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MALARIA AND STROKE

CASE REPORT

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ABSTRACT - Malaria is a parasitic disease with high prevalence in several regions of the world. Infestation by *Plasmodium faciparum* can, in some cases, affect the central nervous system producing encephalitis resulting in death or neurological sequelae. The mechanisms involved in the pathophysiology of the cerebral lesion are not totally clear and there are currently two theories (mechanical and humoral) concerning this. We report a case of malaria with an atypical evolution, with a stroke lesion in the territory of the middle cerebral artery, with no association with encephalitis. We conclude that the mechanical theory is the one applicable to this patient.

KEY WORDS: malaria, stroke, cerebral malaria.

Malária e acidente vascular cerebral: relato de caso

RESUMO - A malária é doença parasitária de alta prevalência em todo o mundo. A infestação pelo *Plasmidim falciparum* pode, em alguns casos, acometer o sistema nervoso central produzindo encefalite grave resultando em óbito ou sequelas isquêmicas. Os mecanismos envolvidos na fisiopatologia da lesão cerebral não estão totalmente esclarecidos e duas teorias (mecânica e humoral) atualmente se somam neste objetivo. Relatamos um caso de malária de evolução atípica, com lesão cerebral isquêmica no território da artéria cerebral média direita, possivelmente não associada a encefalite e o relacionamos à teoria mecânica.

PALAVRAS-CHAVE: malária, acidente vascular cerebral, infarto cerebral, malária cerebral.

Malaria continues to be the most important parasitic disease in the world in terms of both prevalence and mortality. Every year, roughly 489 million people around the world, 80% in Africa, acquire this illness. *Plasmodium falciparum* infects 234 million people and is responsible for 2.5 million deaths per year[1,2]. Infection rates have remained high despite public health measures. That is due to the rise of strains resistant to the available antimalarial medicines, and to social factors (migration, deforestation, irrigation, occupation of areas without programs for vector eradication)[1,3].

Although malaria is produced by several species of *Plasmodium*, the disease produced by *Plasmodium falciparum* is the most severe. Cerebral malaria (CM) encephalopathy with high rates of mortality (up to 50% of the cases) and long-term sequelae is produced exclusively by *P. falciparum*. Even though the clinical, epidemiological and therapeutic aspects of malaria are well known, its pathophysiology is not completely clear despite recent experimental, both in animal and in-vitro models, immunochemical (inflammatory mediators) and postmortem evidences [4,5].

This paper describes an atypical case of malaria with central nervous system involvement and discuss possible phatophysiological mechanisms in the observed lesion.

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CASE REPORT

A white 28-year-old man, originally from the state of Ceará, northern Brazil, has lived in São Paulo, southern Brazil for the last 12 years. The patient was referred to the Division of Cerebrovascular Diseases of Universidade Federal de São Paulo - Escola Paulista de Medicina for evaluation of an acute neurological illness that occurred 4 months before with sudden left hemiparesis as the only neurological symptom. He reported having traveled to a small city in the state of Pará where a febrile sickness overcame during his stay. About the third day of his sickness he experienced a sudden loss of muscular strenghth on the left side of his body, and he was diagnosed as a victim of malaria and stroke. After treatment with antimalarials the fever disappeared, while the neurological problems remained.

The neurological exam showed hemiparesis, with elastic hypertonicity and hyperreflexia on the left side with Babinski's sign.

Computerized axial tomography of the cranium at the onset of neurological symptoms showed a deep right-sided parietal lesion (internal capsule area) with no mass effect that suggested ischemic stroke of middle cerebral artery territory. Normal parameters were obtained from red and white blood cell count, clotting tests, serum lipids, fibrinogen and proteins, sedimentation rate, serology for syphilis and Chagas disease, EKG, transthoracic and transesophagic echocardiogram, thoracic X-ray examination, sickle-cell test, parasithological tests of the feces, Doppler ultrasound of the carotids, and rheumatological tests (antinuclear antibodies, reumathoid factor, complement, crioglobulins, antiphosfolipid antibodies).

The patient is still under physical therapy and his neurological condition is unchanged after 2 years follow-up.

DISCUSSION

Children and young adults living in endemic areas, and adults that come from nonendemic areas seem to be at higher risk of developing cerebral malaria, as are pregnant women and patients with AIDS due to their decreased immunity. This observation led to the hypothesis that immunological considerations could play a major role in the phatophysiology of CM. Repeated exposures to *Plasmodium* does produce progressive resistance to the infections that results in milder cases and even full immunity to the disease. First-time infections and immunological deficiencies could be related to an intense inflammatory response[6-9].

There are currently two theories to explain the effects of malaria on the central nervous system. It is likely that the association of both theories comes closest to the ideal pathophysiological model.

The mechanical theory claims that the obstruction of the capillaries and cerebral venules by parasitized erythrocytes is caused by direct action of the parasite on the erythrocyte, distorting its morphology, diminishing its elasticity and plasticity, and changing its surface properties. By the impaired capillaries flow and adhesion to the endothelium and other blood cells (forming aggregates, "rosettes"), obstruction supervenes. The results are thrombosis, anoxia, stroke, and tissue necrosis. In more serious cases, further endothelial damage produces increase in capillary permeability and even hemorrhages[10,11].

According to the humoral theory the action of non-specific vasoactive inflammatory substances producing changes in the capillary permeability results in compromisement of blood flow, impaired tissue perfusion and cellular hypoxia. Among these substances the tumor necrosis factor (TNF) and interleucine 2 (IL-2) stand out as mediators in the inflammatory process. This theory holds that the more severe cases of malaria, especially CM, are the result of an exacerbated inflammatory response of the host. There are evidences that patients and animal models that have developed CM had high serum TNF, in contrast to lower TNF levels in controls with mild clinical profiles. Moreover, repeated exposures to the parasite result in progressively milder disease with likewise decreasing levels of TNF [6,9-13].

Macroscopic examination of the brain in fatal cases reveals a moderate cerebral edema associated to petechial hemorrhages which are diffuse and occur predominantly in the white matter. There is also a discoloration of the cortex due to hemozoine (malarial pigment). Under microscopic examination the petechiae are seen to be ring-shaped hemorrhages surrounding the arterioles in the white substance[10,11].

The most typical clinical manifestation of MC is encephalitis presenting with impaired level of consciousness (stupor or coma), abnormal postures (decerebration, decortication), convulsions and retinal hemorrhages. CM often accompanies compromisement of other organs and systems: renal failure, shock, pulmonary edema, hepatic dysfunction, metabolic acidosis, hemorrhagic diathesis, severe anemia, sepsis and hypoglycemia. Intracranial hemorrhages, occlusion of the cerebral arteries, extrapyramidal symptoms, benign intercranial hypertension, and psychiatric disturbances are less commonly observed in CM[10-14].

In spite of clinical severity and high mortality, survivors have a good prognosis and even carriers of sequelae in the initial phase of convalescence tend to fully recover within six months of the event.

A common factor in most cases is the encephalitic form that results in a greater or lesser clouding of consciousness, depending on the severity of the pathophysiological process. During the acute phase of CM the identification of focal neurological signs is uncommon, either due to the diffuse nature of brain involvement in the disease, or to the extent of compromisement of other vital functions, what frequently renders the neurological examination inaccurate. Kampfl et al. reported a case compatible with secondary pontine myelinolysis which expressed by vertical nistagmus. The diagnosis was made by magnetic resonance and became a landmark so rare are reports of focal forms in the literature[15].

In the case reported herein there are some noteworthy features. A young patient with no known risk factors for stroke, coming from non-endemic region, developed a cerebral infarct during acute malarial infection. Thus, this stroke was regarded as a result of the malarial infestation and the mechanical theory seems the most suitable to explain the observed neurological compromisement. The acute arterial occlusion could be closer to the mechanical model of malaria where the distortion of the erythrocytes and the formation of “rosettes” could involve arteries of small diameter, despite the clear predilection for capillaries and venules. The humoral model is clearly less defined and does not appear to bear much significance to this case.

As atypical features, this case of malaria had a mild presentation without encephalitis and the brain damage was focal and permanent. A relationship between mild presentation and the short course of the disease that was readily diagnosed and treated might be suggested, but extensive clinical studies on malaria are still needed.

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