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# Renal Cortical Necrosis: An Unusual Complication of *Plasmodium malariae* Malaria

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## Abstract

**Renal cortical necrosis (RCN) is anecdotal in malaria. To our knowledge, RCN secondary to *Plasmodium malariae* has not yet been published. We report a case of severe malaria complicated by RCN. A 29 year old Senegalese patient was transferred to our department for anuria in a context of severe malaria. The diagnosis was RCN secondary to a severe *Plasmodium malariae* malaria. Physical examination showed anuria, anaemic syndrome, haemorrhagic syndrome and a generally impaired condition. There was a normocytic normochromic anaemia aplastic, thrombocytopenia leukocytosis of 11.580/mm$^3$, serum creatinine of 12.45 mg/dl and blood urea of 252 mg/dl. The *Plasmodium malariae* had been shown to thick blood film with high parasite density. The molecular study was able to confirm the infestation of this parasite. Treatment consisted of four haemodialysis sessions and antimalarial molecules. Initial evolution was favourable with a recovery through diuresis and a partial improvement in renal function. Given the persistence of impaired renal function, a renal biopsy was performed. This confirmed the RCN. At last consultation, he had no symptoms and his last glomerular filtration rate (GFR) was 30 mL/min/1.73 m$^2$.**

## Keywords

**Renal Cortical Necrosis, *Plasmodium malariae*, Acute Kidney Injury, Malaria**

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## 1. Introduction

Malaria is a major public health problem with significant morbidity and mortality in sub-Saharan Africa [1]. Life-threatening malaria is mainly determined by visceral effects including kidney damage [1]. These lesions are varied, including renal cortical necrosis (RCN), although this remains anecdotal. Several cases of RCN secondary to infestation by *Plasmodium falciparum* and *Plasmodium vivax* have been published. To our knowledge, RCN secondary to *Plasmodium malariae* (*PM*) has not been published. We propose to present the case of a patient who presents severe malaria with *PM* complicated by kidney failure as RCN.

## 2. Case Report

Mr. D.S., a 29 year old Senegalese patient, was transferred on 09/11/2012 to the Department of Nephrology at Aristide Le Dantec University Hospital in Dakar, for the management of persistent anuria in a context of severe malaria.

He suddenly complained on November 2nd, 2012 of intense and permanent headaches and profuse bilious vomit. This was followed a few hours later by polyarthralgia and intense myalgia. He felt worse on the night of 06 to 07/11/2012 with the appearance of high fever and profuse sweating. He had been prescribed an oral anti-malarial treatment (based on an Artemisinin derivative) at a local health clinic. Generalised tonic-clonic seizures and persistent fever had caused his transfer to the Department of Infectious Diseases at Fann University Hospital Centre where he stayed three days. A gradual break in his diuresis appeared, progressing to persistent anuria which led to a transfer to the Department of Nephrology at the Aristide Le Dantec University Hospital.

At admission, the patient was conscious. He was afebrile. He had a pulse rate of 102/min, respiratory rate of 19/min and his blood pressure was 130/90 mm Hg. Physical examination revealed a total lack of diuresis, bilateral and symmetrical oedema of the lower limbs, anaemic syndrome, haemorrhagic syndrome with bilateral epistaxis and gingival bleeding, and ascites of moderate abundance.

Biological investigations at admission revealed: anaemia normochromic normocytic hypoplastic with haemoglobin at 7.8 g/dl, thrombocytopenia 72,000/mm$^3$, leukocytosis 11,580/mm$^3$, creatinine 12.45 mg/dl, blood urea 252 mg/dl, serum calcium 8.2 mg/dl and hyperphosphatemia 9.67 mg/dl. In blood electrolytes, sodium was 127 mmol/l, potassium 4.5 mmol/l. Transaminases were normal with SGOT 21.6 IU/l, and SGPT 26.9 UI/l. blood sugar was 90 g/dl. CRP was 9.6 mg/dl (**Table 1**).

On the third day after his admission, investigation of urine revealed that 24 h urine volume was 400 ml, urine protein 0.04 g/day, leukocytes 5208/min and erythrocytes 3472/min.

**Table 1.** Showing laboratory values.

| Laboratory parameter | Laboratory result | Normal range |
|---|---|---|
| Hemoglobin (g/dl) | 7.8 | 12 - 16 |
| Total leucocytes count (/mm$^3$) | 11,580 | 4000 - 10,000 |
| Platelet count (/mm$^3$) | 72,000 | 150 - 350,000 |
| Blood urea (mg/dl) | 252 | 15 - 45 |
| Serum creatinine (mg/dl) | 12.45 | 0.6 - 1.2 |
| Serum sodium (mmol/l) | 127 | 135 - 145 |
| Serum potassium (mmol/l) | 4.5 | 3.5 - 5.5 |
| SGPT* (U/l) | 26.9 | 5 - 35 |
| SGOT* (U/l) | 21.6 | 5 - 40 |
| Blood sugar (g/dl) | 90 | 70 - 110 |
| Serum calcium (mg/dl) | 8.5 | 8.5 - 10.5 |
| Serum phosphorus (mg/dl) | 9.67 | 2.5 - 4.5 |
| Parasitemia load (trophozoites/µl) | 18,402 | 0 |

*SGOT: serum glutamic-oxaloacetic transaminase; *SGPT: serum glutamic-pyruvic transaminase.

The *Plasmodium malariae* was highlighted in the thick coloured drop by 10% of Giemsa. This led to the identification of the trophozoites, schizonts and gametocytes of *P. malariae* (**Figure 1**). Molecular diagnostics, based on the amplification of ribosomal gene 18S, had identified a band at 144 bases pair confirming infection with *P. malariae* (**Figure 2**). The parasitemia load was 18,402 trophozoites/µl.

An abdominal ultrasound showed normal sized kidneys with poor cortico-medullary differentiation.

Treatment consisted of: parenteral quinine salt at 250 mg three times daily for five days followed by a relay with oral association Artemether-Lumefantrine, furosemide at a dose of 250 mg/day on Day 1 and 500 mg/day on Day 2 and 3 to stimulate diuresis and fluid restriction.

A worsening of renal impairment (serum creatinine at 16.62 mg/dl, blood urea to 313 mg/dl and hyperkalemia 6.4 mmol/l) occurred on the fourth day of hospitalization. Renal replacement therapy was therefore indicated. In total, the patient received four sessions of haemodialysis. Secondarily, evolution during hospitalisation was favourable with a recovery of diuresis to 2 litres per day, a partial improvement of renal function (creatinine decreased from 12.7 mg/dl on 20/11/2012 at 3.45 mg/dl on 02/12/2013) and a normalisation of the platelets count. Normocytic normochromic anaemia persisted to 9.9 g/dl, however.

Given the persistence of impaired renal function, renal biopsy was realised and showed an abundant and mutilating band of interstitial fibrosis encompassing destroyed glomeruli (**Figure 3**). This fibrosis band around areas of parenchyma preserved tubular atrophy (**Figure 4**) and 80% of nephron reduction, a secondary segmental

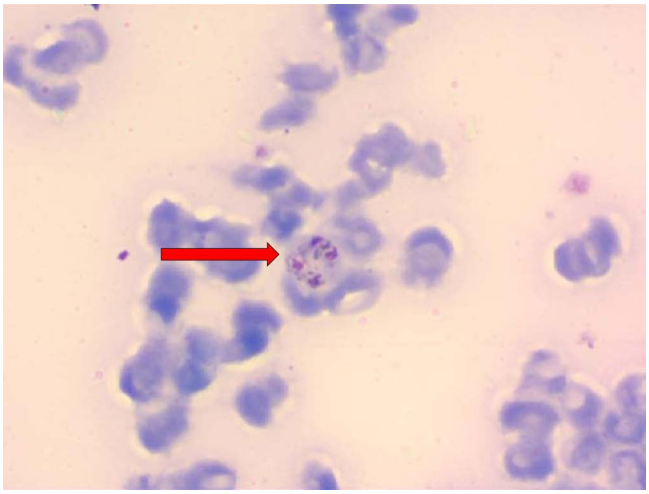

**Figure 1.** Giemsa-stained thin smear of patient'speripheral blood: Trophozoites of *Plasmodium malariae* "Basket-form"(arrow) × 1000.

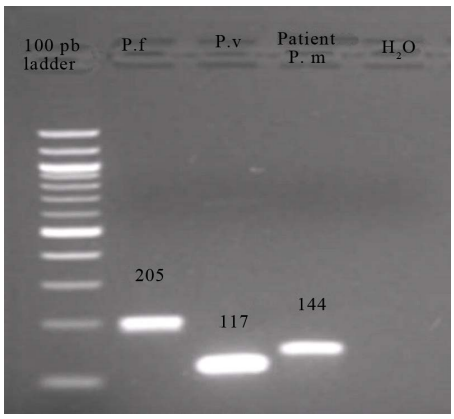


**Figure 2.** Confirmation of *Plasmodium malariae* by molecular biology. *P.v*: *Plasmodium vivax*, *P.f*: *Plasmodium falciparum*, *P.m*: *Plasmodium malariae*.

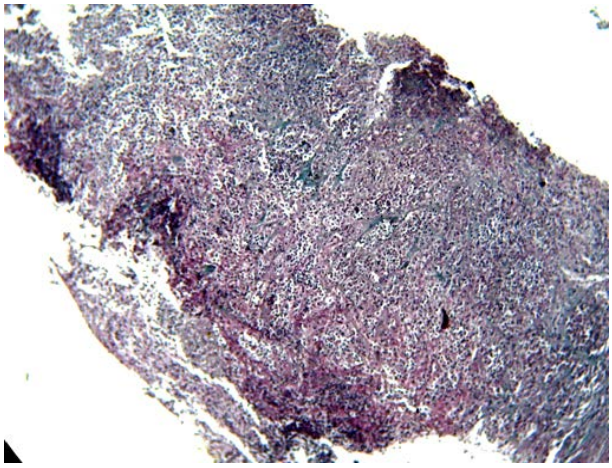

**Figure 3.** Zone of total necrosis of the renal parenchyma. Masson Trichrome × 200.

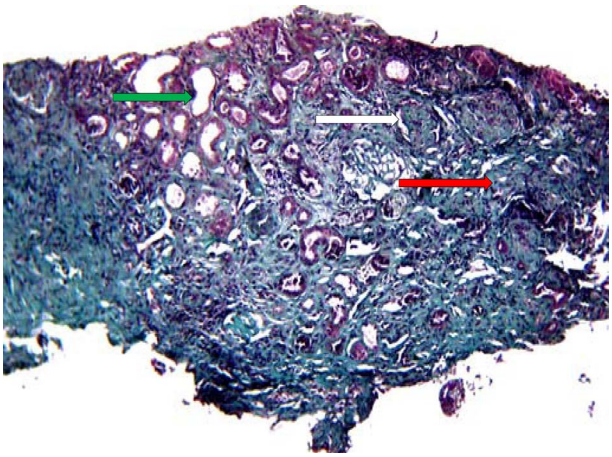

**Figure 4.** Area of diffuse inter stitial fibrosis (red arrow) tubularatrophy (green arrow) and glomerulosclerosis (white arrow). Masson Trichrome × 200.

lesions glomerulosclerosis according to 30% of residual glomeruli. This element was in favour of subtotal cortical necrosis. The patient is currently monitored as a nephrology outpatient. At his last check up, he had a good general condition and his GFR was 30 mL/min/1.73 $m^2$.

## 3. Discussion

Post-malaria renal failure occurs in the context of severe malaria [2]. In developing countries, the incidence of acute kidney injury (AKI) in malaria is not known, but in hospital studies, it ranges from 6% to 30.4% of cases [3] [4].

Acute tubulointerstitial nephropathy is the most common complication [5], however, cortical necrosis is exceptional and prognosis is especially bad in its complete form [3] [5]-[7]. To our knowledge, this clinical case remains the first RCN post-malaria *Plasmodium malariae* reported in sub-Saharan Africa and the world.

RCN is a rare clinicopathological AKI form. It consists of a bilateral ischemic necrosis, symmetrical, "patchy" diffuse to renal cortex, sparing the renal medulla and a thin strip of subscapular cortex [8]. The prognosis of RCN is often pejorative, requiring the use of chronic haemodialysis, apart from cases where segmental renal cortical necrosis and delayed partial recovery can be observed.

RCN post-malaria remains unusual. To our knowledge, four cases have been reported [3] [6] [7] [9]. The first two cases involved the RCN post *Plasmodium falciparum* [3] [7]. The third and fourth cases, published in 2012

and 2014, dealt with *Plasmodium vivax* RCN [6] [9].

RCN in malaria can be explained by four main phenomena: massive intravascular haemolysis causing haemoglobinuria; dehydration and hypovolemia secondary to fever, with profuse sweating, a lack of water intake and digestive disorders resulting in renal hypoperfusion, also cytoadherence and erythrocyte sequestration with intravascular coagulation, head of hypoperfusion, and monocyte activation with release of free radicals. The first two mechanisms were excluded in our patient because there was no clinicobiological evidence for a massive intravascular haemolysis or severe hypovolemia. In our case, the RCN could have been due to cytoadherence and erythrocyte sequestration with intravascular and/or coagulation monocyte activation with the release of free radicals [2].

Clinically, the patient had persistent anuria. In RCN, the main symptom for Chugh and Kleinknecht [10] [11] was anuria that was almost constant. The patient had clinical anaemia on admission. On CBC (count blood cells), this anaemia was normochromic normocytic hypoplastic (reticulocyte count in 5680/mm$^3$) with 7.8 g/dl of haemoglobin. The aplastic anaemia could be explained by dyserythropoiesis. The increase in inflammatory cytokines TH1 has effects on bone marrow, inducing cell hyperplasia and dyserythropoiesis, resulting in a slowing in production of reticulocytes, and anaemia. Some authors believe that the effect of cytokines alone cannot explain the significant morphological changes observed in the spinal cord and suggest that this is a direct effect of haemozoin [12]. Haemorrhagic disease in our patient could be explained by the DIC (disseminated intravascular coagulation). This haemorrhagic syndrome may be missing. Indeed, disorders of haemostasis occur, and about half the time, only by a biological syndrome [13].

In the imaging plane, only renal ultrasonography was performed in our patient. It objectified normal size of kidneys with poor cortico-medullary differentiation. The same result was reported in the observation of Baliga and Singhal [3] [7].

The hypothesis of RCN was raised after unfavourable evolution after three weeks of renal function. Confirmation was made by renal biopsy, although this is not necessary for retaining the diagnosis of RCN. Other paraclinical investigations such as renal Doppler, “microbubble” ultrasound or ultrasound contrast, abdomen and pelvis scan or renal MAG3 scintigraphy [14] may be sufficient.

Our patient had the “patchy” form with striped lesions peppered with normal parenchyma. In all four cases published in the literature, the type of RCN has not been clarified [3] [6] [7] [9]. Our patient also had tubulointerstitial lesions as interstitial fibrosis, and tubular atrophy with a case of tubular ghosts. These lesions were also identified in three of the reported cases of RCN post-malaria [3] [6] [7] [9].

In addition to the lesions described above, this patient had an 80% reduction in nephron lesions, with 30% segmental focal glomerulosclerosis in residual glomeruli. This “secondary” SFG is the result of secondary podocytes lesions, demonstrations of functional adaptation and/or structural. RCN is one of its causes.

*Plasmodium malariae*, which was responsible for RCN in our case, has never been implicated in RCN. Only *Plasmodium falciparum* and *vivax* have been reported so far [3] [6] [7] [9].

Our patient recovered partial renal function. After 18 months of follow-up, he had normal diuresis and stable renal function with a GFR 30 ml/min/1.73 m$^2$ according to MDRD formula. Of the three cases published on RCN post-malaria, one remained on dialysis [7]; change was not reported for the second case [3], and the third and fourth cases partially recovered and were released from dialysis [6] [9]. Cortical necrosis in our patient was associated with subtotal tubular damage may explain the early anuria, the recovery of diuresis and improvement in renal function.

## 4. Conclusion

Our case report demonstrates that *Plasmodium malariae* malaria may cause RCN, similar to other forms secondary to *Plasmodium vivax* and *Plasmodium Falciparum.*

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## Conflit of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

## References


[1] White, N.J., Pukrittayakamee, S., Hien, T.T., Faiz, M.A., *et al.* (2014) Malaria. *The Lancet*, **383**, 723-735. http://dx.doi.org/10.1016/S0140-6736(13)60024-0

[2] Mishra, S.K. and Das, B.S. (2008) Malaria and Acute Kidney Injury. *Seminars in Nephrology*, **28**, 395-408. http://dx.doi.org/10.1016/j.semnephrol.2008.04.007

[3] Baliga, K.V., Narula, A.S., Khanduja, R., Manrai, M., Sharma, P. and Mani, N.S. (2008) Acute Cortical Necrosis in Falciparum Malaria: An Unusual Manifestation. *Renal Failure*, **30**, 461-463. http://dx.doi.org/10.1080/08860220801964293

[4] Kunuanunua, T.S., Nsibu, C.N., Gini-Ehungu, J.-L., Bodi, J.M., Ekulu, P.M., *et al.* (2013) Acute Renal Failure and Severe Malaria in Congolese Children Living in Kinshasa, Democratic Republic of Congo. *Néphrologie & Thérapeutique*, **9**, 160-165. http://dx.doi.org/10.1016/j.nephro.2013.01.001

[5] Brocherion, I. and Ferlicot, S. (2008) Glomérulonéphrite et infections parasitaires. In: Noel, L.-H., Ed., *Atlas de Pathologie Rénale*, Flammarion, Paris, 261-283.

[6] Kute, V.B., Vanikar, A.V., Ghuge, P.P., Patel, M.P., Patel, H.V., *et al.* (2012) Renal Cortical Necrosis and Acute Kidney Injury Associated with *Plasmodium vivax*: A Neglected Human Malaria Parasite. *Parasitology Research*, **111**, 2213-2216. http://dx.doi.org/10.1007/s00436-012-2975-x

[7] Singhal, M.K., Arora, P., Kher, V., Pandey, R., Gulati, S., *et al.* (1997) Acute Cortical Necrosis in Falciparum Malaria: An Unusual Cause of End-Stagerenal Disease. *Renal Failure*, **19**, 491-494. http://dx.doi.org/10.3109/08860229709047736

[8] Laurer, D.P. and Schreiner, G.E. (1958) Bilateral Renal Cortical Necrosis. *American Journal of Medicine*, **24**, 519-529. http://dx.doi.org/10.1016/0002-9343(58)90292-4

[9] Kumar, R., Bansal, N., Jhorawat, R., Kimmatkar, P.D. and Malhotra, V. (2014) Renal Cortical Necrosis: A Rare Complication of *Plasmodium vivax* Malaria. *Indian Journal of Nephrology*, **24**, 390-393. http://dx.doi.org/10.4103/0971-4065.133789

[10] Hiault, C., Dequiedt, P., Benoit, O., *et al.* (1982) Post Partumrenal Cortical Necrosis. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction*, **11**, 839-848.

[11] Kleinknecht, D., Grünfeld, J.P., Gomez, P.C., Moreau, J.-F. and Garcia-Torres, R. (1973) Diagnostic Procedures and Long-Term Prognosis in Bilateral Renal Cortical Necrosis. *Kidney International*, **4**, 390-400. http://dx.doi.org/10.1038/ki.1973.135

[12] Mohandas, N. and An, X. (2012) Malaria and Human Red Blood Cells. *Medical Microbiology and Immunology*, **4**, 593-598. http://dx.doi.org/10.1007/s00430-012-0272-z

[13] Levi, M. (2009) Guidelines for the Diagnosis and Management of Disseminated Intravascular Coagulation. *British Journal of Haematology*, **145**, 24-33. http://dx.doi.org/10.1111/j.1365-2141.2009.07600.x

[14] Pruijm, M., Ponte, B., Hofmann, L., *et al.* (2011) New Radiological Techniques to Investigate Patients Suffering from Chronic Kidney Disease. *Revue Médicale Suisse*, **7**, 505-509.