CLINICAL IMAGES

Awaking a sleeping epidemic

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Two patients with African sleeping sickness (SS) presented to the neurology unit, Pretoria Academic Hospital, during 2004 and 2005. SS has shown a recent resurgence, with epidemics in the Sudan, Angola and the Democratic Republic of Congo. The number of infected people in Africa is currently estimated at more than 500 000. According to the World Health Organization (WHO), about 20 *Trypanosoma brucei gambiense* and 30 *T. b. rhodesiense* infections are diagnosed yearly outside endemic areas in Africa. Migration, tourism, peacekeeping and military interventions and the re-emergence of SS epidemics might increase these numbers.[1]

The electroencephalogram (EEG) is often useful in the diagnosis of coma and delirium, but has not been widely used in the diagnosis of SS. The EEG is proposed as a novel way to follow disease progression, treatment response and treatment-induced encephalopathy.

Case 1

A 27-year-old man presented with a 4-month history of fatigue, loss of appetite, intermittent severe headaches, excessive daytime sleepiness, loss of concentration and insomnia. He had travelled to Malawi 8 months before admission. His temperature was 38.8°C, he had a palpable hepatomegaly and an unremarkable neurological examination although his cognitive response was slow. Diagnosis of African trypanosomiasis was made on a Giemsa-stained blood smear (Fig. 1).

Shortly after admission the patient had a tonic-clonic seizure, with post-ictal confusion. Treatment with suramin was started and repeat blood smears after 48 hours were clear of trypanosomes. The cerebrospinal fluid (CSF) showed no trypanosomes but a total protein level of 1.2 g/l, glucose 2.1 mmol/l, 4 polymorphs and 82 lymphocytes. WHO-recommended treatment with melarsoprol was started.[2]

Since no trypanosomes were isolated from inoculated mice the diagnosis of West African trypanosomiasis (WAT) was made. Eflornithine was unavailable and treatment with melarsoprol continued. The patient recovered well and returned to the UK.

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Five months after discharge he presented to the Hospital for Tropical Diseases in London with fever, sleepiness and an active CSF. Diagnosis of a relapse was made which posed a diagnostic dilemma – recurring *T. b. gambiense*. Treatment with eflornithine was given which cleared his condition.

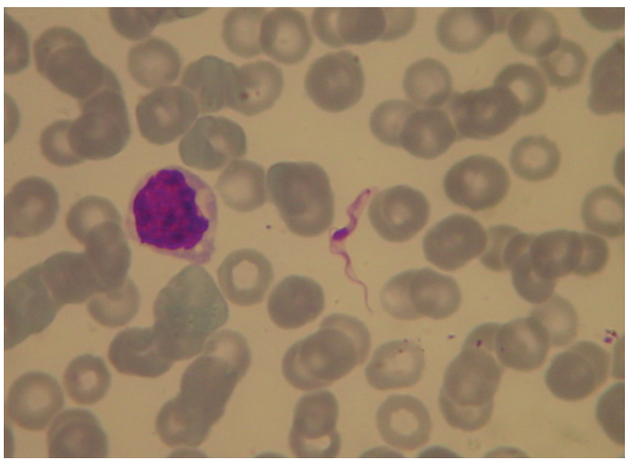

Fig. 1. Giemsa smear (case 1) showing extracellular trypanosomiasis parasite in the peripheral blood.

Case 2

A 53-year-old man presented with a 2-week history of fever, headache and episodic confusion. He was a farmer from Kariba in Zimbabwe where he had been treated for malaria without any clinical improvement. He gave a history of multiple tsetse fly bites but did not have a chancre. A Giemsa-stained blood smear showed *Trypanosoma* spp. On admission his temperature was 39.4°C, but the general examination was unremarkable. He was very sleepy but easily arousable. The diagnosis of East African trypanosomiasis (EAT) was confirmed by isolating *T. b. rhodesiense* from inoculated mice. Treatment with suramin was started and repeated Giemsa-stained blood smears did not show any trypanosomes. The following day he had a fatal cardiac arrhythmia, probably due to myocarditis.

Our first patient had a series of EEG recordings. These indicated a low-voltage mixed-frequency background with episodic, generalised but frontally dominant irregular delta activity (Fig. 2). Follow-up showed a gradual improvement in the frequency of the background. The second patient had an EEG recording shortly after admission showing mild slowing of the background activity with similar episodes of irregular frontally dominant delta activity.

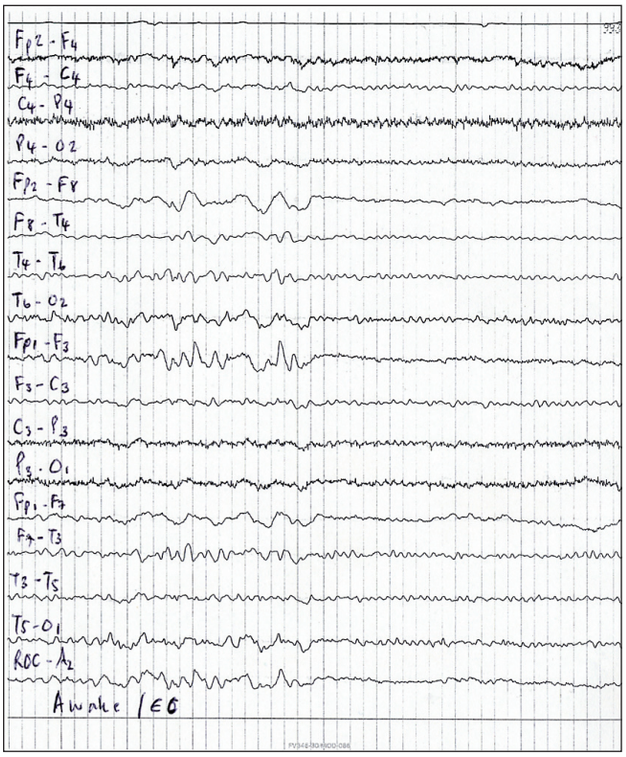

Fig. 2. EEG of case 1 showing mixed-frequency low-voltage background activity with frontally dominant bursts of high-voltage irregular delta activity.

Discussion

WAT, caused by *T. b. gambiense*, is transmitted by tsetse flies inhabiting the forests of Central and West Africa. EAT, caused by *T. b. rhodesiense*, is transmitted by tsetse flies found in the savannah and woodland areas of Central and East Africa.[3] Patients present with a two-phase illness – haemolymphatic and neurological. The course in WAT is more protracted and the outcomes usually more favourable than in EAT.

Giemsa-stained smears of peripheral blood, bone marrow, lymph node aspiration or chancre fluid are used to detect trypanosomes. Serial specimens should be examined as parasitaemia levels may vary.[4] Concentration methods increase the chances for detection (quantitative buffy coat, Becton-Dickenson, NJ).[4] Treatment decisions should be based on demonstration of the parasite since serological assays have variable sensitivity and specificity.[5]

In vivo inoculation of mice distinguishes between EAT and WAT as *T. b. rhodesiense* but not *T. b. gambiense* trypanosomes will be detected.[3]

The diagnosis of WAT in our first patient was surprising, as he had not travelled to Western endemic areas. This raises the possibility of cross-migration of tsetse fly species to other areas.

A lumbar puncture is mandatory after parasite clearance of peripheral blood to exclude stage II (neurological) disease and to individualise treatment. Suramin and pentamidine do not penetrate the central nervous system (CNS) adequately and are only used for the haemolymphatic stage.

The arsenic-based drug melarsoprol is currently the only effective treatment for second-stage EAT but causes an encephalopathic syndrome in 5 - 10% of patients, with a case fatality rate of 50%, and resistance has also been described.[3] Eflornithine should be used in WAT patients with CNS disease.

Development of treatment options is limited. Nifurtimox, a drug used to treat Chagas disease, may be effective, but has not yet been validated for use. Oral eflornithine, the diamidine prodrug DB 289, and the pre-clinical development of megazol seem promising.[5]

1. Cattand P, Jannin J, Lucas P. Sleeping sickness surveillance: an essential step towards elimination. *Trop Med Int Health* 2001; **6:** 348-361.
2. Burri C. Efficacy of new, concise schedule for melarsoprol in treatment of sleeping sickness caused by *Trypanosoma brucei gambiense:* a randomised trial. *Lancet* 2000; **355:** 1419-1425.
3. Kirchhoff LV. Agents of African trypanosomiasis (sleeping sickness). In: Mandell GL, Bennet JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 6th ed. Philadelpia: Elsevier, 2005: 3165-3170.
4. Bailey JW, Smith DH. The use of the acridine orange QBC technique in the diagnosis of African trypanosomiasis. *Trans R Soc Trop Med Hyg* 1992; **86:** 630.
5. Fairlamb AH. Chemotherapy of human African trypanosomiasis: Current and future prospects. *Trends Parasitol* 2003; **19:** 488-494.