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Original Research Article

Autopsy Study of Cerebral Malaria: A Hospital Base Study

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Abstract

Introduction: Malaria is a very stubborn disease which has been taking steady toll of human life even now. It has been mentioned in the literature that many unexpected/ unexplained deaths occurred in malaria endemic regions and on autopsy of these deaths, cause turn out to be malaria.

Material and Methods: This was descriptive observational study conducted for the period of two years. All the diagnosed or suspected cases of cerebral malaria were included in study. Whenever cerebral malaria diagnosed or suspected, brain was removed with usual autopsy technique and fixed with routine techniques.

Results: Out of 3588 autopsies, 60 (1.67%) were the cases of cerebral malaria. On gross examination of brain; the characteristic slate-grey colour was observed in 58.33% (35) cases and presence of malarial pigment seen in other organs.

Conclusion: In malaria endemic areas, unexplained and/or unexpected deaths, should be critically investigated with the autopsy examination

Keywords: Malaria; Autopsy Findings; Cerebral Malaria.

Introduction

From times immortal, malaria has been known to mankind. It is very stubborn disease which has been taking steady toll of human life even now. Malaria is a lethal protozoal disease caused by parasite "plasmodium" and transmitted to man by infected 'female' "Anopheline mosquito" [1]. Malaria existed in India even centuries before Christ. The reference about malarial fever can be found in "Atharva Veda" which dates to 1500 BC [2]. Malaria inflicts a huge health care burden in terms of mortality and morbidity worldwide.

Approximately half of the world population is at risk of malaria. According to 2013 estimates, about 198 million cases of malaria occurred worldwide, out of that 5, 84,000 were succumbed to it [1]. In India, malaria had been the most formidable and serious public health problems for centuries; almost the entire country except the areas above mean sea level are endemic for malaria due to various favourable ecological conditions. In our country about 53% of the infections are reported to be due to P. falciparum, 4-8% due to mixed infection and 49-45 % due to P. vivax [3].

P. malariae is said to be responsible for less than 1% infection. P. ovale is a very rare parasite in man, mostly confined to tropical Africa [1].

Cerebral malaria is the most important one of those manifestations of severe malaria infection, which if not, treated specifically and promptly, leads to death in a short while. Many of these deaths are due to failure of early diagnosis, failure to identify resistant forms and failure to give optimal chemotherapy and supportive treatment.

There has been evidence in the literature where many unexpected and/or unexplained deaths turned out to be related to malaria in endemic regions [4].

In majority of the cases, malaria is well diagnosed in ante-mortem settings and there have been some reported cases in the literature where malaria has been diagnosed as the cause of death posthumously [6-10].

In a number of cases, death takes place even before a proper diagnosis is reached. At autopsy, also the diagnosis is likely to be missed in some cases if a histological examination of brain is not undertaken. With all this background, the present study was conducted to decipher the pattern of cerebral malaria and its histo-pathological characteristic.

Aim

The aim of the present study was; to study the pattern of cerebral malaria and its histo-pathological characteristic

Objectives

The objectives of the present study are,

1. To determine the proportion of cerebral malaria deaths,
2. To study the gross and microscopic pathology of brain in cerebral malaria,
3. To study histo-pathological changes in other organs due to cerebral malaria.

Material and Methods

Institutional ethical committee's approval was obtained before starting study. The present descriptive observational study was conducted in one of the major teaching hospital in North Bombay. All the diagnosed or suspected cases of cerebral malaria were included in study. Cases whose immediate relatives even after counselling; expressed unwillingness were excluded from study. Whenever cerebral malaria was diagnosed or suspected, brain was removed with usual autopsy technique and fixed in 10% formal saline as described by Ludwig [11] after the noting the gross findings. The brains were dissected after 10 days of fixation. The abnormalities on the cut surface were described and sections were taken from different parts of cerebrum, cerebellum and brain stem.

The gross findings of all other organs were also noted. Blood was collected during post-mortem to look for malaria parasite; if malaria was not considered clinically and to confirm the diagnosis if already made. Imprints of bone marrow and spleen were also taken.

All the sections of brain as well as other organs were stained as routine procedure, with haematoxylin and eosin. Special myelin stain was also employed namely Kluver and Barrera Luxol Fast Blue stain for myelin Nissl counter stain and staining by Bancroft [12] was followed. After cutting, sections were brought to water in usual way after dewatering with xyelne; and routine procedure was followed for staining.

Statistical Analysis

Data coding and entry was done, in Microsoft Excel spread sheets and descriptive and inferential statistical analysis was done by using SPSS version 21 (Statistical Package for Social Sciences) software. For descriptive analysis, tables, simple bar graph was used. Qualitative and quantitative data analysis was done using proportion, chi square test, unpaired t test, mean, standard deviation etc.

Results

Total 3588 autopsies were performed during study period. Out of that 60 (1.67%) were the cases of cerebral malaria. In present study; out of total cerebral malaria autopsies cases, 65% (39) and 35% (21) cases were of male and female respectively.

With respect to age wise distribution, youngest patient was 4 months female child, while oldest patient was 75 years old male (Table 1). Out of total 60 cases of cerebral malaria 48.62% (29) patients died within in 06 hrs of hospital admission, where as only 02 (3.3%) patient survived for more than one week (Graph 1).

Cerebral malaria patients had diverse and atypical features; maximum i.e. 95% had central nervous system symptoms; like altered sensorium, convulsion etc., 60% had gastrointestinal symptoms; like loose stool, vomiting etc. Less prevalent symptoms, were of renal system (12%), followed by respiratory system (7.0%). On medical record examination it was found that in 26.6% (16) cases malaria was not suspected at all.

On gross examination of brain; the characteristic slate-grey colour was observed in 58.33% (35) cases and around 8.33% (05) cases, brain was found to be normal. (Table 2) Microscopic changes of brain, on histo-pathological examination; are given in Table 3. On histo-pathological examination the most common changes seen in liver were malarial pigment deposition, Kupffer cell hyperplasia and dilatation of sinusoids and almost every spleen had malarial pigment deposition with congestion (Table 4 & 5). Other organs like lungs and kidneys had pulmonary oedema and cloudy changes on microscopic examination, respectively (Table 6 & 7).

Table 1: Age and Gender wise distribution

Sr. No	Age groups (Yrs)	Gender		Total
		Male	Female	
1.	< 1 Yrs	01	01	02 (3.33%)
2.	1-10 Yrs	01	03	04 (6.66%)
3.	11-20 Yrs	03	02	05 (8.33%)
4.	21-30 Yrs	11	07	18 (30.0%)
5.	31-40 Yrs	09	05	14 (23.33%)
6.	41-50 Yrs	06	02	08 (13.33%)
7.	≥ 51 Yrs	08	01	09 (15.0%)
	Total	**39 (65.0%)**	**21(35.0%)**	**60(100%)**
	$\chi 2$=5.79, d.f=6, P=0.44 Non Significant			
	Mean age wise distribution of gender			
A.	**Male**	29.3±1.6	Unpaired 't' test=23.880, d.f=58, P <0.0001 Significant	
B.	**Female**	18.0±2.0		

Table 2: Macroscopic appearance in brain of cerebral malaria cases (Multiple presentation)

Sr. No	Gross appearance	No. of cases (%)
1.	Dark and Slate grey	35 (58.33%)
2.	Engorgement and congestion	13 (21.66%)
3.	Petechial haemorrhage	17 (28.33%)
4.	Haemorrhages on surface	06 (10.00%)
5.	Pallor	04 (06.66%)
6.	Oedema	11 (18.33%)
7.	Normal	05 (08.33%)

Table 3: Lesion seen in brain microscopy

Sr. No.	Microscopic appearance	No of cases (%)
I.	• Vasculopathy (arteriole, capillary, vein)	
	1: Changes in permeability	
	i. Perivascular oedema	31 (51.06%)
	ii. Parenchymal oedem	46 (76.6%)
	2: Involvement of vessel wall	
	i. Endothelial thickening	08 (13.03%)
	ii. Hyaline microthombosis	18 (30.0%)
	iii. Necrosis of the vein wall	23 (38.03%)
	iv. Perivascular haemorrhage	33 (55.0%)
II.	• Myelinoclasia and reactive gliosis	
	i. Reactive gliosis	11 (18.3%)
	ii. Demyelination	09 (15.0%)
	iii. Malarial granuloma	07 (11.6%)
III.	• Meningeal reaction	12.0 (20.0%)

Table 4: Histopathological changes in liver

Sr. No.	Microscopy	No. of cases
1.	Dilatation of sinusoids	43
2.	Kuffer cell hyperplasia	52
3.	Periportal inflammation	46
4.	Hepatocellular necrosis	03
5.	Cirrhosis	05
6.	Fatty changes	06
7.	Malarial pigment deposition	58

Table 5: Histopathological changes in spleen

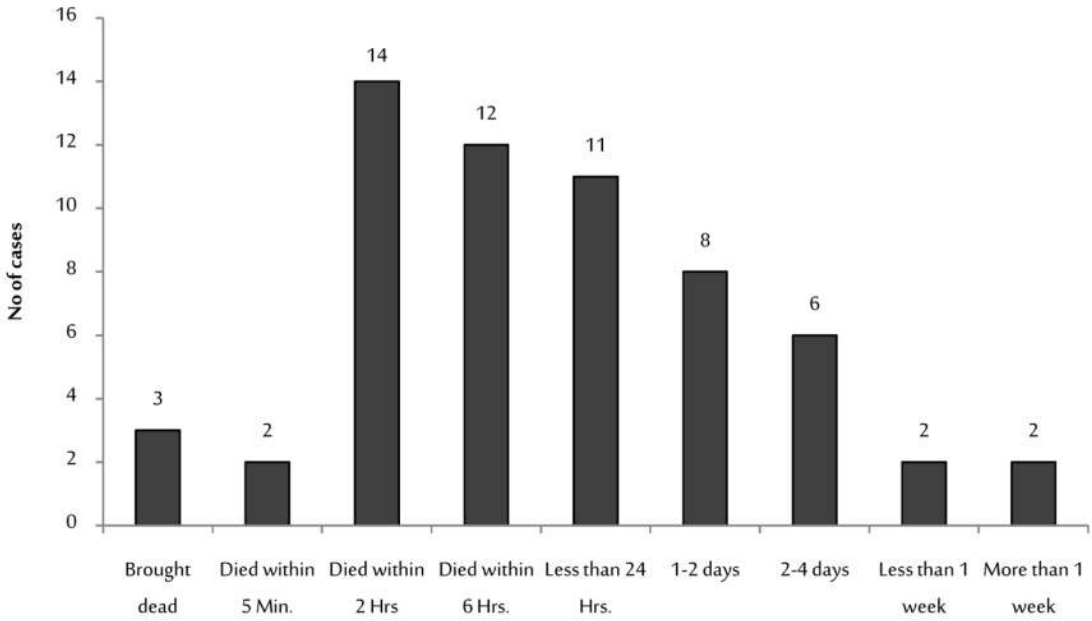
Sr. No.	Microscopy	No. of cases)
1.	Congestion	58
2.	Infarcts	01
3.	Amyloid	02
4.	Malarial pigment deposition	60

Table 6: Histopathological changes in lungs

Sr. No.	Microscopy	No. of cases
1.	Pulmonary oedema	33
2.	Bronchopneumonia	28
3.	Intra-alveolar haemorrhage	16
4.	Fibrin and platelet thrombi	08
5.	Giant cell	02
6.	Associated lesion	
	Emphysema and collapse	09
	Tuberculosis	03
7.	Pigmented macrophages	12

Table 7: Histopathological changes in kidney

Sr. No.	Microscopy	No. of cases
1.	Cloudy changes	53
2.	Tubular necrosis	11
3.	RBC/granular casts	11
4.	Hyaline casts	19
5.	Malarial pigments in glomerular capillaries	26



Graph 1: Duration of stay in the ward

Discussion

Since decades malaria remains the most important parasitic diseases worldwide. Cerebral malaria is a malignant form of P. falciparum infection amenable for sudden deterioration and death. Studies inscribed that, more than 95% of the sudden unexpected malaria deaths, were due to P. falciparum. The reason for complication was, this parasite has capabilities of sequestering into organ capillaries which did not happen in the other types of parasite. In present study, over a period of two years, 3588 autopsies were carried out and out of that 60 were

the cases of cerebral malaria; therefore proportion of cerebral malaria autopsy was 1.67%. In present study out of 60 cases of cerebral malaria, 65% (39) and 35% (21) were the males and females respectively. On analysis, mean age of the male and female patient shown statistical significant difference (P<0.05). In a study conducted by Hathila RN [13] also showed higher proportion of male cases (83.3% vs. 16.6%). In current study youngest patient was 4 month female child while in Surat city study carried out by Hathila RN [13], youngest patients was 5 years male child however elderly involvement remains somewhat similar in both studies. In present study about 48.62% (29) patients were died within 06 hours of hospitalisation and 5% (03) patients had been brought as dead.

In a study conducted by Menezes RG [14] reported highly variable circumstances of death. A case report by Afandi D [15] reported death of patient within 08 hours of hospital admission. In present study on gross examination, dark and slate grey appearance of brain were seen in 58.33% cases and on microscopic examination, in 76.6% cases parenchymal oedema seen, 38.3 cases necrosis of the vein wall was observed and malarial granulomas and demylelination, was seen in 11.6% and 15% cases, respectively.

Study conducted by Menezes RG [14] reported, vascular congestion with malarial pigment laden RBC in capillaries, in the brain sections of all subjects. Study conducted by Hathila RN [13] reported presence of malaria pigments in the brain of all cases. In present study on histopathological examination, In liver Kuffer cell hyperplasia observed in 52 cases, spleenic congestion and malarial pigment deposition seen in almost all cases, pulmonary oedema in lung and cloudy changes in kidney observed in 33 and 53 respectively. Similarly, Menezes RG [14] reported malarial pigment deposits in the liver sinusoids and Kupffer cells in 78% of the cases. These deposits were distributed inside the venous sinuses of the spleen in 67% of the cases. He also noticed alveolitis, pulmonary congestion, haemorrhage and malarial pigment in lungs of 56% cases.

Conclusion

In malaria endemic areas, to confirmed the cause, unexplained and/or unexpected deaths should be critically investigated with the autopsy examination.

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