguria	91.7%	94.1%	1
Acute renal failure	100%	100%	1
Serum creatinine at baseline [mg/dL, mean (SD)]	13.6 (6.4)	18.1 (8.4)	0.1
Systolic blood pressure [mmHg, mean (SD)]	135 (24.7)	127.8 (19.8)	0.4
Haemoglobin [g/dL, mean (SD)]	8.6 (2.3)	7.6 (2.7)	0.3
White blood cell count [mm <sup>3</sup> , mean (SD)]	23 860 (12 579)	16 701 (14 736)	0.17
Platelet count [mm <sup>3</sup> , mean (SD)]	212 600 (72 539)	226 969 (149 744)	0.7
ASAT [U/L, mean (SD)]	482.7 (860)	256.3 (313.9)	0.6
ALAT [U/L, mean (SD)]	363.8 (559.6)	164.3 (162.0)	0.9
Dialysis needed	58.3%	47.0%	0.7
Dialysis sessions [mean (SD)]	1.1 (1.0)	1.9 (2.3)	0.6
Time to death from admission [day, median (range)]	3 (1–6)	–	
Time to recovery from admission [day, median (range)]	–	12 (6–32)	
Serum creatinine at improvement [mg/dL, mean (SD)]	–	2.4 (1.6)	

ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase.

We believe practitioners in tropical health centres should be aware of such complication, and an active investigation of the neurological side effects is needed. In case of inefficient initial treatment, documenting malarial infection is necessary before starting a multimolecular therapy.

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<sup>1</sup>Department of Nephrology, Apollinaire Gnionsahé<sup>1</sup>  
Yopougon Hospital, Mohamed Lamine Kourouma<sup>1</sup>  
Abidjan, Ivory Coast Hassane Izzedine<sup>2</sup>

<sup>2</sup>Department of Nephrology,  
Pitie-Salpetriere Hospital,  
Paris, France  
Email: gnions\_daze@hotmail.com

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### Response of patients with sickle cell anaemia and end-stage renal disease to erythropoietin treatment

Sir,

Generally, end-stage renal disease (ESRD) due to sickle cell anaemia (SCA) occurs in <1% of patients receiving renal replacement treatment. For this reason, data about this patient group are very limited and controversial. Both the unresponsiveness of erythropoietin (Epo) treatments

**Table 1.** Characteristics of SCA and ESRD patients and summary of Epo response

Patient number	Patient characteristics <sup>1</sup>	Epo type and dose (s.c.)	Hb, pre-Epo (g/dl)	Hb, on Epo (g/dl)	Minimum Hb, on Epo (g/dl) <sup>2</sup>	Blood transfusion need and rate pre-Epo	Blood transfusion need and rate on Epo
1	32 years, M, HD	Epoetin beta, 3 × 5000 U/week	6.4	5.9	4.0	16 U/year, 1–3 U per 1–2 M	17 U/year, 1–3 U per 1–2 M
2	41 years, M, HD	Epoetin beta, 2 × 5000 U/week	5.7	5.6	4.2	10 U/year, 1–2 U per 1–2 M	11 U/year, 1–2 U per 1–2 M
3	33 years, M, HD	Epoetin beta, 3 × 4000 U/week	5.1	6.2	4.5	9 U/year, 1–2 U per 2 M	8 U/year, 1–2 U per 2 M
4	43 years, F, PD	Darbepoetin alpha, 50 µg/week	5.4	5.5	4.4	13 U/year, 1–2 U per 1–2 M	12 U/year, 1–2 U per 1–2 M
5	53 years, F, PD	Darbepoetin alpha, 60 µg/week	5.6	5.3	4.5	11 U/year, 1–2 U per 2 M	11 U/year, 1–2 U per 2 M
6	65 years, F, HD	Epoetin beta, 2 × 5000 U/week	6.1	5.7	4.3	14 U/year, 1–3 U per 1–2 M	15 U/year, 1–3 U per 1–2 M
7	38 years, M, HD	Epoetin beta, 3 × 5000 U/week	5.3	5.2	4.0	12 U/year, 1–3 U per 1–2 M	12 U/year, 1–3 U per 1–2 M
8	31 years, F, Stage 4–5	Darbepoetin alpha, 40 µg/week	5.6	5.2	4.5	8 U/year, 1–2 U per 2 M	9 U/year, 1–2 U per 2 M

U, units; M, months.

<sup>1</sup>Age, gender (male/female), haemodialysis (HD), peritoneal dialysis (PD).

<sup>2</sup>Minimum haemoglobin recorded in emergency room.

and their positive effects for extending the blood transfusion intervals of such patients were previously reported in studies with only one to three patients [1–3]. In this study, the responses of eight patients with concurrent SCA and ESRD to Epo treatment were retrospectively investigated.

A total of eight patients (four males, four females; mean age, 42 ± 11.7 years) with ESRD and SCA who were followed up between May 2001 and October 2009 were studied, including one pre-dialysis (Stage 4–5), two peritoneal dialysis and five haemodialysis patients. During the study period, one patient died and one patient was transferred to another centre after renal transplantation. The data of the patients were obtained from the patient records and routine monthly dialysis recordings. Unscheduled haemoglobin measurements recorded in the emergency room during painful episodes and control haemoglobin levels measured after transfusions were recorded but not included in the calculations. The means of the haemoglobin and ferritin levels, transferrin saturation indices, blood transfusion requirements and hospitalizations were recorded before and after Epo treatment over a period of 12 months. The results of pre- and post-Epo treatment were compared using the paired *t*-test.

In four haemodialysis patients, treatment with epoetin beta had been started after blood transfusions when haemoglobin levels rose to approximately 7–8 g/dL, with a dosage of 75 U/kg/week. Despite this therapy, haemoglobin concentrations fell to 5–5.5 g/dL in 2 months. Therefore, the epoetin beta dosage was increased to and maintained at 150 U/kg/week. The other four patients were both started and maintained on Epo therapy at the upper end of the dosage range allowed for ESRD patients, according to guidelines. Haemoglobin levels of all the patients were recorded throughout the study period while they were under the maximum maintenance Epo dosage with the following results: 0.75 µg/kg/week s.c. for darbepoetin alpha (one pre-dialysis and two peritoneal dialysis patients) and 150 U/kg/week s.c. for epoetin beta (five

haemodialysis patients). No patient was receiving iron therapy and only one patient received the hydroxyurea treatment with an adjusted ESRD dose (500 mg/day) during the study period.

There was no significant difference between the means of the haemoglobin (5.6 ± 0.4 vs 5.5 ± 0.4 g/dL) and ferritin levels (>2000 vs >2000 ng/mL), transferrin saturation indices (72.6 ± 19.5 vs 76.5 ± 21.2%), numbers of hospitalizations (5.5 times per year—min. 3, max. 8 vs 6.0 times per year—min. 2, max. 9) and blood transfusion needs and rates (minimum 1–2 U/2–3 months, maximum 1–3 U/1–2 months) before and after Epo treatment. The haemoglobin levels of the patients still decreased to between 4.0 and 4.5 g/dL once or twice during the year Epo was being administered (Table 1). There was no newly developed thromboembolic event in any of the patients during Epo treatment.

Epo treatment was continued (14 ± 2.2 months) in one pre-dialysis and two peritoneal dialysis patients and was ceased in five patients due to unresponsiveness to treatment. In one of the patients in whom Epo treatment was ceased, the treatment had been administered from May 2001 to September 2006, ceased in 2006 and the patient died in 2008. The mean time of Epo treatment in the other four patients in whom Epo had been stopped due to unresponsiveness was 18 ± 6.3 months.

In this retrospective study, the unresponsiveness of Epo treatment, resulting in target haemoglobin levels not being reached in patients with concurrent SCA and ESRD, could possibly be due to the fact that the precise cause of anaemia in this patient group is not Epo insufficiency. On the other hand, since basal endogenous Epo levels in SCA patients are shown to be higher than in the normal population, the Epo requirement may also be much higher than for other ESRD patients following the development of renal failure [4].

With regard to the variable individual response to Epo treatment, until more precise data are available, with a higher number of patients with SCA and ESRD from dif-

ferent centres, it would be appropriate to attempt treatment with the maximum possible dose for a period and then to stop this expensive treatment if the expected response cannot be achieved.

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Nephrology Department, Aysegul Zumrutdal  
Adana Teaching and Research  
Center, Baskent University,  
Adana, Turkey  
Email: azumrutdal@yahoo.  
com

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### Marked improvement in renal function after rectal cancer resection in a case of anti-neutrophil cytoplasmic autoantibody-negative pauci-immune crescentic glomerulonephritis

Sir,

A small number of patients with pauci-immune crescentic glomerulonephritis (CrGN) lack circulating anti-neutrophil cytoplasmic autoantibodies (ANCA) [1], and the significance and pathogenesis of this disorder are not fully understood. A recent paper reported that ANCA-negative

pauci-immune CrGN might represent an independent disease entity, with distinctive features [2]. In contrast to the many reports describing a strong relationship between neoplasms and glomerulopathies, i.e. membranous nephropathy [3], there has been a limited number of reports documenting a possible relationship with rapidly progressive glomerulonephritis (RPGN). Serum ANCA levels also tend to be positive in such cases (Table 1).

A 59-year-old male was hospitalized because of rapid deterioration in renal function over the course of several weeks (Figure 1). Renal impairment was not evident 7 months earlier [serum creatinine (sCr), 78.8 µmol/L]. Although RPGN was indicated, neither myeloperoxidase (MPO)- nor proteinase 3 (PR3)-ANCA was detected in the serum by enzyme-linked immunosorbent assay. A non-specific assay using a commercial fluorescence detection kit also failed to detect serum ANCA. No other organ involvement was evident.

Unexpectedly, a 4-cm rectal tumour was found concurrently and pathologically diagnosed as a well-differentiated adenocarcinoma. Serum carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), cancer antigen 125 (CA125) and alpha-fetoprotein (AFP) were all negative. Because the renal function deteriorated even further (sCr, up to 289.4 µmol/L), low-dose oral steroid therapy, i.e. 20 mg/day (0.28 mg/kg/day) prednisolone, was initiated preoperatively based on the presumptive diagnosis of RPGN.

The principal finding of the biopsy, which was performed at Day 13 of the steroid therapy, was CrGN, with 70–80% of the glomeruli (total = 31 glomeruli) exhibiting fibrocellular or fibrous crescents. No immunoglobulins were detected in the glomeruli by immunofluorescent analysis.

Despite a temporary improvement in renal function after the low-dose prednisolone administration at the time of biopsy, the sCr level started to rise again (Figure 1). Steroid therapy was tapered off to reduce surgery-associated risks, followed by successful resection of the rectal cancer (pT3M0N1). The sCr level declined immediately after the surgery without further medication.

The relapse of progressive renal insufficiency prior to steroid discontinuation and its significant reversal immediately after the surgery suggest that tumour resection rather than the short-term low-dose oral steroid therapy was responsible for the improvement of renal function. Hence, the present

**Table 1.** Published cases of RPGN associated with non-renal solid malignancies

Age (years), gender	Organ	Serum ANCA	Citation
64, M	Stomach	Not mentioned	Intern Med 2008; 47: 1237
57, M	Stomach	pANCA(-)/cANCA(-) <sup>a</sup>	Gastric Cancer 2003; 6:267
60, F	Lung	pANCA(+)	Am J Kidney Dis 2000; 36: E24
64, M	Stomach	cANCA(+)	Int Urol Nephrol 1994; 26: 579
62, M	Lung	cANCA(+)	Clin Nephrol 1993; 40: 22
56, M	Prostate	cANCA(+)	Clin Nephrol 1993; 40: 22
77, M	Prostate	pANCA(+)	Clin Nephrol 1993; 40: 22
50, M	Bladder	cANCA(+)	Clin Nephrol 1993; 40: 22

pANCA, perinuclear anti-neutrophil cytoplasmic autoantibodies; cANCA, cytoplasmic anti-neutrophil cytoplasmic autoantibodies.

<sup>a</sup>The method for detection was not specifically described.