A case of delayed diagnosis of East-African trypanosomiasis in a Dutch traveller

Wijsman, C.A.; Hanssen, J.L.J.; Scheper, H.; Visser, L.G.; Lieshout, L. van

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CA Wijsman, MD, PhD[1], J Hanssen, MD[2], H Scheper, MD[1], LG Visser, MD, PhD[1], L van Lieshout, PhD[3,4]

[1] *Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands*
[2] *Department of Internal Medicine, Alrijne hospital, Leiderdorp, The Netherlands*
[3] *Clinical Microbiology Laboratory, Department of Medical Microbiology, Leiden University Medical Center, Leiden, The Netherlands*
[4] *Department of Parasitology, Leiden University Medical Center, Leiden, The Netherlands*

Abstract
We present a case of East-African trypanosomiasis (EAT). In travellers with fever returning from endemic countries, EAT should always be included as differential diagnosis when malaria has been ruled out. Clinical suspicion of EAT in malaria-negative patients should lead to prompt examination of thin/thick smear diagnostics.

Introduction

East-African trypanosomiasis (EAT) is a very rare travel-associated disease with only a handful of patients outside of Africa every year. In Africa, incidence of EAT is currently around 70 patients per year (1). Awareness of the clinical presentation is of crucial importance for clinicians evaluating travellers returning from endemic countries with fever. Furthermore, distinction between the two clinical phases of EAT is essential in guiding appropriate therapy. Here, we report a patient with EAT after which we will discuss pitfalls in diagnostics and management of patients, which may help clinicians in daily practice to diagnose and treat these patients according to the current standard of care.

Case description

A 56-year-old Dutch woman presented at the emergency department of a peripheral hospital with nausea, vomiting, headache and a fever since five days. Twelve days before presentation she had returned from a holiday trip of 17 days in Tanzania and Kenya where she visited several wildlife parks (Masai Mara, the Ngorongoro and Serengeti). She had used anti-malarial prophylaxis and had not noticed any mosquito or fly bites. On examination she appeared moderately ill without fever. Blood examination showed no abnormalities and the malaria rapid test was negative. A presumptive diagnosis of gastroenteritis was made and she was sent home. The absence of malaria parasites was confirmed by examination of the thick smear at the academic laboratory the next day. Two days after the initial presentation she was admitted with persistent nausea, headache and malaise. This time physical examination revealed fever. There was no lymphadenopathy. Laboratory examination showed a leukocyte count of 1.46 x 10e9/L, thrombocyte count of 48 x 10e9/L and a mild hepatitis with a bilirubin of 51 umol/L (of which 33 umol/L conjugated). Urine examination revealed mild haematuria. Ultrasound of the abdomen was normal. The malaria rapid test was again negative. Revision by microscopy of the blood film the next day revealed trypomastigotes with a density of 1-10 parasites per field in the thin smear. After transferral to the academic hospital a painless erythematous plaque was noticed on her left wrist with a softened centre without central necrosis and a diameter of approximately four cm (figure 1). A lumbar puncture showed one leukocyte, normal protein and absence of trypanosomes. These findings confirmed the diagnosis of a first stage East-African trypanosomiasis. Immediate treatment with suramin was indicated. Due to the non-

availability of suramin in the hospital and nation-wide, treatment with pentamidin 300 mg was started intravenously. Suramin was delivered within 14 hours after admission by transportation from The Swiss Tropical Institute in Basel, after which treatment was continued with a challenge dose of 100 mg suramin followed by another 400 mg the same day, 500 mg on day two, and 1000 mg on day 8, 15 and 22. Apart from some pleural effusions, no adverse events occurred. The amount of trypanosomes in the repeated thick smears showed a decline from day two of treatment, with complete absence of trypanosomes on day four. Retrospectively performed PCR confirmed the microscopy findings, except that *Trypanosoma* DNA levels became undetectable two days after the negative microscopy. The patient improved gradually, and after one week she was discharged from the hospital. At follow-up several months after discharge, she still had mild amnesia and increased fatigue, but had otherwise recovered.

Discussion

We describe a case of East-African trypanosomiasis (EAT) in a traveller returning from Tanzania and Kenya. In our case there was a delay in diagnosis. Firstly due to the lack of suspicion for human African trypanosomiasis (HAT) and secondly because the use of rapid malaria antigen diagnostics postponed immediate analyses of blood microscopy. A detailed travel history and knowledge of the clinical course of East and West-African human trypanosomiasis are of crucial importance for timely diagnosis and treatment. The distinction between East- and West African human trypanosomiasis can be made by clinical presentation and geographic distribution of the parasite (figure 2, adapted from (2)). With the exception of Uganda and Democratic republic of Congo, there is a strict geographic separation between the two parasites. Our patient's travel history including visits to wildlife parks was congruent with EAT. The clinical course of our patient with malaise, fever, headache and cytopenia is typical of the first haemolymphatic stage of EAT. Her presentation shortly after return from travel was consistent with the short incubation time (within days/weeks) seen with EAT. As progression to the second meningo-encephalitic stage may be seen within weeks, we proceeded with analysis of cerebrospinal fluid to establish or exclude CNS involvement, defined as pleiocytosis (>5 leukocytes, trypanosomes or protein content above 370 mg/L). As clinical symptoms are insufficiently specific to distinguish the progression from first to second stage, lumbar puncture should always be performed. The first choice therapy in patients with EAT is suramin which should be given with the shortest possible delay. Due to initial unavailability of suramin, treatment was started with pentamidine 300 mg intravenously, the second drug of choice if suramin is unavalaible. The reported treatment failure rate with pentamidine is approximately 7% for EAT (3). If our patient would have had CNS involvement, the arsenical melarsoprol would have been the first choice, as this drug penetrates the blood-brain barrier. Melarsoprol however is highly toxic with serious metabolic encephalopathy in 10% and a case fatality rate of 5%. In West-African human trypanosomiasis, pentamidine is the drug of choice for first stage human trypanosomiasis, whereas in second stage treatment with nifurtimox-eflornithine has shown good efficacy and safety in recent studies (4, 5). Of note, without treatment both forms of HAT are usually fatal. This illustrates the need for correct definition of type and stage of the disease to guide appropriate therapy. The case report demonstrates the importance of awareness of the possibility of EAT in travellers returning from East-Africa when malaria is ruled out. With the increasing use of malaria rapid diagnostic tests as first line laboratory diagnosis for malaria this awareness becomes even more important. Any delay in microscopic blood examination may increase the risk of progression of EAT to the second stage. Future replacement of blood microscopy by malaria DNA detection procedures within routine

diagnostic laboratories based in non-endemic countries will further increase the risk of misdiagnosing EAT infections. Therefore, clinical suspicion of EAT in malaria-negative patients should lead to prompt examination of thin/thick smear diagnostics and this suspicion should be communicated to the laboratory performing the blood examination. Finally, this case emphasises the need to have access to suramin therapy as soon as possible after the diagnosis is established.

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The authors declare that there is no conflict of interest regarding the publication of this paper.

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Supplemental materials.

Figure 1. Lesion on the patient’s left wrist.

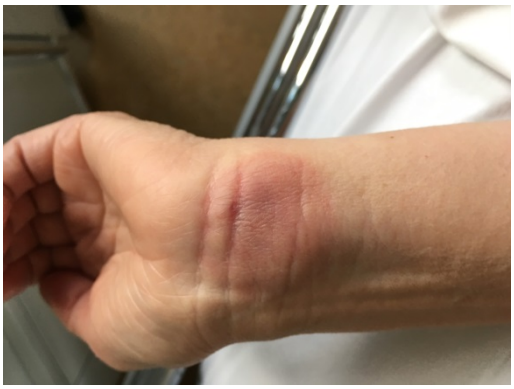

Figure 2. Geographical distribution of East- and West-African Trypanosomiasis (adapted from (2) with permission from the authors)