

Introduction

Cerebral malaria is defined in the WHO 1994 monograph as the "presence of an unarousable coma... exclusion of other encephalopathies... [and the] finding of asexual forms of *Plasmodium falciparum* in the blood film" is common in severe parasitemia (50% incidence) and carries a 20% mortality rate. Naïve adults and immune experienced children may be most susceptible. Conventional management strategies in many cases require transfusions to optimize blood flow. Parameters guiding the use of this and other therapies are incompletely established. This report evaluates the use of dynamic analysis of transcranial Doppler data to evaluate cerebral flow dynamics and perfusion in the critical care setting of 3 patients with cerebral malaria.

Patient Information

Three patients serving in the armed forces in Eastern Africa developed signs and symptoms of malaria and were transported following initial evaluation with blood smears revealing *Plasmodium falciparum* malaria, to the National Naval Medical Center (NNMC) Bethesda, Md. Two patients developed classic signs and symptoms of cerebral malaria and a third developed mental status changes confounded by pulmonary edema. These severe malaria patients had parasitemia 10x as great as that of the remainder of the cohort. Anemia, thrombocytopenia, hepatic injury and dysfunction, and EEG's consistent with diffuse cerebral dysfunction were present in all three patients at presentation to NNMC.

Patient No. 1

-Parasitemia 12%

-Somnolence following a 1 week prodrome of fever, nausea, vomiting. Following 1 day Quinidine became combative resulting in intubation.

Patient No. 2

-Parasitemia 15%

-Several days of fever, malaise, GI disturbance. Following 1 day Quinidine confused, combative resulting in intubation.

Patient No. 3

-Parasitemia 9%

-Developed respiratory distress and showed pulmonary edema after begun on Quinidine for fever and diarrhea. Intubated and sedated for respiratory failure.

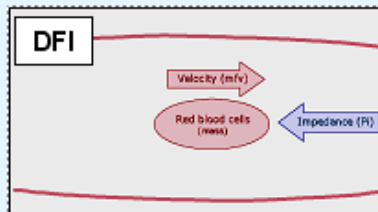
Methods

Patients had transcranial Doppler studies with meanflow velocity (MFV), pulsatility index (PI), and acceleration (SA).

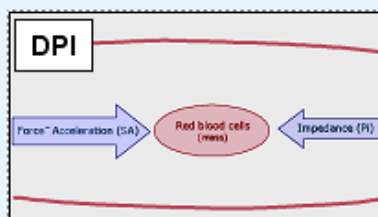
Dynamic Vascular Analysis (DVA) was performed on all Doppler spectral waves yielding the dynamic flow index (DFI), dynamic perfusion index (DPI) and the dynamic work index (DWI). The DVA indices relate the dynamical parameter of acceleration (that is a measure of vessel compliance) to MFV and PI.

3 Doppler studies from two patients in the acute phase and 4 Doppler studies from 3 patients in the convalescent phase.

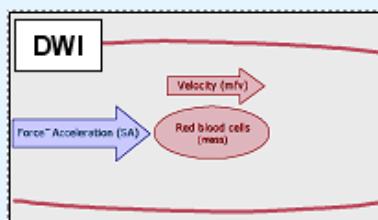
Correlations of DVA patterns with patients' clinical course were performed, and calculated indices were represented as aggregate mean of standard deviation compared to normative data collected at Wake Forest University in young male athletes of comparable age and race.



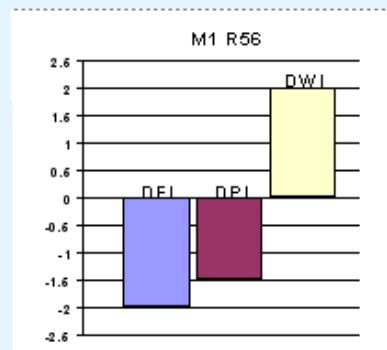
$DFI = MFV/PI$



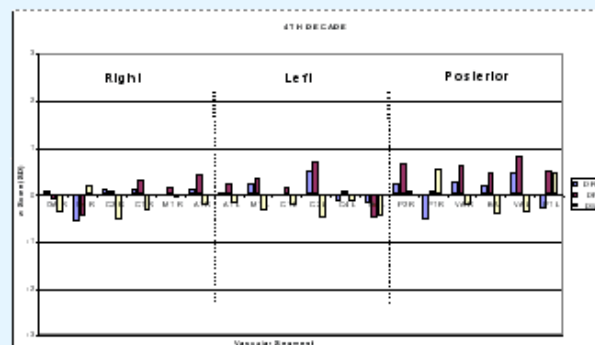
$DPI = \ln SA/PI$



$DWI = \ln SA/MFV$

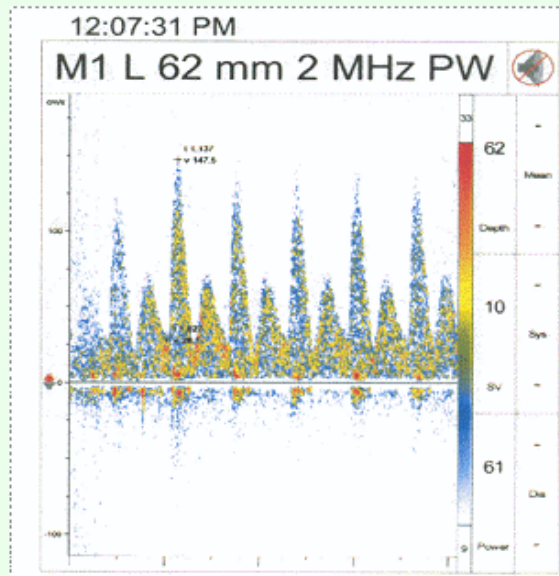


Combined, the three indices, related to mean values from a reference population, generate a segmental z-score bar graph output (above) for an ensemble of segments (below).

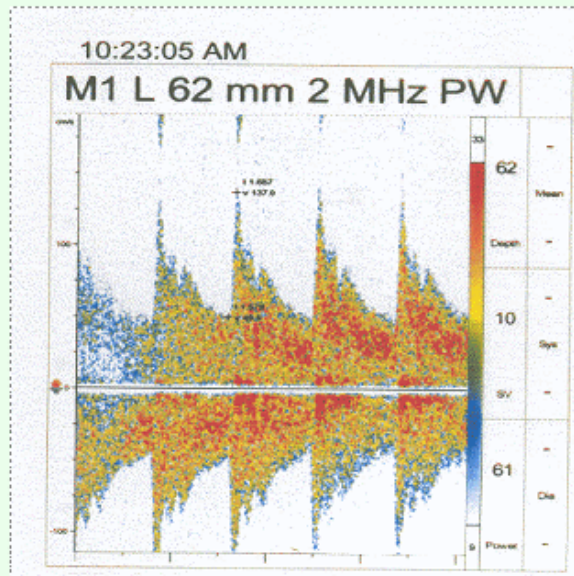


Findings

ACUTE

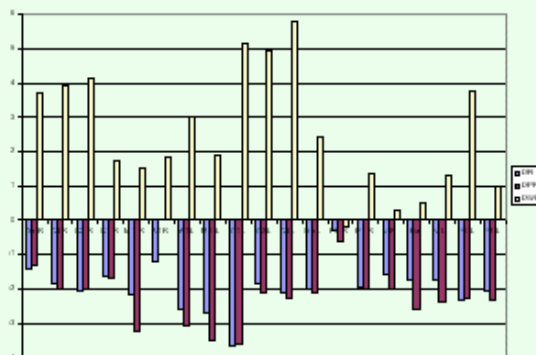


CONVALESCENT

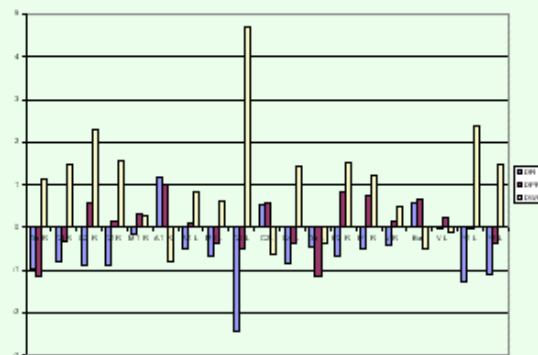


TCD spectral wave morphology differed between the acute and convalescent phases.

ACUTE



CONVALESCENT



DVA analysis with bar graph output shows quantitatively, the differences between acute and convalescent phases.

TCD with DVA revealed increased cerebral vascular impedance in all vessels suggesting the need to augment circulatory volume or raise systemic pressure during clinical management.

Patients were treated successfully with pressure and fluid management without the need for blood transfusions.

DVA indices normalized in the recovery phase.

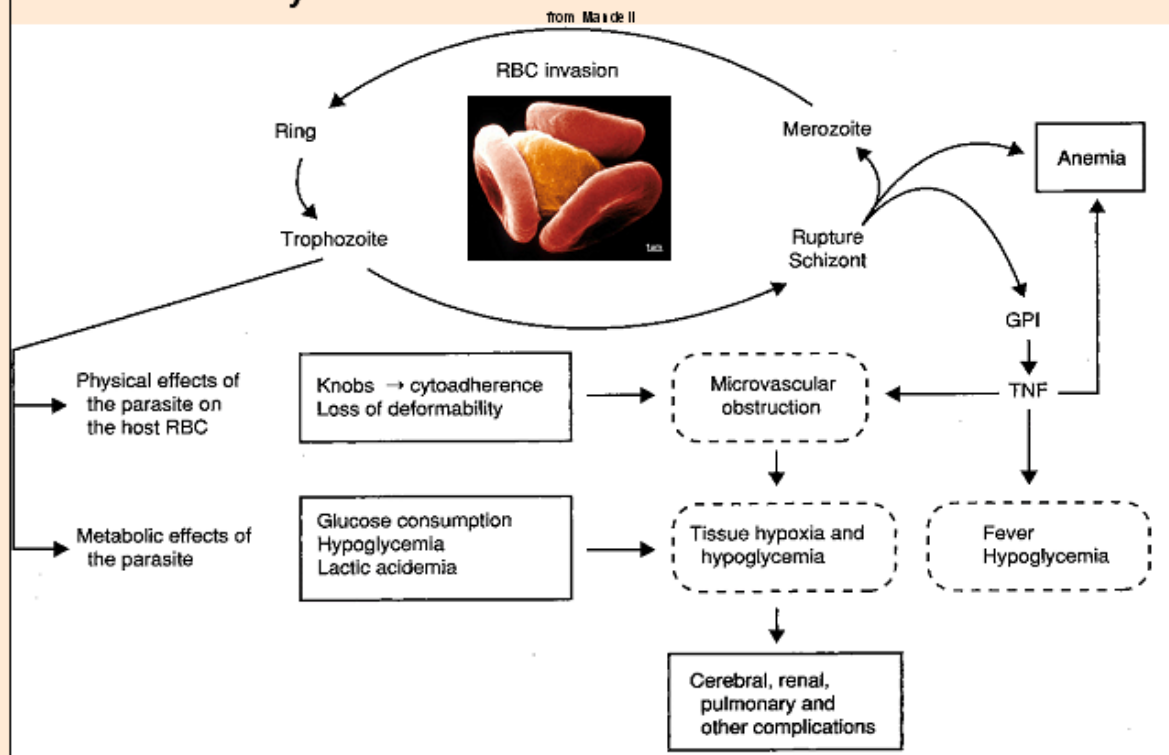
As the patients recovered, with improving clinical appearance and EEG, TCD with DVA revealed a hyperdynamic state suggesting hyperemia.

All three patients recovered following a course of parenteral quinidine and doxycycline in the intensive care unit.

Imaging studies in the acute phase confirmed the lack of cerebral edema.

Discussion

Cytoadherence and PfEMP1



The relationship between parasite activity and clinical disease in cerebral malaria is incompletely understood.

Rosette formation, platelet aggregation, and inflammation induce sluggish flow and obstruct the microvasculature.

As a result, vascular impedance is increased with objective changes noted as decreased DFI, DPI and an increase in the DWI.

Summary

Transcranial Doppler velocimetry was obtainable in the critical phase of cerebral malaria.

DVA indices revealing low flow and increased impedance of the capacitance vessels with an increased work index strongly suggest that the cognitive deficits in cerebral malaria resulted from microvascular occlusive disease and may prove valuable for future strategies in treatment.

Involvement of the ophthalmic arteries suggests a pan-vascular process.

Cerebral Malaria can be treated with conventional critical care management alone.

TCD with DVA may help direct fluid and pressure therapy to optimize cerebral blood flow in the critical care environment.

Dynamic Vascular Analysis (DVA) is the processing method for Doppler data provided by New Health Sciences, Inc., Rockville, Maryland 20850, (240) 453-0430. DVA, Dynamic Flow Index, DFI, Dynamic Altitude Index, DAI are trademarks of New Health Sciences, Inc.

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