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Delayed Cerebellar Ataxia: A Rare Complication of Falciparum Malaria From A Non-Endemic Area

KEYWORDS

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ABSTRACT *PURPOSE - The purpose of this study is to understand the profile of the patients with delayed cerebellar ataxia due to plasmodium falciparum infection in a non-endemic area.*

METHODS - A retrospective chart review of diagnosed cases of malaria who presented with delayed cerebellar ataxia with positive blood smear for plasmodium falciparum between November 2014 and April 2015.

RESULTS - A total of 17 patients were diagnosed to have malaria out of which 9 patients presented with delayed cerebellar ataxia. All the 9 patients were tested positive for plasmodium falciparum. None of these 9 patients had a previous history of malaria infection or its treatment. Mean duration between fever and ataxic symptoms was 14 days (Range: 7-28 days). All patients received artemether and lumifantrin combination.

CONCLUSION - Delayed cerebellar ataxia is a self-limiting neurological complication of falciparum malaria. In a malaria endemic area, all patients with cerebellar ataxia with history of fever in the recent past should be investigated for malaria parasites in the blood. Once the parasite is documented, further evaluation of ataxia may be unnecessary especially in resource constrained regions while anti-malarial treatment should be initiated promptly and effectively to anticipate complete recovery.

INTRODUCTION

Malaria is a major public health problem. As recently as 2014, ongoing malaria transmission is reported from 97 countries and territories. In an estimated 198 million cases of malaria worldwide with 584 000 deaths, almost 90% of all malaria deaths were reported from Africa.[1]India is home to 58% of all cases in the South East Asian Region. Significantly, 89 % of the population lives in the malaria transmission areas with 22% residing in high transmission areas while 67% in the low transmission areas. Nearly 53% of infection is caused by P. falciparum while P. vivax accounts for the remaining.[2]

Severe malaria is acute malaria with major signs of organ dysfunction and/or high level of parasitaemia, most often due to P. falciparum. Life threatening neurological complications following falciparum infection thus, alarm the treating physicians. Cerebral malaria is a sinister clinical syndrome characterized by coma and asexual forms of the parasite on peripheral blood smears.[3] Several neurological complications are associated with severe plasmodium falciparum malaria. Post malaria neurological syndrome is a discrete transient neurological syndrome seen after recovery from malaria infection. Delayed cerebellar ataxia (DCA) is a self-limiting neurological complication following plasmodium falciparum infection and has been reported first in 1984.

DCA is rare following falciparum infection and although reported from Sri Lanka and Africa, only few cases have been reported from India. We report here a retrospective chart review of nine patients with falciparum and vivax infection with ataxic symptoms hailing from a particular geographic area.

MATERIAL AND METHODS

A retrospective chart review was done at the Community Health and Development (CHAD) base hospital, a secondary level hospital run by the Community Health department of a medical college in Southern India between November 2014 and April 2015. All the patients above 18 years of age that were diagnosed to have ataxic symptoms and signs with positive plasmodium falciparum in their peripheral smears were included in the study. History of travel to an endemic area was noted as well the duration of onset of DCA from the first day of febrile illness. Clinically, the patients were evaluated for the signs of cerebellar ataxia viz. truncal ataxia, positive tandem gait, positive knee-heel test, abnormal finger-nose test, and nystagmus. Laboratory evaluation included Haemoglobin, Total White Cell Count, Platelets, and Peripheral Blood Smear for malarial parasites, lumbar puncture and Vitamin B12 levels. When indicated to exclude other causes of ataxia, MRI scan was done.

RESULTS

A retrospective chart review of nine patients out of the 17 patients diagnosed to have malaria between November 2014 and April 2015 was done. Four out of 9 patients had a history of travel to an endemic area. None of the patients had any previous history of malaria infection or its treatment. Mean duration between fever and ataxic symptoms was 14 days (Range: 7-28 days). All the study patients with malaria presented with truncal ataxia, positive tandem gait, and positive knee-heel test, the features consistent with the diagno-

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sis of delayed cerebellar ataxia. (Table 1)

Table 1

	Hb (g%)	TC(/m^3)	Platelets (/mm^3)	MP	CSF	B12	MRI	DCA Onset (Days)	Endemic Area Travel	DCA
Case 1	12.2	7300	22,000	V + F (R)	*	*	*	10	+	+
Case 2	8.1	5200	2,17,000	F + V(R)	*	*	*	21	-	+
Case 3	NA	8900	1,59,000	F (R + G)	*	*	*	28	+	+
Case 4	10.6	4700	1,15,000	F (G)	N	N	*	7	-	+
Case 5	13.1	9300	1,98,000	F (G)	*	*	N	21	+	+
Case 6	11.5	5700	4,19,000	F (R+G)	N	N	N	10	+	+
Case 7	13.3	6600	4,44,000	F (R+G)	*	*	*	10	-	+
Case 8	10.5	7300	2,44,000	F (R+G)	*	N	*	15	-	+
Case 9	8.4	4000	1,75,000	F(G)	*	*	*	7	-	+

Clinical Profile of the study patients. MP-malaria parasite, CSF-cerebrospinal fluid, MRI-magnetic resonance imaging Gametocyte-G; Ring form-R; V-Vivax; F-Falciparum; * clinically not indicated; NA-not available. DCA-Delayed Cerebellar Ataxia; DCA onset-duration between fever and ataxic symptoms

One patient also presented with abnormal finger-nose test and bilateral nystagmus. Mean haemoglobin was 10.96 g% (Range: 8.1-13.3); mean Total White Cell Count was 6555.5 /mm^3 (Range: 4000-9300); and mean platelet count was 234750 /mm^3 (Range: 22000 – 444000). All the 9 patients tested positive for plasmodium falciparum on peripheral blood smear. Additionally, 2 out of 9 patients were tested positive for plasmodium vivax. Two patients underwent lumbar puncture with normal examination while Vitamin B12 levels were measured in 3 patients with normal results and 2 patients underwent MRI scan of brain with normal images. After establishment of the diagnosis, all patients received artemether and lumifantrin combination twice daily for at least 3 days. All the patients recovered completely within 4 -12 weeks.

DISCUSSION

DCA is an unusual complication of falciparum malaria that has an acute onset with signs suggesting a predominantly midline cerebellar lesion without any evidence of cerebral involvement[4]. In this retrospective review, out of 17 diagnosed cases of malaria, 9 patients presented in a span of six months with truncal ataxia, positive tandem gait and heel knee test. One of the 9 patients also had an abnormal finger-nose test and bilateral Nystagmus. It is pertinent to note that four out of nine patients had history of travel to malaria endemic area. None of these 9 patients had any documented evidence of prior history of malaria infection or treatment with anti-malarial medications. The first patient (Case 1) in the series underwent a series of investigations as per the protocol in an academic setting to reach the diagnosis but for the subsequent cases as the experience grew, the investigations were narrowed down to the relevant few. Once the definitive diagnosis was made, all the patients were treated with artemether and lumifantrin combination. The mean duration between fever and ataxic symptoms was 14days (Range: 7-28 days).

Historically, Vellore region is not considered a malaria endemic area. The malaria problem in tribal area of Jawadhi hills appears to have probably been triggered as result of a large scale labour migration to the malaria endemic areas in Andhra Pradesh.

In Vellore, the causes of post-infectious cerebellar ataxia include scrub typhus, Varicella zoster, and typhoid. In a study conducted in Jodhpur amongst the neurological manifestations following enteric fever 19.44 % had cerebellar ataxia.[5] Cerebellar ataxia is one of the neurological complication following varicella infection.[6] Similarly, cerebellar ataxia is also observed following scrub typhus infection (unpublished data from our centre).

In a case series of 18 patients with DCA from Bikaner (Rajasthan), the mean delay between onset of fever and onset of cerebellar ataxia was 13 days (Range: 1-3 weeks with all the patients showing a complete response and eventual recovery after the medical treatment as per the WHO guidelines.[7] These findings and outcomes are consistent with those of the present data.

Delayed cerebellar ataxia is a post-infective neurological syndrome characterized by severe gait and truncal ataxia. It is a self-limiting condition with good prognosis, with spontaneous and complete recovery within 3 -4 months. In our study, seven patients recovered completely within four weeks except two who did show improvement over period but took ten to twelve weeks for complete recovery. Amongst the recognized theories in the pathogenesis of DCA, immune activation with significantly high serum levels of tumour necrosis factor, interleukin 6 and interleukin 2 and cytokine following falciparum malaria seems to be the most accepted one.[8] Consequently, Prochlorperazine and steroids have been used for the symptomatic relief in DCA[9],concomitant to the falciparum infection treatment .

From the foregoing, it appears that the differential diagnosis of acute onset cerebellar ataxia should also include falciparum infection as a cause, especially if the person comes from or has travelled to such a geographic area where incidence of malaria is high and in the absence of more sinister cerebral symptoms. This series of cases presenting from a community with relatively low health awareness is unique from an otherwise sporadically reported condition from the subcontinent. To the best of our knowledge, Cerebellar ataxia in malaria has not been reported from Vellore. Hence the cluster of cerebellar ataxia in malaria in a non-endemic tribal area could suggest a parasite variation or genetically linked immunological mechanism in the tribal community. This needs further study.

Conclusion: Delayed cerebellar ataxia is a rare self-limiting neurological complication of falciparum malaria. In a malaria endemic area, all patients with cerebellar ataxia with his-

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tory of fever in the recent past should be investigated for malaria parasites in the blood. Once the parasite is documented, further evaluation of ataxia may be unnecessary especially in resource constrained regions while anti-malarial treatment should be initiated promptly and effectively to anticipate complete recovery.

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