Case Report

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Unusual CD4+ counts in cerebral malaria-a first of its kind

Abstract

Plasmodium falciparum malaria is recognized to be the deadliest of the four species of Plasmodium.[1] It has the ability to rapidly destroy the red blood cells and also can bind to other organs such as lung, kidney and brain. A major complication of *P. falciparum* is cerebral malaria. This form can lead to coma, neurological effects, and even death. The case report presented here describes a rare case of cerebral malaria with abnormal $CD4^+$ counts. It is common to observe such low counts in opportunistic infections, especially Human Immunodeficiency Virus (HIV). Only a handful of non HIV diseases have shown low CD4 counts indicating its exclusivity of occurrence.

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Case report

A 30 year old male patient presented with history of fever since three weeks associated with joint pain, altered sensorium and vomiting. The patient was diagnosed with malaria-*Plasmodium falciparum*. He was started on Artesunate for seven days along with broad spectrum antibiotics. He was conscious but not oriented. Later he had a sudden onset of respiratory distress and was intubated. Systemic evaluation showed the following:

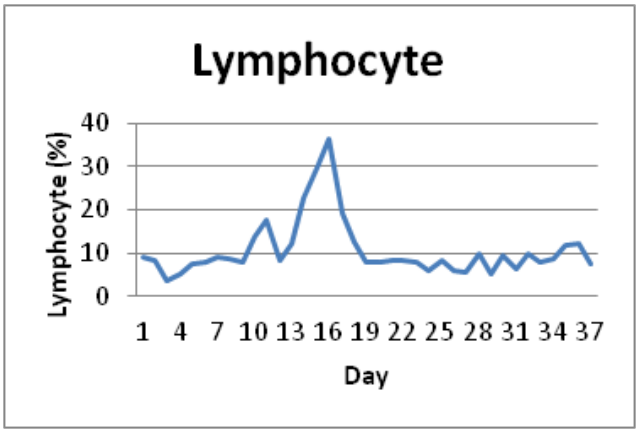
a. Heart rate: 80b/min

b. Blood pressure: 140/70 mmHg

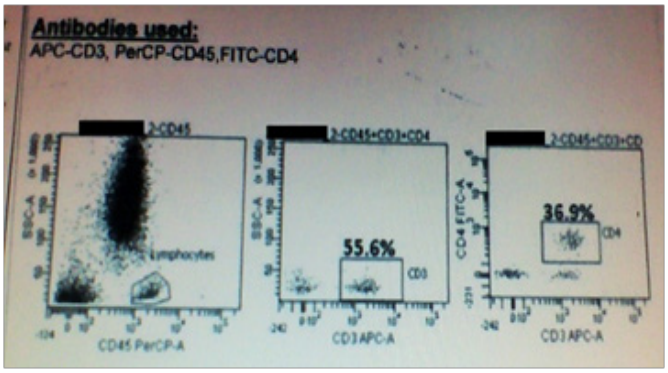
c. SPO_2: 100% on mechanical ventilation

d. Respiratory rate: 18/min

Examination of the respiratory system showed bilateral ronchi with scattered minimal crepitations. A CT chest was done indicating right pneumothorax. CNS examination showed a Glasgow Coma Scale of E2VTM2. Human Immunodeficiency Virus (HIV) screening test was positive and henceforth confirmatory test (MGIT, MTB PCR, ELISA-HIV) were done which reported as negative. In addition, the possibility of Pneumocystis carinii, yeast and Filamentous fungi were also ruled out. Other systemic examinations were within normal limits. CT of brain showed features suggestive of cerebral malaria. Lymphocyte values as shown in the table below were predominantly below normal or just above the normal lower limit. Platelet levels were gradually increasing and esinophils were above the upper limit and was fluctuating.



Since the initial screening for HIV test showed a positive result a CD4 count was done. The table below shows the results of the tests indicating an abnormally low $CD4^+$ count.



Subset	Obtained result
WBC count	10,100 cells/uL
Absolute lymphocyte count	388 cells/uL
T. Lymphocyte ($CD3^+$)%	55.6
T. Lymphocyte ($CD3^+$) absolute count	216 cells/uL
Helper/Inducer T.	36.9%
Lymphocytes ($CD3^+CD4^+$)%	
Helper/Inducer T Lymphocytes ($CD3^+CD4^+$)	143 cells/ul

Other parameters such as renal function tests showed mild increase in urea levels with normal creatinine. Liver function tests were abnormally elevated. In terms of electrolytes, magnesium and sodium levels were usually low or near the normal lower limit. Sources of infection varied and included pleural fluid, bronco-alveolar lavage, urine, and blood therefore indicating in due course sepsis. The patient's condition was worsening progressively and eventually leading to acute respiratory distress syndrome (ARDS). The final diagnosis of the patient was cerebral malaria, right sided empyema, ARDS, and sepsis after staying in the hospital for 47 days, the patient circummed to his death.

Discussion

CD4+ lymphocytopenia is a common condition of HIV infections. However such cases like in this report fall under the category of idiopathic CD4+ lymphocytopenia (ICL). ICL is defined as persistent CD4+ lymphopenia in the absence of HIV-1 or any other causes of immunodeficiency.[2] ICL is found in both adults and children, though more commonly in adults. Reviews of ICL's were seldom, however one study of significance was a 1992 study which reported an outcome of 39 of 47 patients studied had ICL.[3] An assortment of opportunistic infections, malignancies or autoimmune disorders has been reported with low counts. Previous ICL cases that have been reported are mentioned below:

Opportunistic infections	Malignancies	Autoimmune disorders
Cryptococcal meningitis Pneumocystis carinii pneumonia Cryptococcus neoformans Molluscum contagiosum Human papilloma virus Toxoplasmosis Histoplasmosis Hepatitis C Epstein- Barr virus	Non Hodgkin lymphoma Leptomeningeal lymphoma Intravascular cerebral lymphoma EBV- related lymphoproliferative disease and Burkitt lymphomas	Idiopathic thrombocytopenic purpura Autoimmune hemolytic anemia Sjogren's syndrome Systemic lupus erythematosus Antiphospholipid antibody syndrome Polyarteritis/vasculitis Psoriasis Erosive lichen planus of the scalp Autoimmune vitiligo Behcet's like syndrome

[may be consider as a supplementary table][4]

Many infections can lead to conditions of ICL because cells are being consumed in the process. Cerebral malaria occurs when spleen clearance of infected RBCs are not sufficient resulting in greater quantity of mature forms than non-complicated cases.[1,4] It is proposed in few studies that lymphopenia occurs due to the possible reallocation of T cells to the site of inflammation.[4,5] Studies have proposed this hypothesis for the case of malaria since *P. falciparium* is known to rapidly destroy red blood cells hence holding a possible explanation as to why this patient had ICL. For such patients the prognosis depends on the degree and duration of immune suppression and the presence and type of associated infections and comorbidities. Compared to previous case reports regarding opportunistic infections claiming that ICL may be due to a response to anti tumor necrosis factor, this case study differs in reason as to why ICL has occurred.[4] Earlier reports involved the presence of conditions such as opportunistic infections, malignancies, and autoimmune disorders. However this is a case of ICL in a patient with malaria who is neither infected of HIV nor with other malarial, opportunistic infection.

Conclusion

A case of cerebral malaria with low CD4+ counts is probably the first to be reported. In the absence of HIV, opportunistic infection, malignancies, and/or autoimmune infections it has been shown that CD4+ counts can decrease. The actual process of ICL still remains a mystery despite recent studies proposing various hypotheses. Such a topic is clearly in need of further investigation to understand the occurrence of ICL.

Acknowledgments

None.

Conflicts of interest

The author doesn't have any conflict of interest and there is nothing to disclose.

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