**Post-splenectomy acute glomerulonephritis due to a chronic infection with Plasmodium falciparum and malariae.**

Daniel Camprubí[1]*, Leire Balerdi[2], Luis F. Quintana[3], Alex Almuedo-Riera[1,4], M.Eugenia Valls[5], Adriana García-Herrera[6], Natalia Rodriguez-Valero[1], Miriam J. Alvarez-Martínez[1,5], Jose Muñoz[1].

(1) ISGlobal, Hospital Clínic – Universitat de Barcelona, Barcelona, Spain.

(2) Internal Medicine Department, Hospital Universitario Araba, Vitoria-Gasteiz, Spain.

(3) Nephrology and Renal Transplantation Department, Centro de Referencia en Enfermedad Glomerular Compleja del Sistema Nacional de Salud (CSUR), Hospital Clínic-Universitat de Barcelona, Spain.

(4) Internal Medicine Department, Hospital General Granollers, Barcelona, Spain.

(5) Microbiology Department, Hospital Clínic de Barcelona, Spain.

(6) Pathology Department, Hospital Clínic de Barcelona, Spain.

*__Corresponding author__: Daniel Camprubí, e-mail: dcamprub@clinic.cat , telephone number: +34 666 40 20 56, c/ Roselló 132. 08036. Barcelona, Spain. ISGlobal – Hospital Clínic Barcelona.

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A 38-year-old Senegalese man with no travel history for the last 2 years presented with fever and acute kidney injury with nephrotic syndrome after an elective splenectomy. Diagnosis of membranoproliferative glomerulonephritis due to a chronic mixed *Plasmodium* infection triggered by splenectomy in a patient with hyperreactive malarial splenomegaly was confirmed.

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A 38-year-old Senegalese man with no previous medical history and living in Spain since 2004 was admitted due to fever, hypotension and edemas. The patient had not travelled to malaria endemic areas for the last 2 years, and 43 days before this episode he underwent an elective splenectomy in order to rule out a hematologic neoplasm due to a 27 cm splenomegaly and pancytopenia.

Six weeks after surgery, he presented with fever being diagnosed with severe malaria (due to renal failure and metabolic acidosis). Blood smear revealed a 1.5% parasite density of *Plasmodium falciparum* and possible forms compatible with *Plasmodium malariae*, although PCR only confirmed *P. falciparum* infection. Four doses of 2.4 mg/kg endovenous artesunate were

followed by a 3-day course of 320/40 mg oral dihydroartemisinin/piperaquine. Three days after treatment initiation, blood smear was negative.

Despite the good parasitological response, the patient presented progressive ascites and generalized edemas. On the one hand, laboratory tests revealed elevation of C-reactive protein up to 253 mg/l (normal range: <10mg/l), acute kidney injury (AKI) stage 3 with creatinine levels up to 291.2 µmol/l (normal range: 73-107 µmol/l) and 18 ml/min/1.73m$^2$ glomerular filtration rate (normal range: >60 ml/min/1.73m$^2$), non-anion gap metabolic acidosis, hypertriglyceridemia of 4.16 mmol/l (normal range: 0.45-1.71 mmol/l) and proteinuria of 4200 mg/day (normal range: <150 mg/day). On the other hand, polyclonal hypergammaglobulinemia of 40.9% (normal range: 11.1-18.8%) with 29 g/l IgM (normal range: 0.36-2.61 g/l), high antimalarial antibody titers (1/200) and a histological revision of the spleen supported the diagnostic suspicion of hyperreactive malarial splenomegaly (HMS).

For the nephrotic syndrome and the AKI rapid progression, a kidney biopsy was performed, showing a membranoproliferative glomerulonephritis (MPGN) with IgM and C3 immunocomplex (IC) deposits, in addition to acute tubular necrosis (ATN) changes (Figure1). Other causes of MPGN such as common infections, autoimmune and lymphoproliferative disorders were ruled out. Angiotensin II receptor blocker (losartan 25mg/12hours) and corticosteroid treatment at 1mg/kg was then started (and then tapered by 10mg/day every two weeks). Finally, PCR performed on spleen and kidney tissues resulted positive both for *P. falciparum* and *P. malariae*. Diagnosis of MPGN by IC due to a chronic mixed *Plasmodium* infection triggered by splenectomy in a patient with HMS then was confirmed.

Although proteinuria persisted after 2 months after diagnosis, the patient presented progressive clinical improvement with normalization of creatinine levels after one month.

Kidney involvement in *Plasmodium* infections is well established. Classically, two different nephrological syndromes have been described in association with malaria (1). On the one hand, AKI due to ATN has been closely associated with acute *P. falciparum* infections, and it has been defined as a malaria severity criteria by the WHO (2). On the other hand, the progressive glomerulonephritis due to IC deposition - classically described as quartan malarial nephropathy -, has been more associated with subacute and chronic *P. malariae* infections (1). Interestingly, in our patient both syndromes were found.

Another learning point of the case is the role of the spleen in controlling malaria in semi-immune patients. Although *P. falciparum* malaria is usually considered an acute life-threatening infection, "asymptomatic" chronic infections have been well characterized, especially in semi-immune patients with high previous exposure to the infection (3). In some cases, the repetitive *Plasmodium* antigenic stimulus leads to an excessive enlargement and hyperactivity of the spleen, known as HMS (4). A few cases of acute *Plasmodium* infection triggered by elective splenectomy in patients with HMS have been previously reported (5). In fact, elective splenectomy for splenomegaly of uncertain origin is relatively contraindicated in individuals who may have undiagnosed chronic malaria infection with unsuspected HMS. Physicians must be aware of this entity in order to avoid iatrogenia derived from unneeded splenectomies (4).

Finally, our case highlights the complexity of kidney and spleen involvement in *Plasmodium* infections as well as the importance of an expert multidisciplinary approach.

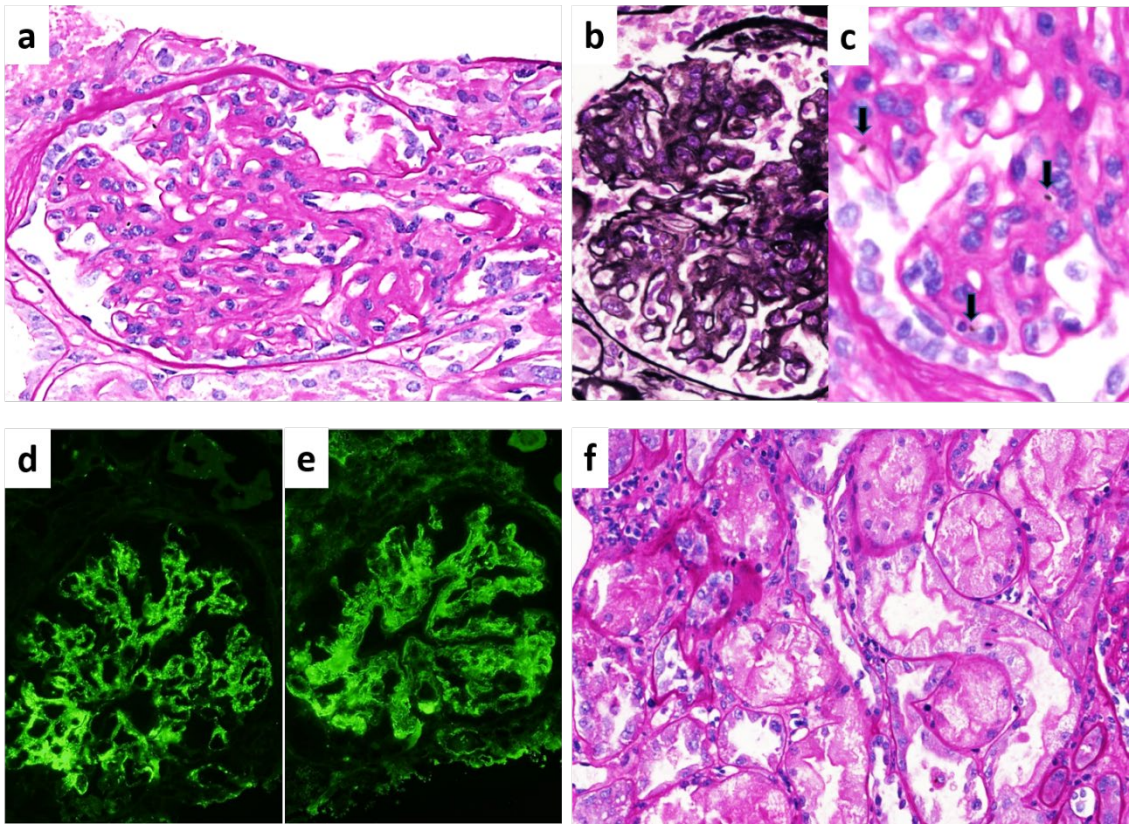


**Figure 1.** (a-b) Kidney biopsy shows membranoproliferative glomerulonephritis (PAS and silver stain 40x) (c) with malarial pigment (black arrow. PAS 60x). Immunofluorescence shows (d) C3 and (e) IgM in the mesangium and along capillary walls. (f) In addition, acute tubular necrosis is manifested in tubules by the lack of the brush border, vacuolated and detached epithelium (PAS 40x).

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