Chapter 20
Case Presentation of Epilepsy Secondary to Cerebral Malaria

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Abstract Epilepsy is the most common neurological disease in Uganda in both children and adults with a the prevalence of 2–5/1,000 of the general population and as high as 70 % in onchocerciasis volvulus affected populations. The causes are multiple but in the Ugandan and other African settings, the most common causes are usually infections in childhood (cerebral malaria, HIV etc.), birth trauma, brain injury in adulthood and substance abuse. Cerebral malaria, characterised by high fever, convulsions and /or coma is one of the deadliest forms of malaria and is caused by the Plasmodium falciparum malaria haemoparasite.

Epilepsy is a common sequel of cerebral malaria in highly endemic areas as is the case in most sub-Saharan African regions and it occurs mostly in children. It is postulated that red blood cells infected with malaria parasites sequestrate and clog brain capillaries which appear as petechial haemorrhages in the brain causing brain hypoxia and edema leading to convulsions and coma. Children with cerebral malaria are at risk of developing several adverse neurological outcomes including epilepsy, disruptive behaviour disorders (e.g. ADHD) and disabilities characterised by motor, sensory or language and learning deficits. These affect approximately 10 % of survivors of cerebral malaria and represent a form of injury to the brain or brain degeneration pointing. Epilepsy is highly stigmatised in Africa pointing to a need to educate the people and increase public awareness about epilepsy facts to demystify the disease so that the sufferers are not treated as outcasts and not to be stigmatized. This is in addition to malaria eradication programs.

Keywords Cerebral malaria • Epilepsy • Convulsions • Coma • Brain damage • Stigma • Prevention

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Abbreviations

HIV	Human Immunodeficiency Virus
MHC	Mental Health Clinic
SVD	Spontaneous Vertex Delivery
EEG	Electroencephalogram
RBS	Random Blood Sugar
WBC	White Blood Cells
FBC	Full Blood Count
FBS	Fasting Blood Sugar
Hb	Hemoglobin
CM	Cerebral Malaria

Introduction

Epilepsy is the most common neurological disease in Uganda in both children and adults as it affects individuals of all age groups. In Uganda the prevalence is 2–5/1,000 of the general population and as high as 70 % in onchocerciasis volvulus affected populations. The causes are multiple but in the Ugandan and other African settings, the most common causes are usually birth trauma, infections in childhood (cerebral malaria, HIV etc.), brain trauma in adulthood and substance abuse [1]. Cerebral malaria, characterised by high fever, convulsions and /or coma is one of the deadliest forms of malaria and is caused by the Plasmodium falciparum malaria hemoparasite. Epilepsy is a common sequel of cerebral malaria where there is a high prevalence of malaria as happens in Africa's malaria-endemic regions [1, 2].

Cerebral malaria is the most severe neurological complication of infection with Plasmodium falciparum. With >575,000 cases annually, children in sub-Saharan Africa are the most affected worldwide. Surviving patients have an increased risk of neurological and cognitive deficits, behavioral difficulties and epilepsy making cerebral malaria a leading cause of childhood neurodisability in the African sub-Saharan region [3]. The pathogenesis of the neurocognitive sequel is poorly understood: coma develops through multiple mechanisms and there may be several mechanisms of brain injury. It is unclear how an intravascular parasite causes such brain injury. However it is postulated that red blood cells infected with malaria parasites sequestrate and clog brain capillaries which appear as petechial haemorrhages in the brain causing brain hypoxia and edema leading to convulsions and coma. Understanding these mechanisms is important to develop appropriate neuroprotective interventions. This chapter examines the sequelae of brain injury in cerebral malaria, relating this to the pathogenesis of epilepsy as a long term outcome. The chapter explores prospects for improved neurocognitive interventions to reduce on this brain degeneration which is a leading cause of neuro-disability in sub-Saharan Africa [1, 4].

Cerebral malaria is a medical emergency demanding immediate diagnosis and treatment since it is highly fatal or often leads to long-term complications. This severe or complicated form of malaria affecting the brain, occurs predominantly in children, with a mortality rate of 15–25 %. It affects about one million children every year, primarily in sub-Saharan Africa. Coma, headaches, seizures and impaired consciousness are frequent manifestations of this infection. Children less than 5 years of age are particularly susceptible because of their low levels of immunity. It only takes one bite from an infected mosquito to contract the disease that directly affects the brain, causing fever, vomiting, chills, and coma [4, 5].

Although this type of malaria is most common in children living in sub-Saharan Africa, it should be considered in anybody with impaired consciousness that has recently travelled in a malaria-endemic area [6]. Cerebral malaria has few specific features, but there are differences in clinical presentation between African children and non-immune adults. Subsequent neurological impairments are also most common and severe in children.

The malaria parasite is usually found circulating in the blood stream causing fever, vomiting, chills and rigours. In severe cases, these parasites would go through the blood to the brain and the infected red blood cells sequester in the capillaries in the brain, and block these blood vessels, causing swelling of the brain (brain edema) [1, 2]. When this happens, the child may become unconscious, but a number of them recover to full consciousness. Also, other factors such as convulsions, acidosis and/or hypoglycemia can impair consciousness. Cerebral malaria is highly fatal and can kill rapidly when with poor management, or it is not recognised early or when it involves a non-immune person who has not been in a malaria-endemic area.

Children with cerebral malaria are at risk of developing several adverse neurological outcomes indicating brain degeneration. These include epilepsy, disruptive behaviour disorders (e.g. ADHD) and disabilities characterised by motor, sensory or language deficits. These affect approximately 10 % of survivors of cerebral malaria and represent a form of injury to the brain or brain degeneration.

Treatment of Cerebral Malaria

Cerebral malaria is a medical emergency. Treatment is tripartite:

- Specific antimalarial therapy (I.V quinine, quinidine, artimesinine etc.)
- Management of coexistent malarial complications including seizures, fluid and electrolyte imbalances, hypoglycemia, hyperpyrexia etc.
- Treatment of associated super infections [2].

At best, initial management should be in an intensive care unit. Generalized seizures can be followed by rapid neurologic deterioration, so prompt treatment is required. Subclinical or non-convulsive seizures should be suspected in patients with persistent coma [3]. Convulsions can be prevented by controlling fever and through judicious use of prophylactic anticonvulsants [4, 5].

It is important to support the family of a child suffering from Cerebral Malaria (CM). Many lay people in Africa may feel that CM is caused by supernatural forces (witchcraft) and attend traditional healers and faith healers to the detriment of the affected child as death may soon ensue. The long-term outcome of cerebral malaria is the highly stigmatised epilepsy and the affected children are often treated as outcasts in their communities and even families. The usual management of epilepsy should thus be multidisciplinary involving not only psychiatrists or neurologists, but also psychologists, social workers, nurses, O.Ts, educationists and the community (village) health team. Below is an illustrative case of epilepsy which was caused by cerebral malaria.

Case Report

Presentation and History

NP was a 21 year old female hair dresser, Catholic and single who stopped school in senior three (Grade 10). At the age of 4 years, she developed convulsions associated with a febrile illness which were managed as cerebral malaria at Nsambya Missionary Hospital in Kampala, Uganda. Months later, she developed recurrent unprovoked seizures but which she treated with local herbs as she invoked witchcraft for having brought on this "unfortunate disease" to her which she did not like to call epilepsy for fear of stigma. Nine years ago, she was formally diagnosed with epilepsy, after she presented to the Mulago hospital's Mental Health Clinic, (MHC). NP's fits were usually preceded by a right sided headache which lasted for 10 min, lip smacking, blank starring, thereafter paralysis of the left lower limb followed by paralysis of the left upper limb, then dizziness and eventually generalized tonic-clonic convulsions with loss of consciousness.

NP reported associated but occasional tongue biting, no foam formation and she denied a history of fecal or urine incontinence. The rate of the fits was 4 per week. She reported history of multiple injuries especially on the forehead following the falls. No burns. She denied a history of smoking, alcohol or use of any other drugs. She had no history of head trauma. She did not have Sickle Cell Disease.

NP had never had a history of hearing voices, seeing things or smelling things which other people could not hear, see or smell prior to the fits or after gaining consciousness. On gaining consciousness, she often wandered away from home. She missed many of her school days and could not concentrate in class. This interfered with her school performance. She faced a lot of stigma and segregation from her peers where no one wanted to sit next to her or discuss with her which led her to attain poor grades at school. Eventually, she dropped out of school in Grade 10.

NP was born normally by Spontaneous Vaginal Delivery from Nsambya Missionary Hospital in Kampala, Uganda. Her mother reported that labor lasted for only 5 h and the baby cried immediately and there was no need for resuscitation of the baby. Initially, she had normal developmental milestones and was not sickly in

her childhood till when she had the cerebral malaria, developed epilepsy and everything in her life changed. She was educated up to Senior Secondary 3 (Grade 10), quit high school and went to hair dressing vocational training where she obtained a certificate in hairdressing. People often described her as being reserved. She lived with her mother and was single. She had had a boyfriend for 2 years but who left her after finding out that she had epilepsy. She had no family history of mental illness.

Examination Findings

On physical examination all findings and systems were normal. On Mental Status Examination, in appearance and behavior, she was a young lady in a good nutritional state and who was well kempt with no mannerisms and no scars on her body. Her speech was normal, logical and coherent. Her mood and affect were normal and euthymic. She had no suicidal or homicidal ideations. Her thoughts were well connected with no of flight of ideas or loosening of associations and no blockage. There were no delusions, no obsessions, no overvalued ideas and no thought insertion or withdrawal. She was preoccupied with the stigma of her epilepsy illness and she lamented on how it had interfered with her schooling and relationships as well as her future plans including getting a spouse. She also worried about its chronicity and incurability and hence poor prognosis. Perceptually, she had no hallucinations, no illusions, no derealization and no depersonalization. In her cognition, she was well oriented in time, place and person. Her memory, immediate and 5-min recall, as well as intermediate, short and long term memory were all intact. Her judgment for safety, social situations and abstraction were all intact. She had normal average intelligence and her attention and concentration were intact. She had insight into her illness and lamented the problems it had caused her.

Diagnosis

A DSM IV-TR multi-axial formulation was carried out. On AXIS I she had Complex partial seizures with generalization. On AXIS II, there was no overt personality disorder; but she was withdrawn, isolative, socially avoidant and with low self esteem and low confidence. On AXIS III, she had past Cerebral malaria which was also on AXIS IV as her predisposing factor to the epilepsy. Her perpetuating and precipitating factors were not being on any antiepileptic medications and beliefs in the supernatural as causing her epilepsy. However, she was protected by having had some education, having a hairdressing vocation and a supportive mother. On AXIS V, she scored 80 %. She was currently functioning well, had her hairdressing job, could be self supporting and had been able to keep a boyfriend for over 2 years although he had left.

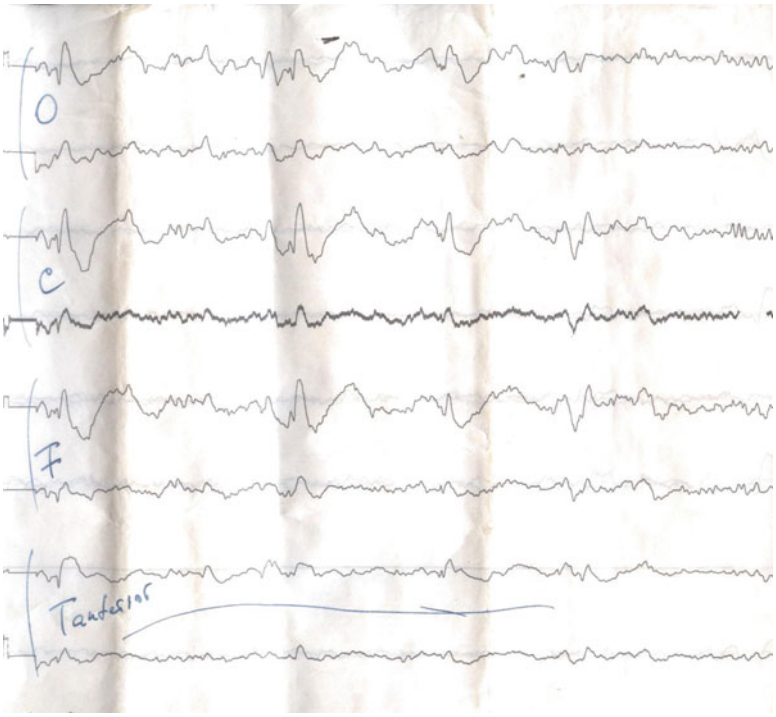

Fig. 20.1 EEG trace findings of NP

Investigations

The investigations carried out revealed normal CBC no haemoparasites, a FBS of 113 mg/dl, Hb electrophoresis-AS and her HIV and Syphilis serology were both negative. EEG findings showed mild diffuse slowing of activity and prominent paroxysmal abnormality consisting of slow waves and epileptiform discharges lasting from 2 up to 8 s in the left posterior temporal region (Fig. 20.1). The EEG diagnostic conclusion was Left Temporal Lobe epilepsy.

Treatment and Outcome

Before visiting the Mulago hospital MHC because her epilepsy illness, NP was being managed by traditional healers where she used to bath with herbs or take them orally. She had attributed what was happening to her to be witchcraft from her stepmother. At the Mulago hospital MHC, she was managed on carbamazepine and the frequency of her fits greatly reduced to only an occasional one once in a blue moon. She was initiated on carbamazepine and reviewed at monthly intervals as an outpatient.

NP and her family were psycho-educated about epilepsy, the fits, trigger factors, treatment and what to do with an aura. The epilepsy was demystified and its relationship to her childhood cerebral malaria was explained.

During her follow up on subsequent visits, she reported that the seizures had been adequately controlled to 2 fits a year. After 4 years on treatment, the carbamazepine dose was increased to better control the fits. Unfortunately, we could not do blood levels at Mulago hospital at the time. The patient was then followed up at 6 months intervals and she did well.

Discussion

This is a case of epilepsy secondary to cerebral malaria. The causes of epilepsy are multiple but the commonest in the sub-Saharan African setting are infections like malaria and onchocerciasis. This patient got convulsions in early childhood but later developed overt epilepsy as described above. The sequel of cerebral malaria may not be evident immediately after the infection but may occur years later. This patient she suffered the cerebral malaria at 4 years of age but the epilepsy developed at 9 years of age, 5 years later after the cerebral malaria.

When a child develops a chronic condition like epilepsy, their concentration and academic performance is often affected and many quit school as was this case. If they are still at school, many miss class. In this case, this was made worse by the fact that she used to be segregated at school and no one wanted to sit next to her in class, this is because in the African setting epilepsy is considered as a curse and the sufferers are often stigmatized and treated as outcasts in the community, even in their own homes.

There are several myths about epilepsy in the African setting. For example in Uganda there is a myth that the saliva of an epileptic is highly infectious. This translates into being avoided by others in fear of being infected. If an epileptic happens to get a fit even on a busy street, no one comes to his or her rescue due to such myths. In many African settings including Uganda, people have a tendency to seek alternative modes of treatment especially if diagnosed with chronic illnesses with no cure. This was seen in this patient who first sought treatment from traditional healers where she obtained herbs because the illness was attributed to witchcraft from the step mother.

In order to make a diagnosis of epilepsy, a high index of suscipicion is required as there are often no findings on examination or laboratory tests. In this patient the diagnosis was made basing on the history, In most Low and Middle Income Countries (LMIC) as are found in sub-Sahara Africa sophisticated investigations are not usually available, and in centers where they are available the cost is often prohibitive, forcing the clinician to rely on his/her clinical acumen. In epilepsy investigations, the EEG is informative in only 25–50 % of cases. The EEG confirmed the diagnosis in this patient. One also needs to carry out a series of investigations to look for any possible etiological factors responsible for the condition or at least to exclude them, e.g. HIV or Syphilis serology. Classifying the type of seizure is

useful in making the choice of drug for the patient. Thus focal seizures tend to do well on Carbamazepine or Sodium valproate. This patient responded well to Carbamazepine. Management is usually by psychiatrists and neurologists and is biological. However involving psychologists, social workers, nurses and mental health counselors is very important for the patient's and family's psycho-education and support.

Biological management involves use of various drugs selected depending on the seizure type and condition of the specific patient bearing in mind the drug interactions. A single drug at a low dose should be started with. If this is unable to control the fits, then the dose of the antiepileptic drug should be increased or consider adding another drug. This patient, she was started on a low dose of carbamazepine of 200 mg once a day, then to 400 mg nocte and lastly to 400 mg twice a day and the seizures were finally well controlled. There were no facilities to do serum carbamazepine levels.

Psychological management involved educating the patient about the disease, its trigger factors, aura and the need to comply with the treatment plus ways in which she could deal with the stigma associated with the illness. In this patient, the aura was the right sided headache and once experienced the patient stayed away from dangerous items like sharp instruments and fire to avoid being injured. However the trigger factor to her fits could not be identified.

Social management involves educating the care givers about the illness, teachers, and parents like it was done in this patient for support. For this patient, the mother was advised to keep her in school to get a vocation and she was able to attain a certificate in hairdressing thus enabling her to earn a living. The patient also neede social skills in how to be open and come out forthright in handling relationships when affected by a stigmatized condition.

Conclusion

Epilepsy in Africa is mainly due to infectious causes followed by trauma (birth injury, HIV, Syphilis etc.). These are all highly preventable and, therefore, point to the need to control them and manage them urgently and effectively in order to bring down the number of epileptic cases. This case illustrated brain degeneration from Cerebral Malaria, a disease wiped out in western countries, hence posing a challenge to Ugandans to also eradicate the malady. There is also need to educate the people and increase public awareness about epilepsy facts to demystify the disease so that the sufferers are not treated as outcasts and not to be stigmatized.

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