

CASE REPORT

PATHOLOGY AND BIOLOGY

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An Autopsy Case of Sudden Unexplained Death Caused by Malaria*

ABSTRACT: Sudden unexplained deaths, especially those unwitnessed can lead to forensic issues and would necessitate the need for a meticulous and complete postmortem examination including ancillary investigations to discover the cause of death. We herein report a case of sudden unexplained death caused by malaria in an apparently healthy individual. This fatal case is presented to remind the forensic pathologist of the possibility of malaria as a cause of sudden unexplained death in malaria-endemic regions. In the present case, histopathological examination demonstrated the presence of parasitized red blood cells with malarial pigment in the blood capillaries in the brain, myocardium, pericardium, lungs, kidneys, liver, and the spleen. Cerebral malaria with acute renal insufficiency or pulmonary edema with an acute respiratory distress syndrome might have been the cause of death.

KEYWORDS: forensic science, forensic pathology, medicolegal autopsy, forensic histopathology, sudden unexplained death, *Plasmodium falciparum*, malaria, malaria-endemic region

Sudden unexplained deaths, especially those unwitnessed can lead to forensic issues and would necessitate the need for a meticulous and complete postmortem examination including ancillary investigations to discover the cause and manner of death (1). Globally, autopsy is often seen as the gold standard for the diagnosis of the cause of death in cases wherein individuals are found dead without anybody having witnessed their death. We herein report one such case of unwitnessed death of an adult male who was found dead near a railway station. Autopsy revealed the cause of death to be malaria. This fatal case is presented to remind the forensic pathologist of the possibility of malaria as a cause of sudden unexplained death in malaria-endemic regions. In the present case, histopathological examination demonstrated the presence of parasitized red blood cells (PRBC) with malarial pigment in the blood capillaries in the brain, myocardium, pericardium, lungs, kidneys, liver, and the spleen.

Case Report

An unknown elderly man aged about 60 was found lying dead near the Mangalore railway station in the district of South Canara

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in southwest India on 20th August 2007, in the early morning hours. The body was subjected to a medicolegal autopsy on the same day. External examination revealed a good physical state and the absence of traumatic injuries. Examination of the pleural cavities did not reveal any effusions or adhesions. The left lung weighed 500 g and the right 620 g. On cut section, both the edematous lungs showed no evidence of any focal lesions. The pericardial sac was unremarkable with no effusions or adhesions. The myocardium and endocardium were unremarkable. The coronary arteries had a normal anatomic course with no significant atherosclerotic disease. The enlarged spleen that weighed 350 g was unusually soft. The cut sections of the liver that weighed 1300 g were congested. The edematous brain weighed 1500 g. Macroscopically, the remaining organs were unremarkable.

Histopathologic examination of the lungs revealed alveolar exudate with focal pleural fibrosis and lymphocytic infiltrate. PRBC with malarial pigment were present in the pulmonary septal vessels (Fig. 1). Sections from the heart (Figs. 2 and 3) demonstrated congested vessels with PRBC in the myocardial and pericardial vessels, and focal inflammatory infiltrate. The spleen showed congestion and macrophages with engulfed parasites and brownish-black malarial pigment (Fig. 4). Sections from the brain demonstrated PRBC marginating within cerebral vessels (Fig. 5). The kidneys showed PRBC within blood vessels and congested glomeruli with malarial pigment (Fig. 6). Focal inflammatory infiltrate was present in the renal tissue. Sections from the liver (Fig. 7) demonstrated dilated sinusoids, Kupffer cells laden with malarial pigment, hepatocytes with malarial pigment, and periportal inflammatory infiltrate.

Routine postmortem toxicological screening utilizing chromatography and mass spectrometry was undertaken without detecting common illicit or prescribed drugs or pesticides.

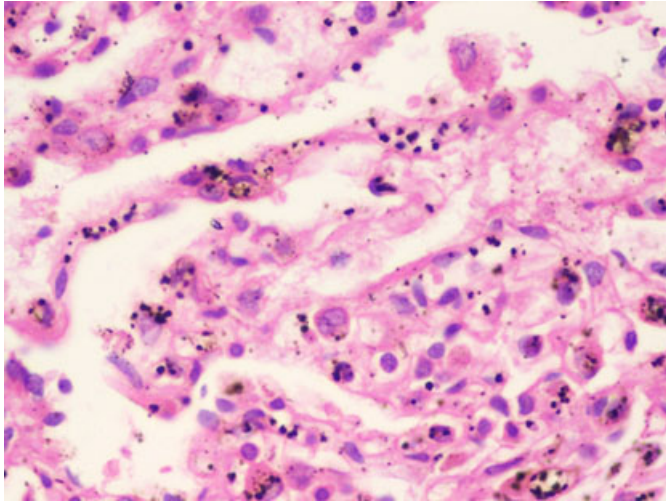


FIG. 1—Pulmonary tissue showing parasitized red blood cells with malarial pigment in the septal vessels (Hematoxylin and Eosin 40 \times).

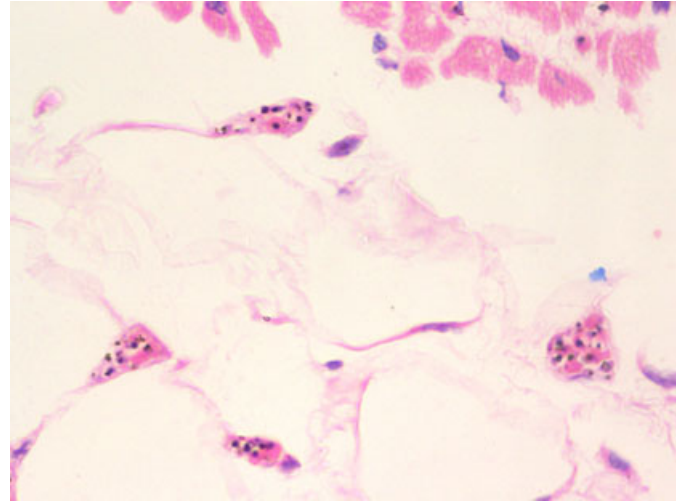


FIG. 3—Congested vessels with parasitized red blood cells in the pericardium (Hematoxylin and Eosin 40 \times).

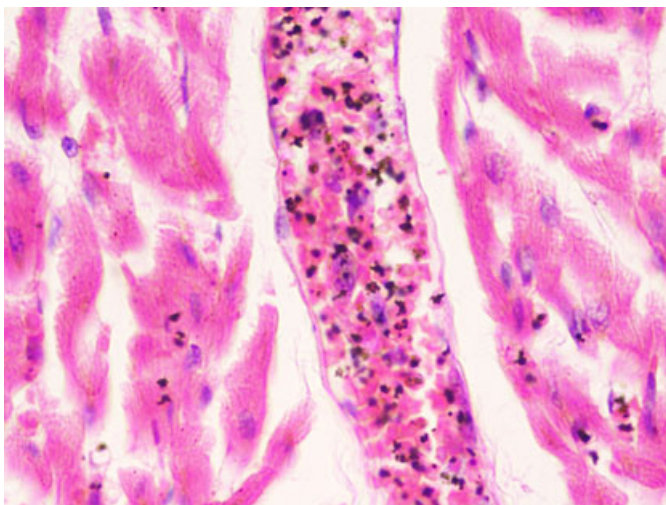


FIG. 2—Congested vessels with parasitized red blood cells in the myocardium (Hematoxylin and Eosin 40 \times).

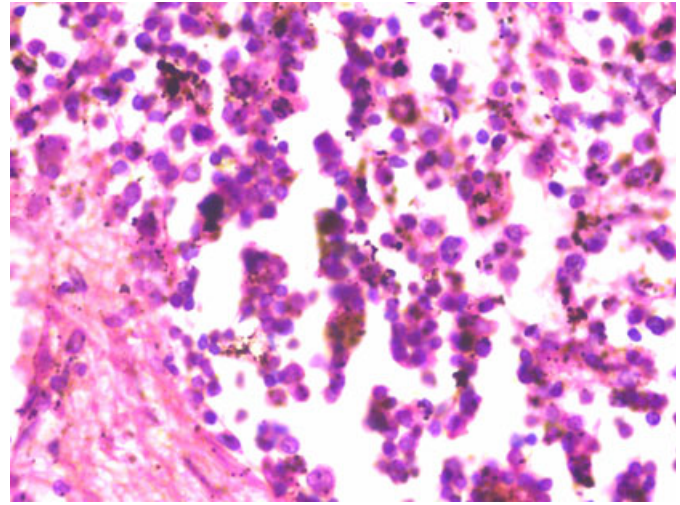


FIG. 4—Macrophages with engulfed parasites and brownish-black malarial pigment in the splenic tissue (Hematoxylin and Eosin 40 \times).

Discussion

Not uncommonly, medicolegal autopsies are conducted in cases of sudden unexplained deaths primarily to establish the cause and manner of death in cases where such deaths have occurred in apparently healthy individuals under suspicious circumstances (1). Sudden unexplained deaths are mainly attributed to the cardiovascular system and the respiratory system (2,3). Nevertheless, autopsies have revealed that sudden deaths are occasionally attributed to parasitic infections like malaria (4).

Malaria, caused by the protozoal parasite *Plasmodium* (P) and transmitted by the female anopheline mosquitoes, is the world's most important parasitic infection ranking among the major public health challenges (5). Four species of malarial parasite (*Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*) cause malaria (5,6), but *P. falciparum* is the main cause of complicated severe form of malaria (7).

Malaria is endemic in India with the bulk of cases found in the flood plains of northern India and coastal plains of the east and

west coasts (8). Studies on resurgence of malaria in India revealed countrywide presence and spread of *P. falciparum* (9). *P. falciparum* is found in all states and union territories except the Lakshadweep Islands off the south-western coast of India (10). The countrywide presence of *P. falciparum* is facilitated by rural urban migration, and inter- and intra-state movement of population, particularly for civil works and rail road construction (11,12), thus providing openings for the mutant strains of *P. falciparum* to disseminate across the country (11). The present case is reported from Mangalore, the headquarters of South Canara district, a coastal city located along the west coast of South India. Mangalore is a region highly endemic for malaria transmission. Anecdotal media reports suggest that, in Mangalore, malaria transmission persists throughout the year with the peak season from June to August, which corresponds to the months of heavy rainfall in the region. The present case of sudden unexpected death as a result of malaria occurred in the month of August when the incidence of malaria cases in the city of Mangalore is reported to be very high.

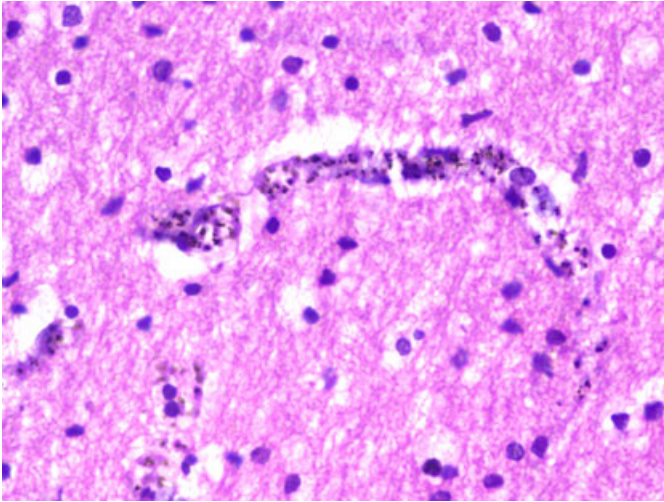


FIG. 5—Parasitized red blood cells seen marginating within cerebral vessels (Hematoxylin and Eosin 40 \times).

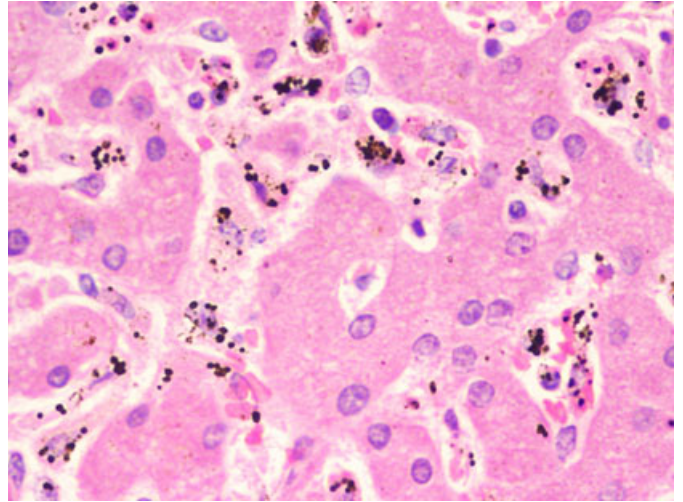


FIG. 7—Hepatic tissue showing dilated sinusoids and Kupffer cells laden with malarial pigment (Hematoxylin and Eosin 40 \times).

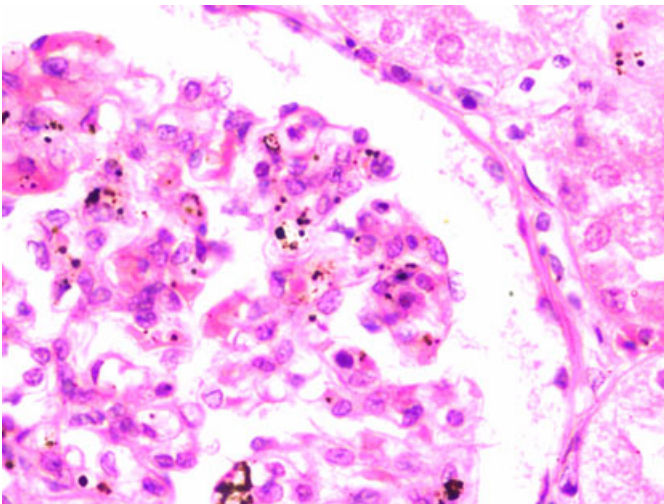


FIG. 6—Parasitized red blood cells within renal vessels and congested glomeruli with malarial pigment (Hematoxylin and Eosin 40 \times).

The clinical features of malaria vary from nonspecific symptoms resulting in diagnosis only at autopsy to severe life-threatening systemic manifestations. Nonspecific symptoms include headache, myalgia, anxiety, and mental confusion with or without fever. In cases from endemic areas or travelers to such regions, malaria must be considered in the differential diagnosis along with other causes of fever such as viral, bacterial, and rickettsial infections. Jet lag as a risk factor for the development of malaria in inter-continental travelers visiting malaria-endemic regions is debated (13,14). Travelers from a nonendemic malaria region entering an endemic region for the first time are susceptible to malaria because they lack the necessary preformed antibodies (14). In the recent past, acute renal and multi-organ failures are important changes in disease outcomes recognized in patients with *P. falciparum* infections (9). Severe falciparum malaria often affects individuals with low or even absent immunity to malaria resulting in multi-organ failure. In the present case, histopathology revealed multi-organ involvement. Severe falciparum malaria is a

multi-system disease with diverse manifestations including cerebral malaria, renal failure, pulmonary edema, severe anemia, lactic acidosis, and hypoglycemia (15). In the present case, postmortem diagnoses of cerebral malaria, renal malaria, and pulmonary edema were made. Cerebral malaria, renal malaria, and pulmonary malaria are the three most common causes of death in adults with severe form of falciparum malaria (16). In the present case, cerebral, renal, and pulmonary malarial involvement may have caused the sudden unexplained death.

The red blood cells infected by late developmental stages of *P. falciparum* preferentially sequester in the deep vascular beds adhering to the endothelial cells of the capillaries and venules of vital organs, including the brain, kidney, lung, liver, spleen, and intestine, the hallmark of *P. falciparum* infection (17,18). Sequestration results in lower peripheral blood parasitemia underestimating the severity of the disease; however, histopathological findings demonstrate the multi-organ involvement associated with very high mortality (19). In the present case, histopathology revealed PRBC with accumulation of malarial pigment, in the brain, kidney, lung, liver, spleen, myocardium, and pericardium. In the brain, site of biopsy is important to assess the parasite burden as differential sequestration occurs between gray and white matter and between cerebral and cerebellar cortex based on the differences in the anatomy of blood supply to these areas (19). The gross pathological findings in the affected kidney include enlargement and congestion with formation of characteristic hemoglobin casts in the tubules. The spleen and the liver become progressively enlarged and pigmented. The heart shows focal nonspecific hypoxic changes caused by anemia and circulatory stasis in chronically infected cases (20).

In the present case of sudden unexplained death, postmortem diagnosis of malaria was primarily based on histopathological examination of the various organs. Therefore, the possibility of parasitic infections such as malaria as the cause of sudden death should be explored at autopsy by the forensic pathologist throughout the tropics and sub-tropics where malaria is endemic. In cases of sudden unexplained death, in malaria-endemic regions, tissues for histopathological examination should be obtained. The demonstration of PRBC with malarial pigment in the blood capillaries of internal organs by histopathology is a reliable method of postmortem diagnosis of malaria.

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