A PARASITE’S HERITAGE: PERSONALITY CHANGES AFTER MALARIA

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INTRODUCTION

Malaria remains the most prevalent parasitic disease in the world. In 2018, the WHO reported 219 million cases of malaria occurring worldwide.¹ Detailed reports in the literature described a set of **neuropsychiatric complications emerging in patients following treatment and resolution** of acute malaria infection, that were attributed to both severe and mild forms of the disease² and that range from a reversible post-malaria neurological syndrome to permanent deficits³. Yet similarly, **anti-malarial drugs**, particularly mefloquine and quinine, have also been associated with acute and potentially chronic psychiatric adverse effects, therefore creating a confounding role in the attribution of the psychiatric sequelae.^{2,4}

	Psychiatric sequelae attributed to malaria in the literature ^{2,4,5}
Consciousness	Dream-like states.
Personality	Lasting changes in personality.
Behaviour	Impairment in executive functioning, inappropriate speech and behaviour, aggressiveness, impulsiveness, agitation, self-injurious and destructive behaviours.
Orientation	Temporospatial disorientation.
Attention	Difficulties with concentration.
Memory	Forgetfulness, word-finding difficulty, anterograde amnesia, transient amnesia, impairments in working memory and verbal learning.
Speech and Language	Aphasia, acalculia, impairments in pragmatics (use of language), receptive and expressive speech, vocabulary and phonology.
Thought	Confusion, impairment in abstract reasoning, persecutory delusions, grandiose delusions.
Perception	Transient psychosis with visual hallucinations.
Mood	Mania, irritability, anxiety and depressive symptoms.
Neurovegetative	Insomnia, anorexia.
Neurologic complications	Headache, epilepsy (generalized tonic clonic seizures; focal seizures, with or without secondary generalization; subtle or purely electrographic seizures), motor disorders (cerebellar ataxia, fine postural tremors, hemiparesis) and visual disorders.

CASE REPORT

Identification

- 43-year-old male, flight attendant, with no past psychiatric follow up.

Acute severe malaria (2012)

- Diagnosed with a mixed *P. falciparum* and *P. ovale* infection, following his work trip to Equatorial Guinea with no malaria prophylaxis.
- He completed 12 days of IV quinine and doxycycline, followed by 14 days of oral primaquine (to prevent *P. ovale* relapse).
- Plasmodium antigen was negative 2 months after hospital discharge.

Psychiatric Symptoms following successful malaria treatment

- Personality changes: he gets easily irritated, verbally aggressive and he became very obsessive, organizing everything by colour.
- Anxiety, irritability and aerophobia.
- Nocturnal agitation and insomnia or poor-quality sleep.
- Fluctuations in appetite and weight, from hyperfagia to anorexia.
- Lack of concentration, forgetfulness and word-finding difficulties.
- Frequent headache, and dizziness.
- Episodes described as “absences” during work flights (2013), with lapses in awareness and transient amnesia, along with diaphoresis and palpitations.

Observation (2018)

- The neurological examination revealed no changes.
- At his first psychiatric observation, he presented with motor unrest, distractibility, short-term memory disturbances with poor recall memory, phobic content of thought, and anxious mood.

Tests

- Blood tests, brain MRI, CT-scan and EEG were all normal.
- Malaria recurrence was excluded by the absence of parasitaemia.

Clinical Follow-up (2018-2019)

- 4 months**
 - Sertraline 50mg at breakfast + Mexazolam 1mg at breakfast (+SOS, if needed) + Clonazepam 0,5mg at bedtime.
 - He noticed some improvements in short-term memory and only a slight improvement in his mood.
- 1 month**
 - Sertraline 100mg + Risperidone 1mg 3x/day + Quetiapine 100mg at bedtime.
 - He said he felt overall better and less irritated.
 - However, he described having nightmares that caused him to wake up terrified in the middle of the night.
 - At observation, he was more restless and anxious compared to previous appointments.
- He is still waiting for the neuropsychological evaluation and psychology consultation.

DISCUSSION

We may consider the following diagnostic hypotheses:

- Chronic malaria sequelae** – The patient presents with psychiatric effects attributed in the literature to a past history of malaria, as we can see highlighted in the table shown.
- Anti-malarial drugs side-effects** – Doxycycline and primaquine rarely produce psychiatric effects, but there are reports of amnesia following treatment with primaquine, and insomnia, nightmares and anxiety after treatment with doxycycline. Quinine is much more frequently associated with psychiatric side-effects, including irritability and personality changes.
- Post-malaria neurological syndrome** – Some symptoms are observed, such as behavioural abnormalities, headache, dizziness, drowsiness and, maybe, seizures. However, this is a predominantly self-limited disorder (~13 days) and the EEG is usually abnormal.

CONCLUSIONS

Despite the temporal relation, we couldn’t find a definitive causal relation between malaria and this case. The diagnosis is not easy in the absence of encephalopathy EEG signs. Nevertheless, it should be considered in this case, even knowing that there are other possible diagnosis. There is still a need for more studies on the psychiatric complications following malaria, especially concerning the long-term sequelae and the pathophysiological mechanisms involved.

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