Who "SIADH" Malaria Doesn't Cause Hyponatremia?

According to World Health Organization (WHO), patients with untreated severe malaria have a mortality rate near 100% which decreases to approximately 10-20% with appropriate treatment. The risk is greater in patients who have more complications due to malaria. Hyponatremia is a well-known complication of severe malaria; however, this electrolyte imbalance has been studied mostly in children in endemic regions and is thought to be secondary to dehydration and renal impairment. The impact and physiology of persistent hyponatremia in the presence of severe *Plasmodium falciparum* infection in an adult patient with normal kidney function and adequate hydration has not been extensively studied.

Patient is a 65-year-old female with a past medical history of type II diabetes on insulin presenting with acute mental status changes, generalized weakness, and cyclical fevers starting one week after arrival to the US from Nigeria. Patient is a resident of Nigeria, however, was in the UK and now is visiting the US. The vitals at presentation were notable for a temperature of 39.4 °C (103 °F) and blood pressure of 159/67 mmHg. Initial workup revealed pancytopenia (white blood count of 3.7 K/uL, hemoglobin of 9.7 g/dL and platelets of 36 K/uL), hyperglycemia with blood glucose of 239 mg/dL, hyponatremia with sodium of 125 mmol/L, BUN 11 mg/dL, and venous lactate of 3.20 mmol/L. On admission, she was resuscitated with isotonic fluids with initial improvement of her sodium to 130 mmol/L given her sepsis presentation. Imaging including CT of the brain, chest, abdomen, and pelvis were unremarkable. Lumbar puncture was negative for parasites and did not suggest bacterial or viral meningitis. The presenting creatinine was 0.79 mg/dL and urinalysis showed moderate ketones and 1+ protein. Infectious workup was significant for *Plasmodium falciparum* detected on parasite examination with 9.8% parasite load and she was diagnosed with severe *Plasmodium falciparum* infection. Treatment with artesunate and supportive care led to clinical improvement including resolution of encephalopathy, pancytopenia, and fevers. After therapy, the parasite load dropped to being undetectable. Despite initial improvement of sodium to 130 mmol/L with adequate isotonic fluid resuscitation, her hyponatremia worsened to 126 mmol/L. Urine studies showed serum osmolality of 268 mosm/kg, urine osmolality of 276 mosm/kg H_2O, and urine sodium of 57 mmol/L consistent with syndrome of inappropriate ADH (SIADH) pathophysiology. After a period of fluid restriction and ongoing treatment of malaria, the patient's sodium improved to 132 mmol/L.

It is important to highlight SIADH as an etiology of persistent hyponatremia in malaria patients since, on initial presentation, their clinical picture may suggest hypovolemia as the primary etiology. Failure to recognize hyponatremia from SIADH may lead to excessive fluid resuscitation and worsening of the hyponatremia, The pathophysiology of SIADH in malaria is poorly understood. Of note, sodium levels of $\leq$126 mEq/L, can be a mortality predictor in cases of severe malaria. Further studies to understand the prevalence of SIADH in severe malaria infections may be beneficial to avoid additional complications associated with severe hyponatremia.