It is the same scenario for previously reported cases of hypocomplementaemic idiopathic immune complex tubulointerstitial nephritis (TBIN) that we mentioned in our case report [1,2]. In the absence of this evidence, presence or absence of IgG4 disease in reference to our case remains a speculation.

On reviewing the literature of IgG4 disease, we noted some important differences. Most of the cases of IgG4 disease have concurrent or subsequent systemic involvement [3]. On the contrary, there was no evidence of systemic or extrarenal disease in our case even after a follow-up of 18 months [1]. In the largest reported series of cases of hypocomplementaemic idiopathic immune complex TBIN by Kambham et al., there were two cases of sclerosing cholangitis which could be potentially indicative of IgG4 disease [2]. However, autoimmune pancreatitis, which is one of the most commonly reported features of IgG4 disease, was conspicuous by its absence in all the reported cases of idiopathic TBIN [1–3]. Also, no significant glomerular disease has been reported in cases of idiopathic TBIN, while membranous and membranoproliferative glomerulonephritis have been reported with IgG4 disease [1,2,4,5]. We could not find any reported case of IgG4 disease with tubulointerstitial nephritis and no extrarenal involvement. There are cases described without pancreatitis, but even they have some extrarenal involvement in terms of sialadenitis and lymphadenopathy [6].

In conclusion, it is difficult to say whether our case has IgG4 disease as etiology due to lack of IgG4 levels and tissue staining and in the light of available literature.

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1. Gupta A, Jothy S, Somerville P et al. Hypocomplementaemic immune complex tubulointerstitial nephritis. NDT Plus 2010; 3: 78–80
2. Kambham N, Markowitz GS, Tanji N et al. Idiopathic hypocomplementemic interstitial nephritis with extensive tubulointerstitial deposits. Am J Kidney Dis 2001; 37: 388–399
3. Kamisawa T, Okamoto A. IgG4-related sclerosing disease. World J Gastroenterol 2008; 14: 3948–3955
4. Hill P, Russell P, Sammartino C et al. Acute kidney injury and proteinuria in a patient with diabetes and a submandibular mass. Am J Kidney Dis 2009; 54: 375–380
5. Morimoto J, Hasegawa Y, Fukushima H et al. Membranoproliferative glomerulonephritis-like glomerular disease and concurrent tubulointerstitial nephritis complicating IgG4-related autoimmune pancreatitis. Inter Med 2009; 48: 157–162
6. Seiki T, Saito A, Yamazaki H et al. Tubulointerstitial nephritis associated with IgG4-related systemic disease. Clin Exp Nephrol 2007; 11: 168–173

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Fatal acute hepatorenal failure during antimalarial-based combination treatment

Dear Editor,

Artemisinin and its derivatives are the most rapidly acting antimalarial drugs. Randomized trials suggest that these drugs are remarkably nontoxic [1–3]. However, we report here 12 deaths occurring under an artemisinin-based combination treatment.

Between March and December 2008, a total of 46 Ivorian adult patients (78.3% of whom were men; mean age, 33 years) who received a 3-day regimen of oral artemisinin-based combination (ABC) [lumefantrine (20), amodiaquine (13), mefloquine (7), piperaquine/trimethoprim (6)] treatment for malaria were retrospectively studied (Table 1). Concomitant prescribed drugs included quinine (33) and paracetamol (16). All patients were admitted for acute hepatorenal failure under treatment (median time, 2 days), and half of them required haemodialysis (1.7 ± 2.1 sessions). The ABC treatment was withdrawn on admission for all. Twelve patients (26%, Group 1) died, and 34 patients (74%, Group 2) recovered within a median of 3 and 12 days from admission, respectively (Table 1). Comparison of variables between the treated groups was done using Student’s t-test. Of the patients alive, renal improvement was confirmed after a 3-month follow-up (mean serum creatinine 1.5 mg/dL).

The case fatality rate in severe malaria treated with either quinine or artemisinin can be expected to be 10–25% even under optimal conditions [4]. However, whether malaria and/or drug side effects are causes of acute hepatorenal failure (AHRF) in our study is unclear. Multiple antimalarial drugs, normal temperature and negative malaria blood film as well as bacteriological investigations on admission plead for an iatrogenic effect rather than a progression of the infectious illness. The mechanism underlying this severe complication remains to be established. Only the presence of coma on admission was found to be an independent risk factor of mortality in our cohort (P = 0.0006) (Table 1). The potential neurological toxicity of an artemisinin-based treatment has already been suspected in both animal and human studies. When administered daily in high doses to dogs and rats, artemether and arteether caused neuropathic lesions in the caudal brain stem [5]. In randomized clinical trials, coma associated with increased incidence of convulsions (39% vs. 28%, P = 0.01) was significantly prolonged [1,2] in the arteether group [1], indicating the need for an active investigation of the neurologic side effects of these drugs.
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.

Conflict of interest statement. None declared.

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

| Variable                                           | Death | Survivor | P |
|----------------------------------------------------|-------|----------|---|
| 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 [×10^3, mean (SD)]          | 23 860 (12 579) | 16 701 (14 736) | 0.17 |
| Platelet count [×10^3, 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.

Conflict of interest statement. None declared.

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1. van Hensbroek MB, Onyiorah E, Jaffar S et al. A trial of artesunate or quinine in children with cerebral malaria. N Engl J Med 1996; 335: 69–75
2. Hien TT, Day NPI, Phu NH et al. A controlled trial of artesunate or quinine in Vietnamese adults with severe falciparum malaria. N Engl J Med 1996; 335: 76–83
3. Karunajeewa HA, Mueller I, Senn M et al. A trial of artemether or quinine in children with cerebral malaria. N Engl J Med 1996; 335: 69–75
4. Hoffman SL. Artemether in severe malaria—still too many deaths. N Engl J Med 1996; 335: 124–126
5. Brewer TG, Peggins JO, Grate SJ et al. Neurotoxicity in animals due to arteether and artemether. Trans R Soc Trop Med Hyg 1994; 88: S33–S36
6. Brewer TG, Peggins JO, Grate SJ et al. Neurotoxicity in animals due to arteether and artemether. Trans R Soc Trop Med Hyg 1994; 88: S33–S36

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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