

Autopsy findings in severe malaria – a case report

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Abstract

Severe malaria, caused by Plasmodium falciparum infection, has a high mortality rate and is the main cause of death in malaria. Since clinical autopsy is unpopular in Indonesia, autopsy examination in malaria cases is rarely done. We reported a forty three year old woman from non endemic area that was dead because of severe malaria. Diagnosis was concluded from autopsy, histopathology, and toxicology. (Med J Indones 2008; 17: 210-5)

Abstrak

Malaria berat yang disebabkan oleh infeksi Plasmodium falciparum memiliki angka mortalitas yang tinggi dan merupakan penyebab utama kematian pada malaria. Pada kematian akibat malaria jarang dilakukan pemeriksaan otopsi karena belum populernya otopsi klinis di Indonesia. Dilaporkan seorang perempuan berusia 43 tahun dari daerah non endemik dengan penyebab kematian malaria berat. Diagnosis ditegakkan melalui otopsi, pemeriksaan histopatologi, dan toksikologi. (Med J Indones 2008; 17: 210-5)

Keywords: *Plasmodium falciparum, cerebral malaria, black water fever*

Malaria has caused over 1.2 million deaths all over the world in year 2002, it's the fourth among deaths caused by infectious and parasitic diseases. There are approximately 400 million new malaria cases all over the world and 7% of those numbers were found in Asia (World Health Organization, 2002). More than 45% of world population is contacted with malaria. In Indonesia, Malaria spreads all over the island particularly in the eastern islands.^{1,2,3}

Diagnosis of severe malaria is based on the appearance of asexual forms of *Plasmodium falciparum* in a patient with a potentially fatal manifestation or complication

of malaria, in whom other diagnosis have been excluded (WHO, 1990). The potentially fatal manifestations and complications are: (1) cerebral malaria, (2) severe anemia, (3) renal failure, (4) hypoglycemia, (5) Adult Respiratory Distress Syndrome (ARDS)/pulmonary edema, (6) circulatory collapse, (7) bleeding and blood clotting disturbance, (8) convulsion, (9) acid-base disturbance, (10) hemoglobinuria (black water fever) in acute malaria.^{2,5}

Due to rarity in complete clinical autopsy examination in Indonesia, particularly in malaria case, we reported a complete clinical autopsy in a case of severe malaria.^{4,5,6}

CASE

A 43 year old American woman traveler died and was sent to the Department of Forensic Medicine and Medicolegal, Faculty of Medicine, University of Indonesia to go through an autopsy to determine the cause of death. She lived in Florida until her visit to Jakarta. Six days after she arrived in Jakarta, she experienced fever and arthritis. She went to a doctor and got some medicine but did not get better. Two days

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later, she went to a hospital and got hospitalized by the recommendation of the doctor there. Five hours after hospitalized, she started to have convulsions and her general condition was deteriorating. She then died 3 hours later. Her family was suspicious that her death was due to improper medical treatment, so they reported the case to the police for some investigation.

We did external examination on the corpse. Further, standard procedure for toxicology and histopathology was done. All organ samples were taken including brain, liver, and blood. Further, urine, gastric content and bladder content were withdrawn.

RESULTS

External examination

External examination was done 10 hours post mortem. The corpse was an oriental female, well nourished, 43 years old, white to yellow skin color, with black hair, 154 cm in height. She was naked. The lower left second molar was missing, no denture was observed. The irises were brown in color, the pupils were measuring 5 mm in diameter; the conjunctives were white in color. *Rigor mortis* had fully developed; *Livor mortis* was found on the back, red-purple in color and bleached by pressure. Putrefaction signs were not observed. There was no sign of injuries. Cyanosis was found on finger nails. The skin was not icteric. Needle-marks were found on both of cubital regions.

Autopsy findings

Autopsy was done 30 minutes after external examination.

Head:

Brain and skull were intact. The brain weighed 1250 grams. Venous congestion on the surface of the brain was observed. No injury was found.

Neck, trachea and esophagus:

The hyoid bone, thyroid and cricoid cartilages were intact. The esophagus and trachea contained red mucous and food remnant. The tracheal mucous was hyperemia. No signs of injuries on the esophagus and trachea walls.

Thorax:

There was dark red fluid in the thoracic cavities, 80 cc in the right and 15 cc in the left one. There were no signs of injury on the thoracic wall.

Lungs: Upper lobes of both lungs were purple red in color and spongy; many petechial hemorrhages were found on their surfaces. Lower lobes of both lungs were dark red in color; and hematomas were found on their back surface. The right lung weighed 300 grams and the left one 330 grams.

The heart was brownish red in color. The circumference of tricuspid valve was 10 cm, and the mitral, pulmonary, and aortic valve circumference were 9 cm, 5.5 cm, and 5 cm respectively. The right ventricle wall was 2 mm thick and the left was 9 mm. The coronary vessels were not sclerotic or narrowed. The inter-ventricular septum, the left wall and the right wall of ventricles showed no remarkable changes. The heart weighed 300 grams. There were many petechial hemorrhages on the back surface of the heart.

Abdomen and pelvis:

Stomach contained 50 ml of food remnant. Spleen was grey-purple in color, showed no remarkable change and weighed 120 grams.

The liver was extremely big, far from normal, yellowish brown in color, soft and brittle (fragile), with rather blunt edges, and weighed 1420 grams. Further, the cut surface structure was unclear.

Duodenum, intestines, colon and adrenal glands showed no remarkable changes. Pancreas was yellow brown in color, showed no remarkable change, and weighed 80 grams.

Renal capsule was easily detached. It contained red dark fluid and longitudinal section appearance was changed. Petechia was found in renal pelvis.

Both of ovarium showed no remarkable changes. Uterus measures 10 cm x 7 cm x 3.5 cm and contained a small amount of blood.

Histopathological findings

Histopathological examination was done at the Department of Anatomical Pathology, Faculty of Medicine, University of Indonesia. We did not find intravascular thrombus formation in the blood vessels of the organs.

Brain:

The brain was edematous and hyperemic, especially in the white matter. The blood vessels were congested and clogged by erythrocytes cluster. There were fine black pigments in the erythrocytes and inside the capillary lumens (Figure 1), which did not disappear by bleaching technique, was not blue on Yzer staining method, and negative on Fontana-Masson staining method. It was confirmed that the pigments were malaria pigments.

Heart:

The heart was edematous and hyperemic. The morphology of the cardiac muscle fibers showed no remarkable changes. There were no signs of bleeding or inflammation, but the parenchyma contained pigments inside and outside the capillary lumen.

Lungs:

The anterior parts of the lungs were slightly emphysematous and hyperemic, but the posterior ones were severely congested and edematous (Figure 2). There was no leucocyte proliferation (signs of inflammation).

Liver:

The liver showed varying appearance, especially at R3 area which was diffusely necrotic and bleeding. There were degenerative and fatty liver processes. Pigments were found every where in the parenchyma (Figure 3).

Pancreas, intestines and spleen:

The pancreas contained moderate necrotic tissue. Intestines contained early necrotic tissue and pigments especially at the mucous membrane. Spleen were congested and contained pigments.

Kidneys:

The kidneys were severely congested. There were pigments inside the glomerulus. Some tubular epithelia were necrotic and sloughed off into the lumen on some places. These findings are consistent with early acute tubular necrosis (Figure 4).

Uterus:

The uterus showed pigments in the erythrocytes inside the capillaries, and there were occlusion of capillaries by erythrocyte clusters, but there was no stromal breakdown except at the upper endometrium that showed necrosis and sloughing (Figure 5).

Toxicological examination

Toxicological examination was done at Forensic Laboratory Center, Police Department of the Republic of Indonesia, Jakarta. The examination findings: There were no poison found in the blood, stomach content, urine, brain, and liver.

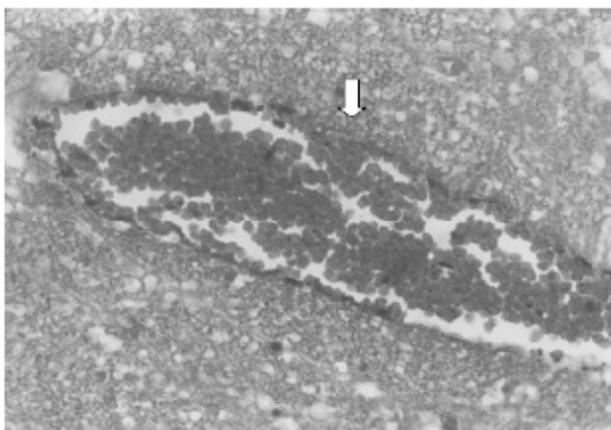


Figure 1. Malaria pigments in the capillary of the brain (H&E after bleaching X 100)

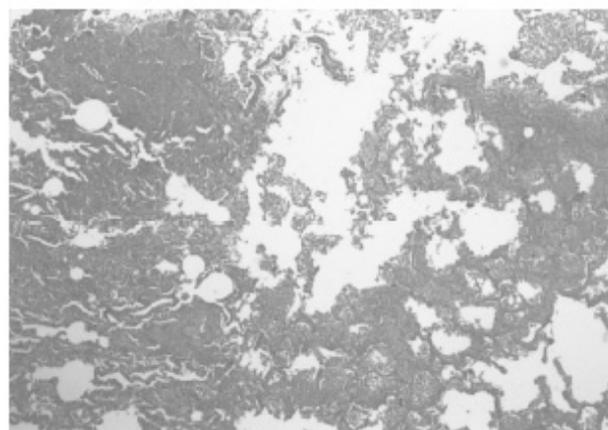


Figure 2. Lung microphotograph with no sign of inflammation (H&E after bleaching x 40)

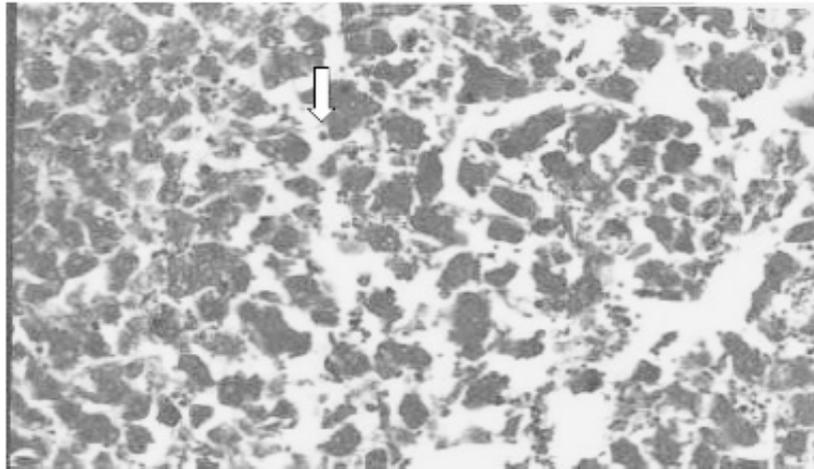


Figure 1. Malaria pigments in liver (H&E after bleaching X 100)

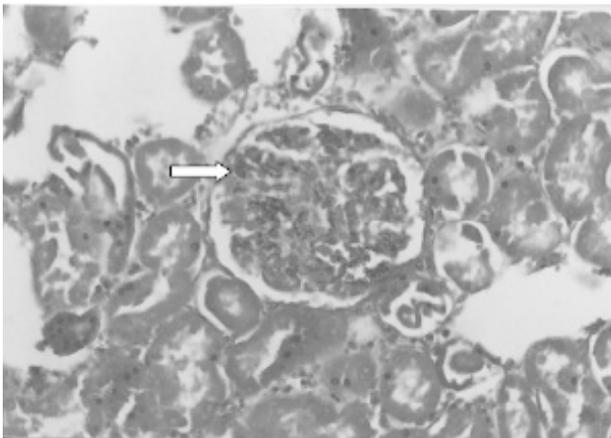


Figure 2. Renal microphotograph showing acute tubular necrosis with malaria pigments (H&E after bleaching x 100)

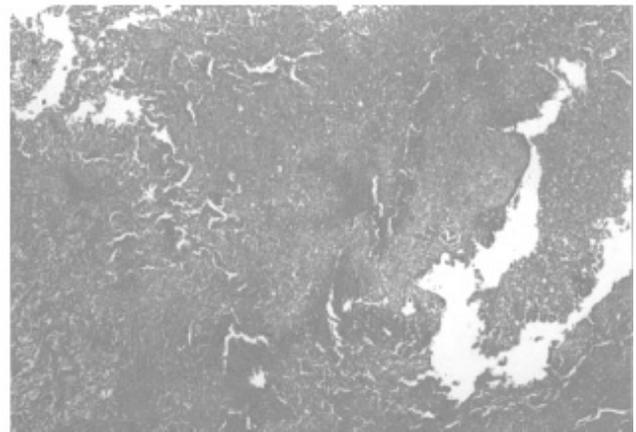


Figure 3. Malaria pigments in uterus with spontaneous bleeding (H&E after bleaching x 40)

DISCUSSION

There were 4 types of malaria found in human based on the types of parasite. Mortality of malaria is often caused by complication of severe malaria due to *P. falciparum* infection. The complication happened because the parasite had the capability of sequestering into organ capillaries which did not happen in the other types of parasite. The effects of sequestration could cause function disturbance of the organs and lead to organ failure.^{2,3,6-8}

After external examination, we still couldn't determine the cause of death and had to wait for histopathological and toxicological examination findings. At this time we

were thinking that her death was caused by some kinds of disease while keeping the probability that she was poisoned.

Although statistically cardiovascular disease is the most common cause of silent death (more than 50% is caused by ischemic heart disease),⁹ we could not find any heart abnormality in this case. Macroscopically there was no thickening or plug in the coronary artery and no sign of old or new infarct. Microscopically, though there was no sign of inflammation or even bleeding in the myocardium, malaria pigments were found.

We started to think about the possibility of severe malaria for this case. Histopathological examination

was very important at this time. To make the finding definite, we did 4 staining methods for all organ samples: (1) Hematoxylin and Eosin to show malaria pigment that was molasses-yellow to black in color.¹⁰ (2) Hematoxylin and Eosin staining after bleaching to exclude formalin pigment, (3) Yzer staining to exclude hemosiderin pigment, and (4) Fontana-Masson staining to exclude melanin pigment.

Malaria pigments were found in the brain, heart, liver, intestines, spleen and kidney. Multiple organ failures were found on heart, lungs and kidneys and spontaneous bleeding was showed inside the uterus. All data were consistent with severe malaria.^{2-5,8}

The brain was edematous and hyperemic especially in the white matter which differ cerebral malaria from viral encephalitis where the hyperemia was found mostly in substansia grisea.^{7,10} Brain blood vessels was congested and clogged by erythrocyte clusters. Fine black pigments were found in the erythrocytes and inside the capillary lumen. These findings fit the signs of cerebral malaria where the malarial pigment was only found inside the capillary lumen and never been in the brain tissue.¹¹

The liver showed blunt edges; the surface was yellowish brown and smooth but fragile, while the cut surface structure was unclear. Necrosis was found under microscope especially in R3 area, the closest part to the center of the lobule. These findings showed liver failure which also fit with malaria falciparum case theoretically which show degeneration and central lobular necrosis.^{2,6} Histopathological examination showed malaria pigments at the parenchyma, that was diffusely necrotic and showed fatty liver processes. Study in Jodphur,¹² reported that histopathological feature in liver due to *P. falciparum* showed malaria pigments (90%), liver cell necrosis (18,3%) and fatty change (15%).

The spleen was normal in size, no splenomegaly was found. This finding is in line with the theory stating that splenomegaly is usually found in chronic malaria, children and semi-immune people, but not in severe malaria. No abnormality was found microscopically. This fact may happen when the disease is acute due to the difference in the ability to sequester in different organ. From a prospective study,¹³ Chotovanich et al reported that ring-infected erythrocyte surface antigen (RESA) was not found in red blood cells (RBCs) in splenic blood smears from 5 patients with acute falciparum malaria.

In this case, macroscopic appearance of the kidneys and microscopic findings revealing early acute tubular necrosis and malaria pigment in the glomerulus indicated an acute attack of falciparum malaria.⁴ Newman et al,¹⁴ reported that renal failure and cerebral malaria was common clinical complication among U.S. travellers (43.9% and 48% respectively), and malaria pigments were found in some organs in autopsy findings (in 18 out of 50 cases).

Disseminated intravascular coagulation was supposed to happen in this patient, based on the many petechiae that were found in the heart and lung, confirmed microscopic findings in some organs, and uterus spontaneous bleeding.^{4,11} The negative finding of thrombus in blood vessels of the organs might be due to increasing post mortem fibrinolysin activity.

Post mortem diagnosis of severe malaria was determined by the appearance of the parasite and or malaria pigment in the organs. The most accurate prove for the presence of the parasite involve polymerase chain reaction tests for plasmodium DNA and TaqMan real-time PCR methodology. Laser light depolarization analysis for malarial pigment (hemozoin) in white blood cells is also specific for malarial infection and has a sensitivity of 80%.⁵ Sometimes, the parasite can be found in peripheral blood smear by using malaria detection method (thin and thick film).^{5,6,10}

According to WHO criteria, diagnosing cerebral malaria as the cause of death should be carefully considered, and should be based on the finding of malaria parasite or pigment in the brain, that is usually hard to find in post mortem examination. In this case, we found malaria pigments in the brain, but we diagnosed the case as severe malaria, since the finding of malaria parasite or pigment in the brain might give various symptoms depending on the sequestration density, while death could be due to other organ failure.

In conclusion, the cause of death for this patient was multiple organ failure due to severe malaria.

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