Human African trypanosomiasis in two historical foci of the estuaire province, gabon: A case report

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Abstract
Human African Trypanosomiasis (HAT) is an infectious disease due to a protozoa parasite of the Trypanosoma genus. In West and Central Africa, this disease is caused by the subspecies Trypanosoma brucei gambiense. Several foci of this disease are currently active and causing the death of hundreds of people in endemic areas. In this article, we report two cases of gambiense HAT in one Indonesian and one Gabonese men in two historical foci of Gabon in 2019. Both patients had fever with temperatures above 38°C, an altered state of consciousness, cachexia, and multiple dermabrasions on the abdomen related to scratching lesions. The diagnostic revealed second-stage infection of both patients with T. b. gambiense; this result was confirmed by a polymerase chain reaction assay. Despite treatment with a combination of eflornithine and nifurtimox, as recommended by the World Health Organization for late-stage T. b. gambiense HAT, one of the two patients died. Thus, these cases highlight the importance of early HAT diagnosis and prompt patient care to fight effectively against this disease.

Keywords
Human African trypanosomiasis, Trypanosoma brucei gambiense, Noya, Komo, northwestern Gabon

Introduction
Human African Trypanosomiasis (HAT) is a neglected tropical disease transmitted by tsetse flies that occur in sub-Saharan Africa.1,2 Two forms of this disease exist: the slow-progressing form, caused by Trypanosoma brucei gambiense and the faster progressing form, caused by Trypanosoma brucei rhodesiense.3 T. b. gambiense accounts for 98% of reported cases of sleeping sickness.

In Gabon, trypanosomiasis is endemic4 and the disease has been reported in seven of the nine provinces during the last century.5 The Komo-Mondah department, in Estuaire Province, is identified as the most active foci of HAT in Gabon with an average of 20 cases per year.6 Indeed, the Gabon estuary is known to be an overflowing tsetse-infested area7 and the extension of cities has brought tsetse-populated sites closer to urban populations. Colonization of these areas for diverse activities exposes people to HAT due to the contact between human and Glossina flies becoming more regular.

Here, we report and describe two cases of HAT due to T. b. gambiense in the towns of Kango and Cocobeach in Estuaire Province in the northwestern area of Gabon.

Cases presentation
The first patient, a 28-year-old man native to Gabon was living in the Noya region (Figure 1). This patient was received and examined in April 2019. He was characterized by a severe and violent headache with a fever of 39°C. He took paracetamol for symptoms relief, but no improvement was noted. HBV, HCV, HIV, syphilis, and malaria testing were all negative. The diagnosis was done by microscopic analysis.

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and revealed the presence of trypanosomes in aspiration fluid of the ganglion (Figure 2). Later on, the diagnosis of phase 2 HAT was confirmed based on the presence of trypanosomes in the cerebrospinal fluid (CSF). The cerebrospinal fluid analysis revealed clear liquid and pleocytosis at 27/mm³. He was admitted at the intensive care unit due to altered state of consciousness. The clinical examinations on admission revealed cachexia; multiple dermabrasion on the abdomen related to scratching lesions; impaired consciousness with a Glasgow Coma Scale of 9/15 and a meningeal syndrome, and motor deficit. The biological assessment revealed severe anemia with a hemoglobin level of 8.7 g/dL, an important inflammatory syndrome with a C-reactive protein (CRP) at 243 mg/L and leukocytes: 15,700/mm³. The brain computed tomographic (CT) scan showed a meningoencephalitis aspect with multiple capsulo-lenticulo-insular hypodensities. The patient received a specific combination treatment of eflornithine and nifurtimox (NECT) for the HAT as recommended by the World Health Organization (WHO) for second-stage T. b. gambiense infection for all endemic countries. During the course of intensive care treatment, the patient died of complications, eschars stage 4 wound, and malnutrition.

The second patient, a 41-year-old man, originally from Indonesia, living in Gabon for the past 8 years, in the Kango town in the Komo department (Figure 1) working in the Gabonese forest for the Olam company. He was admitted in July 2019 to the Hospital for altered state of consciousness. Upon his arrival at the hospital, the clinical picture was marked by intermittent fever (peak of temperature at 39.7°C) associated with chills, headaches, polyarthralgia, sleeping disorders and we found also this patient with acute mastoiditis. After a microscopic analysis which was negative, an analysis of the CSF revealed the presence of trypanosomes by the card agglutination test for trypanosomiasis (CATT +) (+1/16)
and analysis of the cerebrospinal fluid reveals clear crystalline fluid, glycorrhachia at 2.76 mmol/L with a capillary blood glucose of 4.78 mmol/L, CSF protein level of 1.7 mmol/L, and a leucocytes count of 9,000/mm³. The presence of trypanosoma parasites in CSF suggests second-stage HAT. The blood count showed neutrophils (2,070/mm³), hemoglobin (10 g/dL), and a CRP at 123 mg/L. As with the first patient, several clinical examinations were done (HBV, HCV, HIV, syphilis, malaria test), but all were negative. However, cytobacteriological urine examination revealed the presence of Enterobacter aerogenes. The patient was treated with ceftriaxone antibiotic for its bacterial infection. Regarding the treatment of HAT, the patient received NECT as per WHO recommendations. The neurological evolution was favorable, marked by a normal consciousness after treatment. The patient return to his country safely.

To confirm the diagnosis of HAT, polymerase chain reaction (PCR) was performed to characterize the *Trypanosoma* species. The sequences obtained (around 1,200 nucleotides) have been deposited in Genbank under the accession numbers MT460094-MT460095. We used maximum likelihood (ML) as described previously,⁸,⁹ to examine the relationship of both sequences obtained with the different trypanosome species known. The tree was built (Figure 3) using MEGA software.

**Figure 3.** Phylogenetic relationships among *Trypanosoma* parasites sequences obtained and the sequences from Genbank. Sequences obtained from the different patients are included in red. The sequences reported in this study were deposited in Genbank under the following accession numbers: MT460094-MT460095.
Discussion

HAT is one of the most complex parasitic diseases occurring in Africa. West and Central Africa are endemic areas and the major agent of HAT in this region is *T. b. gambiense.*\(^{10}\) Trypanosomiasis caused by *T. b. gambiense* is a chronic disease with progression to a final central nervous system stage that occurs over months or even years.\(^ {10}\) Several cases of infection were reported in people living in Gabon\(^ {11–13}\) and HAT remains a public health problem. Recent result shows that Komo-Mondah, Noya, and Komo are also active foci.\(^ {6,12}\)

In this article, we reported two cases of second meningo-encephalitic stage HAT, characterized by the trypanosomes crossing the blood-brain barrier and invading the central nervous system, caused by *T. b. gambiense* in two patients of different origins (African and Asian). The identified cases where from people residing in Komo-Kango and Noya region. These regions are known to be high-risk zones for transmission of *T. b. gambiense.*\(^ {12}\) Thus, our result supports previous studies that reported human infections with this *Trypanosoma* parasite species.\(^ {3,11}\) Gabon reported to the WHO 16 new cases in 2018.\(^ {14}\) This confirms that transmission is still active. Infection of the patients with *Trypanosoma* parasites could be explained by the fact that they have been exposed to tsetse fly bites (both males and females are hematophagous) during their activities in the forest or mangrove during the day. Thus, because of the human activities in forest and mangrove, populations in contact with these areas are more likely to be exposed to HAT infections. Setting up a monitoring system and/or awareness campaigns in these localities is likely to be beneficial to reduce the HAT burden. But also to prevent a possible re-emergence of this disease in populations living in regions at risk. Moreover, infected individuals who remain undiagnosed due to inadequate surveillance could constitute a reservoir, thus favoring the upholding of the disease. Moreover, it would be important to identify non-human reservoir hosts of this parasite, evidence suggesting animals could play an important part in sustaining these historical foci active.\(^ {15}\)

Regarding clinical presentations, our study revealed that clinical symptoms seem to be similar for both patients. Indeed, we observed that patients presented intermittent fevers with peaks around 39°C, arthralgia, and headache were present. Some signs such as the presence of an altered gait, incontinence, a reduced Glasgow Coma Scale, that is, altered state of consciousness, could suggest a neurologic evolution of the disease.\(^ {16}\) However, a small difference in symptom between the two patients exist, the first patient presented impaired consciousness with Glasgow Coma Scale 9/15 and a meningeal syndrome. The second patient had acute mastoiditis. These symptoms are not really for HAT. Thus, early-stage symptoms may be vague and non-specific which may delay the clinical suspicion and diagnosis\(^ {17,18}\) and with no clear clinical indication to distinguish between the two different stages of the disease, disease can evolve from hemolymphatic to encephalitic stage insidiously.\(^ {17}\)

The two patients received a combination of eflornithine and nifurtimox (NECT) which is the first-line anti-parasitic treatment recommended by the WHO for the treatment of second-stage of HAT due to *T. b. gambiense.*\(^ {19–21}\) After treatment, only one patient (Indonesian) recovered successfully with the improvement of his biological markers CRP and hemoglobin. However, the second patient who was native of Gabon died, despite that the clinical portrait was improving. We believe that this is due to the late management of the disease, indeed this patient presented himself with an advanced infection showing general health degradation, second-stage of HAT with altered state of consciousness, severe anemia and a high CRP.

Conclusion

We report here two cases of HAT caused by *T. b. gambiense* in two historical foci of the disease. This case report testifies that HAT remains a public health problem in Gabon and that prompt management of infected people is necessary to prevent mortality and morbidity. Despite the death of one of two patients reported here, this study reveals the effectiveness of the treatment recommended by WHO in case of HAT infection. However, there remains a pressing need to develop a strategy for surveillance of this disease. To finish, we suggest that the Public Health Department of Gabon engage in awareness campaigns for at-risk populations living near high-risk areas of transmission such as the forest, mangrove, swamp, and also for workers or people transiting through those areas.

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Author contributions

All authors made substantial contributions to the investigations presented in this manuscript. LB and BAI drafted the manuscript, analyzed, and interpreted the data. MGD supervised this work, drafted, and revised the manuscript. BBM analyzed the samples and revised the first draft. BAI and LGM participated in sanitary surveillance of patients in the acquisition of the clinical data with contributions of JRN. All authors have critically revised and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

This study was done according to the Declaration of Helsinki II. It was approved by the Ethics Committee of our institute (Hôpital d’Instruction des Armées Omar Bongo Ondimba).
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**Informed consent**

Written informed consent was obtained from the patient and family of the deceased patient.

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