International Journal of Infectious Diseases 79 (2019) 34–36

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Human African trypanosomiasis caused by *Trypanosoma brucei gambiense*: The first case report in China

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ARTICLE INFO

Article history:
Received 18 July 2018
Received in revised form 31 October 2018
Accepted 3 November 2018
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Human African Trypanosomiasis
Diagnosis
Treatment
Relapse

ABSTRACT

We report the first imported case in China of human African trypanosomiasis (HAT), caused by *Trypanosoma brucei gambiense*, in a sailor returning from Gabon in 2014. The diagnosis was delayed and relapse led to death, despite treatment with eflornithine, as recommended by the World Health Organization for late-stage HAT. This case shows that early diagnosis of HAT and close follow-up with proper retreatment are critical.

Introduction

Human African trypanosomiasis (HAT), also known as sleeping sickness, is a vector-borne parasitic disease endemic to Africa during the 20th century (Anon, 2018). The disease is transmitted by the tsetse fly and can be fatal if untreated or treatment is delayed. We report the first confirmed imported case in China of late-stage HAT, caused by *Trypanosoma brucei gambiense*, in a sailor returning from Gabon in 2014.

Case report

A 45-year-old Chinese sailor, returning from Gabon, was admitted to The First Affiliated Hospital of Nanjing Medical University on September 15, 2014, after experiencing 21 months of low-grade fever, 5 months of progressive lymphadenopathy, and 2 weeks of somnolence. The patient had worked as a sailor in inland navigation near Omboue and Ndougou in western Gabon, Africa, from July 8, 2010 to July 15, 2014. At the end of 2012, he had suffered a fever (peak temperature of 38 °C) accompanied by skin pruritus, but no rash, chills, headache, cough, or night sweats. In the following years, he had continued to suffer repeated episodes of mild fever and had undergone several medical examinations in Gabon and China. HIV testing and blood cultures were both negative; Plasmodium was not found in the blood smear. The diagnosis was not clear and no treatments were administered.

In April 2014, the patient presented lymphadenopathy; the swellings in the axilla, neck, and inguinal regions ranged from 0.5 cm to 3 cm in diameter. The patient also complained of fatigue, apathy, paralysis of the lower limbs, progressive weight loss of 20 kg, visual deterioration, and somnolence in recent months. He was not actively eating and had experienced changes in mental status, cognitive impairment, and occasional urinary incontinence.

Lymph node biopsies were performed at two different hospitals in China on July 16, 2014 and August 31, 2014 to rule out lymphoma. Both biopsies were considered to show lymphoid reactive hyperplasia. An enhanced abdominal computed tomography scan revealed lymphadenopathy in multiple regions of the abdomen, as well as splenomegaly. Bone marrow smears showed no obvious abnormality. However, microscopic analysis of blood smears revealed the possibility of African trypanosomiasis. The patient was then admitted to The First Affiliated Hospital of Nanjing Medical University for further medical evaluation and treatment.

Examination upon admission showed a patient with apathy and somnolence. A mini-mental state examination (MMSE) indicated moderate cognitive impairment (the patient scored 15 out of 30). Another lymph node biopsy showed the presence of trypanosomes in the smear (Figure 1). A rapid diagnostic test was positive for HAT-specific antibody (Büscher et al., 2014; Kennedy, 2013).

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https://doi.org/10.1016/j.ijid.2018.11.004

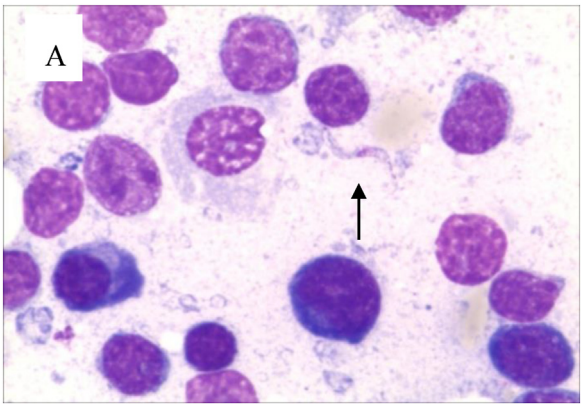

Figure 1. *Trypanosoma brucei gambiense* is shown (arrow) in a section from the lymph node biopsy.

Peripheral blood and cerebrospinal fluid (CSF) tested positive for *T. b. gambiense* DNA. CSF testing showed IgG of 306.00 mg/l, a white blood cell count (WBC) of 60×10^6/l, mainly with small lymphocytes, and protein of 1.39 g/l. The patient was then diagnosed with late-stage HAT (meningoencephalitis stage) and was given a standard regimen of intravenous eflornithine (100 mg/kg every 6 h for 14 days) (Eperon et al., 2014). By the end of treatment, the patient was fully conscious and his sleep pattern was normal. His MMSE score increased to 28 (recall −1, language −1), indicating minimal cognitive impairment. The lymph node swelling was reversed and the patient's weight increased by 2 kg. Routine CSF testing showed a WBC of 35×10^6/l, protein of 0.59 g/l, and IgG (CSF) of 253.0 mg/l.

Two months after the end of treatment, the patient complained of gait instability and recurrence of his sleep disorder. CSF testing showed a WBC of 70×10^6/l, protein of 1.46 g/l, and IgG of 174.0 mg/l. Due to the clinical manifestations of relapse, including the progressive increase in CSF WBC (Mumba Ngoyi et al., 2010), a half course of treatment with eflornithine was administered (Pépin et al., 2000). The patient's condition improved rapidly, however long-term follow-up was suggested.

At the beginning of the following year (January 6, 2015 to April 1, 2015), the patient's CSF WBC dropped below 10×10^6/l, protein fluctuated between 0.6 g/l and 0.76 g/l, and HAT-specific antibody was negative in the blood. At this time, the patient was completely asymptomatic.

On July 3, 2015, the patient's CSF WBC rose to 93×10^6/l. From August to September of 2015, the gait instability reappeared and the patient was frequently fatigued. He was advised to return to the hospital. On October 3, 2015, the patient suddenly lost consciousness at dinner. He was hospitalized as an emergency, with his condition deteriorating rapidly. Routine CSF tests showed a WBC of 210×10^6/l, protein of 1.39 g/l, and IgG (CSF) of 364 mg/l. The patient's blood oxygen saturation level dropped and he was placed on a ventilator. He was treated intravenously with 132 mg melarsoprol (2–3.6 mg/kg/day, on days 1, 2, 3, 4, 11, 12, and 13) provided by the World Health Organization (Kennedy, 2013). Unfortunately, treatment was unsuccessful; the patient showed brain death and died on October 28, 2015.

Discussion

HAT caused by *T. b. gambiense* is endemic in West and Central Africa. This disease is characterized by two stages: hemolymphatic presentation and central nervous system (CNS) involvement. West African trypanosomiasis is a chronic disease with progression to the final CNS stage occurring over months or even years. A case of HAT caused by *T. b. gambiense* that was confirmed by lymph node biopsies is reported here. The patient had no diagnosis until the disease progressed to the late stage. Although HAT is not endemic in China, when an unexplained fever occurs along with lymphadenopathy, HAT should be considered if the patient has visited Sub-Saharan Africa (Sudarshi and Brown, 2015; Kennedy, 2013). As the density of trypanosomes in lymph nodes is higher than that in peripheral blood, specimens should be taken from multiple sites, especially from enlarged lymph nodes. If a HAT-specific antibody is available, serology is a useful screening test (Büscher et al., 2014; Kennedy, 2013).

Eflornithine, commonly known as the 'resurrection drug', is the first-line anti-parasitic treatment, as it is able to pass through the blood–brain barrier and is an effective drug recommended by the World Health Organization for the treatment of late-stage HAT (Anon, 2018; Eperon et al., 2014; Kennedy, 2013; Sekhar et al., 2014). The patient was treated with a standard regimen and a half course regimen of eflornithine (Kennedy, 2013; Pépin et al., 2000). He recovered successfully and his CSF WBC dropped to 10×10^6/l (Kennedy, 2013). However, the patient unexpectedly relapsed and progressed rapidly to brain death. Previous research has shown that positive lymph node aspirate and a CSF WBC $>50 \times 10^6$/l at 6 months post-treatment are predictors of treatment failure (Mumba Ngoyi et al., 2010). The patient's diagnosis was delayed, his lymph nodes were reduced but did not disappear, and CSF WBC was $>50 \times 10^6$/l at 6 months after the second course of eflornithine treatment. Changes in the CSF WBC and increases in CSF protein and IgG content are all indicators of relapse. Therefore, the CSF WBC, CSF protein, and CSF IgG should be monitored during follow-up. It has been reported that a negative blood test with HAT-specific antibody post-treatment does not always indicate cure. Thus, blood testing for HAT-specific antibody should not be used to monitor the treatment outcome (Lejon et al., 2010).

This case shows that early diagnosis and close follow-up with proper retreatment are critical for survival in patients with HAT.

Although HAT is not endemic in China, a large number of people from the country have been visiting Africa in recent years, and there remains a pressing need to develop a strategy for early diagnosis, timely treatment, and medication reserves for HAT.

Acknowledgements

We would like to express our thanks to Jiangsu Provincial Institute of Parasitic Diseases, National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, the World Health Organization Representative Office in China, and Department of Pathogenic Biology at Nanjing Medical University.

Funding sources

The authors received no specific funding for this work.

Ethical approval

This work was approved by the patient's widow.

Conflict of interest

All authors declare no potential conflict of interest.

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