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Post-malaria neurological syndrome: report of 3 cases from a Portuguese malaria reference centre

André Silva-Pinto¹, Andreia Costa², Joana Alves¹, Nélia Neves Silva³, Pedro Miguel Paredes Abreu², Cândida Abreu³, Lurdes Santos^{*1}, António Sarmiento¹

¹*Centro Hospitalar São João; Infectious Diseases*

²*Centro Hospitalar São João; Faculdade de Medicina Da Universidade Do Porto; Neurology*

³*Centro Hospitalar São João*

Background: Post-malaria neurological syndrome (PMNS) is rare (only 38 cases reported in the literature). It occurs after recovery from malaria (mainly a severe *P. falciparum* malaria) probably due to crossed immunoreactivity. The clinical picture is mainly characterized by confusion and behaviour dysfunction, but also higher nervous functions impairment and focal neurological deficits. The treatment is controversial since it has normally benign evolution. However, in severe cases corticotherapy can be necessary.

Material/methods: We performed a retrospective study of patients with PMNS. We searched on our Department's database for cases of neurological deterioration after a malaria recovery.

Results: From 248 patients hospitalized with malaria in our Department between 2004 and 2016, we found 3 patients with PMNS. The patients' characterization is shown in table below. All patients had a history of *P. falciparum* malaria with high parasitemia treated with intravenous quinine dihydrochloride and doxycycline. Eleven days after the malaria treatment, they began neuropsychiatric symptoms. The cerebrospinal fluid showed lymphocytic pleocytosis with hyperproteinorrachia and the brain MRI showed abnormalities in two patients. An extensive workout to find an infectious cause was performed in all patients. Two patients need corticosteroids and in all of them a clinical improvement was progressively observed.

Conclusions: We report 3 cases of PMNS pretending to call the attention and add the knowledge about the clinical manifestations, laboratory and imaging findings as well as treatment and prognosis of this rare and not completely understood entity.

	Case 1	Case 2	Case 3
Diagnosis date(mm/yy)	09/2004	01/2016	10/2016
Age (years)	38	45	57
Gender	Male	Male	Male
Malaria characterization			
Acquisition localization	Angola	Ivory Coast	Angola
<i>Plasmodium spp.</i>	<i>P. falciparum</i>	<i>P. falciparum</i>	<i>P. falciparum</i>
Parasitemia (%)	70	25	8
WHO severity criteria	Hyperparasitemia; impaired consciousness; renal impairment.	Hyperparasitemia; impaired consciousness; jaundice; pulmonary oedema; shock.	None
Malaria treatment	Quinine / doxycycline	Quinine / doxycycline	Quinine / doxycycline
Post-malaria neurological syndrome			
Elapsed time since end of malaria treatment (days)	11	11	11
Clinical picture	Headache, behaviour impairment, myoclonic jerks	Fever, behaviour impairment, visual hallucinations and myoclonic jerks	Fever, behaviour impairment, circadian rhythm disruption and myoclonic jerks
Neurological examination	Decreased consciousness, ataxic gait	Decreased consciousness, working memory deficit.	Inattention, mental identification, working memory deficit, visualconstruction inability
Lumbar puncture			
Cells (ug/L)	75 (> mononuclear)	99 (> mononuclear)	159 (> mononuclear)
Proteins (g/L)	1.14	2.09	2.12
Glucose (% CSF/serum)	60	70	60
Brain MRI (T2/T2FLAIR)	Periventricular, lenticular, thalamic and pons hypersignal	No abnormalities	Bilateral mild caudadolenticulocapsular hypersignal
Electroencephalography	Not available	Global lentification	Severe subcortical diffuse dysfunction
Treatment	Methylprednisolone 1g/day, 3 days	No specific treatment	Methylprednisolone 1g/day, 5 days
Clinical evolution	Gradual improvement Recovery to normal status ten months later	Gradual improvement Mild cognitive dysfunction after six months	Fast improvement Persistence of slight attention deficit.

Table