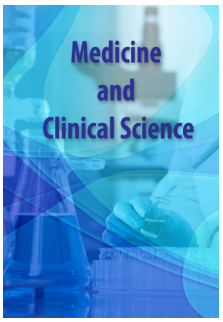
Medicine & Clinical Science

Case Report



Post Malaria Neurological Syndrome: Unknown, Underestimated, or Underdiagnosed? First Report Done in Gambia

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Abstract

Post-malaria neurological syndrome (PMNS) is a rare self-limiting neurological complication that can occur after recovery from malaria, usually severe falciparum malaria. It is characterized by a myriad of neuropsychiatric manifestations including mild neurological deficit to severe encephalopathy. PMNS is a debated entity, is a rare complication of severe malaria that might be underreported. It can develop up to 2 months after clearance of parasitemia. Clinical features can be variable. Most cases are self-limited, but more severe cases may benefit from steroid therapy. There are several neurological syndromes that can occur following complete recovery from malaria, in particular Plasmodium falciparum. These PMNS include, delayed cerebellar ataxia (DCA), acute inflammatory demyelinating polyneuropathy (AIDP) and acute disseminated encephalomyelitis (ADEM). In 2021 according to WHO report, the African region was home to 95% of all malaria cases and 96% of deaths. Paradoxically, reports of post malaria neurological syndrome in west Africa sub region are practically null, it is not clear if it is due to lack of knowledge regarding the disease, underdiagnosis or combination of factors, the first case of post malaria neurological syndrome in Gambia is described below. The objective is to show that cases exist, but due to lack of knowledge by health personnel they are overwhelmingly underdiagnosed.

Introduction

Malaria occupies a unique place in the annals of history. Over millennia, its victims have included Neolithic dwellers, later on Hippocrates, described in a medical text. However, it was not until 1718 that the term malaria was coined by Italian physician Francisco Torti. In 2018, an estimated 228 million cases of malaria occurred worldwide, most malaria cases in 2018 were in the African Region, followed by the WHO South-East Asia Region [1-3] Despite malaria and its disastrous complications being well known since ancient times, it has taken centuries to diagnose PMNS as rare neurological complication that can occur after recovery from malaria, usually severe falciparum malaria. PMNS was first described in 1996, since then no more than 200 cases have been reported in English literature [4,5], on the other hand it is also contradictory that fewer are reported cases in the endemic areas and that representing Africa more than 80% of the cases is practically insignificant, the reported incidence and those that have occurred are limited to anecdotal cases of travelers coming from areas without malaria[6-10]. Reports are practically non-existent in the West African region and in Gambia no health institution, either from the private or public sector, has been diagnosed cases [11]. In order to inform and sensitize the medical community and its institutions, the following case is shared.

Case presentation

He is a 56-year-old patient from Italy with a history of high blood pressure treated with lisinopril 10 mg a day, a smoker of less than 1 pack of cigarettes a day for more than 30 years. Family arrived in Gambia as a tourist 3 weeks ago and he wasn't undergoing chemo prophylaxis for malaria. Three days prior admission, he began to present fever with chills, generalized weakness, joints pain, and severe headache. On physical examination, was febrile, lightly pale, temperature of 39.50 C, with chills and profuse sweating. Pain on light palpation in the right hypochondrium. Central nervous system without motor or sensory focus, and completeness of consciousness, Glasgow 15/15. Rest of physical examination irrelevant. Considering the level of hyperparasitemia by Plasmodium Falciparum in a patient from a non-endemic area, admission at the ICU was done with a diagnosis of severe malaria. .

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Analytical studies

A blood film showed Plasmodium falciparum infection 4+

- **Hb:** 9.6 g/l
- **WCC**: 12.5x 109/L
- **Plt:** 75000 mcl
- **CRP:** 80 mg/l
- **LDH:** 550 IU/L
- **ASAT**: 45 u/l
- **ALAT:** 56 u/l and LDH
- **RBS:** 3.5 mmol/l
- **Creatinine:** 72 mmol/l.
- **Liver echography**: Reactive hepatomegaly

Treatment

Fluid replacement, IV Paracetamol, IV artesunate and oral doxycycline. On the 4th day of admission patient became asymptomatic blood study turned negative for malaria, then artesunate stopped and started with oral coartem, patient was transferred to medical ward. On the seventh day of admission and after being asymptomatic for 72 hours prior to hospital discharge, the family escort complained about night restless, incoherent words, and talking nonsense sentences.

On medical examination, the patient appears incoherent in his verbal expression and poor coordination, presents evident difficulties in carrying out manual activities and standing without losing his balance, as well as an unstable gait with his feet far apart, in addition to difficulty in walking. Fine motor tasks, such as eating, writing, or buttoning the shirt and dysmetria in the upper limbs with aditoocokinesia, however, on physical examination no tremor, dysarthria or nystagmus have been observed. Rest of the exam rule out jaundice, anemia, fever, sweating or chills. However, considering the acute cerebral injury (encephalic and cerebellar), it was decided to re-admit at the intensive care unit. Computed tomography of the brain reported as normal. The thick smear was negative for malaria, the white blood cell test, as well as the renal function tests, also remained normal, the inflammatory response markers were moderately elevated (CRP, ESR) but considerably lower than the previous values. After re assessment diagnose of post-malaria acute neurological syndrome was raised. IV dexamethasone, vitamin B and haloperidol were given, after 48 hours of treatment the patient began gradual clinical improvement of the encephalic functions, so it was transferred to medicine ward, few days later he recovered his balance and motor coordination, fine movements took a little longer and after 6 days of onset of the neurological picture the patient was discharged with restitution ad integrum of all neurological functions, diagnosis at discharge upon discharge Post falciparum malaria neurological syndrome.

Discussion

Malaria induces neurological manifestations including axonal and sensory neuropathy, cerebral venous and arterial thrombosis. Neurological syndromes may occur after recovery from malaria, with no parasitemia, usually following Plasmodium falciparum malaria and occurring after an interval of 2 days to 2 months. PMNS is characterized by three neurological syndromes after recovery from malaria, with no parasitemia, usually following Plasmodium falciparum and occurring after an interval of 2 days to 2 months. The syndromes are an acute disseminated encephalopathy, known as post-malaria neurological syndrome; a delayed cerebellar syndrome; and an acute idiopathic demyelinating polyneuropathy (AIDP), aphasia, tremors, myoclonus, or psychiatric manifestations are also described as part of the picture. In acute phase is common rapid onset of confusion with aphasia, psychosis, myoclonus, or epilepsy, with visual hallucinations, tremor and ophthalmoplegia. MRI of the brain and spinal cord may be normal or may show widespread white matter lesions [12-17].

In principle, all conditions that acutely develop brain or cerebellar dysfunction without apparent origin such as viral, bacterial or post vaccinal are potentially consider as probable diagnose, newly of multiple sclerosis, neurosyphilis, or ataxia of toxic origin could tentatively be part of the differential. Acute disseminated encephalomyelitis is a monophasic acute demyelinating disorder, characterized by diffuse neurologic signs and symptoms, coupled with evidence of multifocal lesions of demyelination on neuroimaging, in PMNS, CT scan could be normal, nonetheless alternatively diffuse cerebral edema might be seen. [18] According to Mohsen et al., there are no specific identifiable clinical or radiologic lesions to distinguish PMNS from ADEM [19].

First syndrome to be described was delayed cerebellar ataxia in1986, then Guillain–Barré (AIDP) in 1992 and later on PMNS in 1996. However, without there being a logical explanation, the number of diagnosed cases remains low [10], and in West Africa it is practically nil. Information about it by the health authorities as well as in medical publications remind scanty. Therefore, looks like be under diagnosed and underreported, patients may return home and later on developing subsequent illness either not described or not attributed to a complication of malaria. Probably because there are no long-term sequelae, and the condition does not relapse or recur because is self-limiting.

Differential diagnosis is complex considering not pathognomonic studies available to confirm or rule out the condition, only clue elements increase the level of suspicious and are paramount in the diagnosis such as:

1. Recent episode of severe falciparum malaria.
2. Negative studies for current malaria infection
3. Sudden onset of unexplained neurological symptoms that cannot be explained by a focal lesion.
4. Drastic spontaneous recovering after steroid treatment.
5. Restitution ad integrum of the CNS
6. Could be associated with mefloquine prophylaxis.

In Gambia history, only Stephen D. Lawn reported 2 cases, both British patients and happened in 2003 after they arrived at UK. [11] In our case, diagnosis was made in Gambia, the patient described was not undergoing prophylaxis for malaria, so there is no association with the consumption of mefloquine. PMNS symptoms began around 72 hours after being asymptomatic and with a negative test for malaria, similar to that reported by the reviewed literature. Another concordance is the spectacular response to steroid treatment, fully recovered of all previously affected neurological functions, this being almost a paradigm in the cases reviewed.

The acute onset of neurological symptoms, predominantly diffuse encephalic (confusion, incoherence, and misbehavior) with cerebellar ataxia, has been our seen pattern. Nevertheless, it is opportune to recognize that there are several forms of clinical presentation, which can vary from a single presentation or in combination of the three mains described above (encephalic,

cerebellar, and peripheral), however by far the first two are the most commonly reported.

Conclusion

Since the first report PMNS has behaved as uncommon, reported disease. According 2021 WHO malaria report total malaria cases increased from 213 million to 228 million [3], Consequently, the following questions arise:

1. Where are the cases of PMNS?

2. Why are they not reported, especially in endemic countries?

3. What is the level of awareness among doctors from endemic malaria countries?

Unfortunately, in its etiology and pathophysiology there are more questions than answers. On the other hand, from epidemiological point of view only few cases are reported in endemic countries, except for the series described in Vietnam[7], The disproportion is greater in the African continent, where the autochthonous published cases are usually purely anecdotal, and the vast majority of reports correspond to travelers from non-endemic areas who may or may not have taken mefloquine and who, after being cured, developed symptoms and signs corresponding to the PMNS.

At this point, we can infer, that at least in our geographic area cases of PMNS have never been reported before because:

1. The level of awareness about the diseases is still low among health workers.

2. There is an enormous sub-registration of the cases. Probably because it is a self-limited entity with spontaneous resolution or after the use of steroids,

3. Nonetheless the impact reminds undervalued, and the risk is still underestimated.

Therefore, the main objective is to achieve greater and better knowledge in relation to the PMNS, to ensure that especially our new generations of medical professionals take this entity into consideration, reducing its underdiagnosis and under registration, achieving a direct impact on the health of the population.

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