Case Report

Challenges in the diagnosis and management of sleeping sickness in Tanzania: a case report

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Abstract: In Tanzania sleeping sickness presents a serious threat to human health with a country-wide average of 400 cases reported annually. Both wild and domestic animals have been found to play a significant role in the epidemiology of sleeping sickness. Serengeti National Park in northern Tanzania, has experienced a number of sleeping sickness epidemics since 1922. The epidemics were associated with abundant game animals in the areas and *Glossina swynnertoni* was incriminated as the main vector. However since 2001 there has been no case of sleeping sickness reported from the park. This case report highlights on the possibility of resurgence and challenges in the diagnosis and management of sleeping sickness in Serengeti. A 38 years old Tanzanian man working in the Serengeti National Park who had experienced various tsetse bites was presented with a febrile condition and history of unsuccessful case management at different health facilities. Blood and cerebrospinal fluid (CSF) samples were examined for the presence of trypanosomes using wet film, Field's stain and concentration techniques. *Typanosoma brucei rhodesiense* were detected in both the blood and CSF samples. The patient was treated successfully with melarsoprol. The results of this case study highlight the possibility of resurgence of sleeping sickness in the park hence calls for the need to create more awareness among the community and clinicians. There is need for early reporting to health facility and strengthening the diagnostic capacity of healthcare facilities in and around national parks endemic for sleeping sickness.

Key words: Diagnosis, treatment, sleeping sickness, trypanosomiasis, Tanzania

Introduction

Sleeping sickness also known as Human African trypanosomiasis is a disease of human which exists in two forms and is caused by infection with either *Trypanosoma brucei rhodesiense* (acute sleeping sickness, endemic in East and South Africa) or *T.b. gambiense* (chronic sleeping sickness, endemic in West and Central Africa) (Welburn *et al*., 2001). In Tanzania sleeping sickness presents a serious threat to human health with an annual incidence of 400 cases (Mcharo & Kitua 2001). Tanzania has experienced several major epidemics of sleeping sickness since the disease was first documented at the turn of the last century (Kihamia *et al*., 1991). The animal reservoir for *T. b. rhodesiense* in Tanzania comprises both wild animals and domestic livestock, all of which are incriminated to play a role in maintaining the disease (Mwambu & Mayende, 1971).

Game parks in Tanzania have long been considered to be low-risk areas for sleeping sickness (Ponce de Leon *et al*., 1996). However the number of cases of sleeping sickness reported among tourists visiting the Tanzanian National Parks increased from six cases between 1998 and 2000 to 13 in 2001 (Kaare *et al* 2006).

Initial outbreaks of sleeping sickness occurred in Ikoma in the north-western part of Serengeti National Park in 1922 and Maswa in the southern part in 1919-1921 (Davey, 1924). The outbreaks were associated with abundant game animals in the areas and *Glossina swynnertoni* was incriminated as the main vector (Swynnerton, 1923, 1925). Then the Tanganyika government instituted rigorous control measures including clearing of vegetation, regrouping of isolated villages in reclaimed land, isolation and treatment of patients to prevent spread of infection, health education, destruction of wild animals, and closure of goldmines in Ikoma-Serengeti area. These measures led to a significant decrease in the incidence of the disease in the mid 1950s and early 1960s (Onyango & Woo 1971). The disease did not disappear completely as there was resurgence in 1964 (2 cases), 1965 (1 case), 1966 (4 cases), 1967 (6 cases), 1968 (14 cases) and 1969 (6 cases) (Moloo *et al*., 1971). This was followed by three decades during which no case was reported. By 1993, the Ikoma sleeping sickness focus was designated as inactive (Kilonzo & Komba 1993). A mass screening survey of 3,216

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individuals conducted in 2006 within SENAPA and the villages bordering the park revealed no any sleeping sickness cases (L.E. Matemba, *unpubl*.). This case report highlights on the possibility of resurgence and challenges in the diagnosis and management of sleeping sickness in Tanzania.

Case presentation

A 38-year-old Tanzanian man who has been working in Serengeti National Park since 1998 had a febrile condition that was clinically and symptomatically suspected to be a case of malaria at a dispensary in the Serengeti National Park in December 2007.The case was unsuccessfully managed using sulfadoxine pyrimethamine, amodiaquine and coartem in that order, at different times. Because of poor health improvement, the patient went to a hospital in Arusha complaining of somnolence, fever and headache. He was diagnosed microscopically to suffer from malaria. The patient returned home to complete a coartem dose that was given at this hospital.

The patient stayed at home with persistent febrile condition and headache for two weeks. Then he went to a referral hospital in Mwanza complaining of high fever, severe headache and sleep disorder. He was diagnosed to be suffering from malaria and meningitis and was hospitalised for three weeks. During this time the patient developed hallucination. Thereafter, following health improvement the patient was discharged and went back home.

After a week he had a fatigue, fever and severe headache once again. He went to the nearby hospital in Mara region where he had his blood sample tested microscopically positive for malaria. Following the administration of anti-malarial, the patient recovered and was discharged. However, thereafter he experienced sleep disorders and went back to the hospital in Mwanza. He was diagnosed to suffer from malaria and severe sleep disorders. The patient was treated with anti-malarial drugs and was instructed to complete the dose at home. The health condition did not improve. The patient was then advised by his family members to test for HIV/AIDS. The test was done and the results were negative.

Thereafter the mental disorder resurged with hallucination and loss of memory more pronounced. The patient reported back to Serengeti National Park dispensary from where he was referred to a nearby hospital in Mara (where he was once diagnosed with malaria) where the results of blood sample analysis indicated that the patient was suffering from the early/first (haemolymphatic) stage of sleeping sickness. However, staging of the disease was not performed at this hospital to ascertain the central nervous system involvement for the late/second (encephalitic) stage of the disease essential for the correct choice of treatment.

Because there were no drugs for managing cases of sleeping sickness in Mara, the patient was referred to Tabora Medical Research Centre in Tabora for further management in March 2008. Narrating his history, the patients reported experiencing intermittent sleep disorder (from January to March 2008) that was accompanied with general body weakness, loss of appetite and day and night sweats. He further recalled to have received several tsetse fly and mosquito bites during his stay in Serengeti since 1998 although he had never suffered from sleeping sickness before. Although the patient was distressed, he was still alert and oriented. On clinical examination, he had fever (38.2^{o}C) and his blood pressure was 110/70 mmHg. The posterior cervical and axillary lymphnode palpation findings were normal. Determination of the packed cell volume (PCV) was carried out using the technique described by England *et al*. (1980).

Wet film preparation, Field's stain and haematocrit centrifugation methods were employed in the examination of blood samples for the presence of trypanosomes. A drop of blood was applied on duplicate slides that were soon examined microscopically for the trypanosome movements under a cover slip at magnification of 10 times and 40 times. A drop of blood was applied on a slide to make thin and thick blood smear (each in duplicate) that were air dried. A drop of oil immersion was applied on the smear and the examination for the presence of trypanosomes was done using light microscope at the magnification of 100 times.

Haematocrit centrifugation technique was conducted as described by Woo (1970). After centrifugation, the capillary tubes were examined for the presence of trypanosomes, by direct examination of the buffy coat/plasma junction using light microscope at the magnification of 10 times. CSF sample was collected by lumbar puncture. Staging of the disease was carried through the determination of total white blood cell (WBC) count and demonstration of the parasites in the CSF (WHO 1998). White blood cell count was carried out using Neubauer hemacytometer and a method described by Cattand *et al* (1988) was adapted in the detection of the parasites in the CSF. Five millilitres of the collected CSF was centrifuged using hematocrit centrifuge at 4,000rpm for 10 minutes. Then the supernatant was removed and the sediment was taken by capillary force into two microhaematocrit tubes and centrifuged again using the procedure similar to that described above for the PCV determination.

The PCV was 36% and the results of a peripheral blood smear for malaria were negative, but *Trypanosoma brucei rhodesiense* were detected in the thin blood smear (1 parasite per field). Microscopic examination of cerebrospinal fluid (CSF) revealed presence of trypanosomes (one per field at x100 magnification) and total white blood cell count of 127cells/µl. The results from the CSF indicate that the patient was in the second/late (encephalitic) stage of the disease.

The patient was hospitalized at Tabora Regional hospital to complete a course of melarsoprol that was administered in incremental doses to 3.6mg/kg, in three series of three daily doses, each followed by a 7-day rest period i.e. Series 1=1.44, 1.8 and 2.16mg/kg/day; rest for seven days then Series 2= 2.52, 2.88 and 3.24mg/kg/day; rest for seven days then Series 3= 3.6 mg/kg/day for the last three injections. A follow-up monitoring was carried out during the time of hospitalisation. After the patient had received the first and second series of treatment, the PCV was 38%, the results of blood smears became persistently negative for trypanosomes and body temperature was 36.5 ^{o}C and blood pressure was 110/60mmHg. The appetite had improved during this time and the patient was more alert and able to perform light physical exercises. After completion of the third series dosage, the blood pressure was 110/70mmHg and PCV was 38%. The patient recovered successfully without obvious side effects resulting from melarsoprol and was discharged after 24 days of hospitalization.

Discussion

Serengeti National Park has been designated as amongst inactive sleeping sickness foci because of an absence of reported cases since 2002. The current case of sleeping sickness highlights the possibility of the resurgence of this disease in Serengeti National Park. *T. brucei rhodesiense* infection causes high fever and systemic symptoms days after the infectious bite and progresses from early haemolymphatic to late central nervous system disease over weeks to a few months (Greenwood & Whittle, 1980). However, the transition from the early to the late stage is not always distinct in *T. brucei rhodesiense* infection (Atouguia, 2000). The definitive diagnosis of sleeping sickness requires detection of the causative parasite in the blood and/or cerebrospinal fluid of the patient. This relies on conventional techniques such as lymph node puncture, blood film examination, or various more elaborate techniques to concentrate parasites in the blood and CSF (Bailey & Smith, 1992). The combination of clinical manifestations and context of a geographical location where sleeping sickness is endemic are key diagnostic clues.

To differentiate between haemolymphatic and encephalitic stages, essential for the correct choice of treatment when the trypanosomes have been detected/ not detected in blood or lymph, the diagnosis needs staging by lumbar puncture. Most health facilities in Tanzania have inadequate capacity in human resource and diagnostic services. Clinical diagnosis, which is the mainstay of most diagnosis in the country, may lead to misdiagnosis. Finding malarial parasites in the blood of a patient with sleeping sickness as it was with the described case is not unusual (Malele *et al*., 2006), and can mislead clinicians, diverting their attention from the diagnosis of trypanosomiasis and other haemoparasites. The non-specific nature of many of the clinical features makes it imperative to exclude (from sleeping sickness) other infections such as malaria, tuberculosis, HIV infection, leishmaniasis, toxoplasmosis, hookworm infection, typhoid, and viral encephalitis (Atouguia *et al*., 2000). Like in our case, a particular pitfall is that antimalarial treatment may actually reduce the fever due to sleeping sickness, thus confounding and delaying the correct diagnosis (Atouguia *et al*., 2000), and these two conditions may also co-exist. This may partly explain the reasons for the delay in the confirmatory diagnosis of this sleeping sickness case.

Accurate staging of sleeping sickness is critical because failure to treat a patient with CNS involvement will lead inevitably to death from the disease, yet inappropriate CNS treatment in an early-stage patient carries a high risk of unnecessary drug toxicity. The increased WBC count beyond the normal values and presence of the trypanosomes in the CSF of the patient indicates CNS involvement. However, when there is an increase in WBC count in the CSF and a microscopic examination reveals no evidence of trypanosomes, then the particularly useful technique to rule out the CNS involvement is the inoculation of specimens of blood, CSF, or lymph node aspirate into mice or rats, in which parasitaemia may take up to 2 weeks to develops (Aerts *et al*., 1992). The high cost and the long delay before obtaining the result are definite obstacles to routine field use of this technique. The persistently negative blood smear for trypanosomes following the administration of the second series dosage of melarsoprol indicates the effectiveness of the drug against trypanosomes in this patient.

There are some challenges with treatment of sleeping sickness. For the treatment of late-stage sleeping sickness, melarsoprol is the only drug of choice (Panosian *et al.*, 1991). Although this patient did not develop any obvious adverse effect related to melarsoprol or resistance to melarsoprol during the period

of hospitalization, this does no rule out the possibility of experiencing some adverse effects such as intermittent/persistent backbone-ache and headache. Another major drawback of melarsoprol therapy is the specific treatment regimen that is based on empiric development, and typically a course of three series of three intravenous injections of increasing doses spaced by rest periods (WHO, 1998). This empiric treatment regimen results in a long hospitalization period of up to a month, which poses major social and economic burden to the patients and their care givers.

Conclusion

The recent occurrence of sleeping sickness case in Serengeti National Park signifies the presence of active focus, most likely with the infections perpetuating in the tsetse flies and wild animals as reported recently by Kaare *et al.* (2007). These findings highlight the importance of the Serengeti as a potential sleeping sickness focus, with risks to local communities as well as tourists. Local communities living in and around the Serengeti ecosystem are exposed to high risk of infection due to their interaction with tsetse and wild animals. Moreover, though the hospitals and other health facilities are equipped with facilities for microscopic diagnosis of trypanosomes, the fact that sleeping sickness is not anticipated may result in delays in making the early diagnosis and prompt treatment. These observations suggest the need to raise the profile and awareness of sleeping sickness among both medical personnel and the community. There is thus a strong need to strengthen the capacity health workers and healthcare facility in the diagnosis and management of sleeping sickness.

Consent

Written informed consent was obtained from the patient for publication of this case report.

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