CASE REPORT

West-African trypanosomiasis in a returned traveller from Ghana: an unusual cause of progressive neurological decline

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SUMMARY

West-African trypanosomiasis caused by *Trypanosoma brucei gambiense* is a rare imported infection presenting with somnolence, lymphadenopathy and wide-ranging neurological symptoms. A 67-year-old Caucasian man presented with a 10-month history of cognitive deterioration, ataxic gait, somnolence and urinary incontinence. His symptoms had progressed more rapidly over the course of a month prior to admission. Serological testing confirmed a diagnosis of West-African trypanosomiasis. The patient was successfully treated with eflornithine and made a good recovery. West-African trypanosomiasis should be considered in the differential diagnosis of unexplained cognitive decline in those with a relevant travel history. If left untreated, the condition is universally fatal.

BACKGROUND

Progressive neurological deterioration is not an uncommon scenario faced by clinicians. This case highlights the importance of taking a full and accurate travel history from all patients. As international travel becomes increasingly frequent and accessible, rare imported infections may be seen. Trypanosomiasis is relatively easily diagnosed and treated with a high-cure rate.

CASE PRESENTATION

A 67-year-old Caucasian man with a background of type 2 diabetes presented to hospital with rapidly progressive cognitive deterioration, an unsteady gait, urinary incontinence and increased somnolence. The patient was a retired engineer who had been visiting Ghana for a few weeks annually over the past 4 years. He had been developing a caravan park in a rural coastal region of western Ghana and had never travelled further than 60 km inland. He had not travelled elsewhere in Africa. He had suffered numerous insect bites on his trips. He cut short his last visit to Ghana, 2 months before admission to hospital, as he was feeling cold, shivery and persistently sleepy. Symptoms began about 10 months prior to hospital admission. There were several instances of uncharacteristic memory problems such as being unable to find the way to his mother's care home by car at a location he knew well. He became more irritable and developed balance problems, falling once in his garden. His symptoms progressed more rapidly over the month prior to admission to hospital.

On admission, he was confused, drowsy, with a variable Glasgow Coma Score of 7–14, unsteady on his feet and doubly incontinent. He had a global deficit of cognition particularly affecting the frontal lobe executive function and visuospatial skills. There was significant short-term and long-term memory impairment with an abbreviated mental score (AMT) of 1/10. Initially, he was able to obey 2-stage commands and was apraxic, more so on the left. He became more ataxic with global hypertonia and hyper-reflexia over a period of 2 weeks. He fell several times on the ward. The rest of his examination was unremarkable, and in particular he had no lymphadenopathy or skin lesions. He was afebrile throughout.

INVESTIGATIONS

Routine laboratory studies revealed a thrombocytopenia of $137 \times 10^9/L$ with normal haemoglobin and white cell count. The erythrocyte sedimentation rate was 23 mm/h and C reactive protein <5 mg/L. A vasculitic screen, including an antinuclear antibody and an antineutrophil cytoplasmic antibody, and HIV testing were negative. An MRI of the brain demonstrated diffuse white matter T2 hyperintensity involving the frontal and parietal white matter with further changes in the internal capsules and some patchy changes in the brainstem (figure 1A, B). Patchy grey matter changes were present in the globus pallidus and both thalami. There was no pathological meningeal or parenchymal enhancement or haemorrhage. EEG showed a slow background rhythm. Initially, the lumbar puncture revealed a cerebrospinal fluid (CSF) protein level of 1.97 g/dL (0.15–0.45 g/dL), glucose 3.8 mmol/L (no serum reference taken), 5000 red blood cells, 35 lymphocytes and 3 polymorphonuclear leucocytes. The raised red blood cell count was compatible with a traumatic tap. The opening pressure was not recorded. The bacterial and mycobacterial culture and PCR for herpes viruses were all negative. Given his travel history, an immunofluorescent antibody test (IFAT) was performed and was positive for antibodies to *Trypanosoma brucei gambiense* with a titre of 1:400.

DIFFERENTIAL DIAGNOSIS

Confusion and drowsiness may be due to intracranial or extracranial causes and may be due to infectious or non-infectious causes at these two sites. This patient's neurological features suggested an intracranial problem and the long time course

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Figure 1 (A) Axial T2 MRI of the brain before treatment. Arrows demonstrate the cerebral white matter T2 hyperintensity. (B) Axial T2 MRI slice through the pons before treatment. The white arrow demonstrates patchy T2 hyperintensity in the pons. The black arrow demonstrates an incidental arachnoid cyst. (C, D) Post-treatment Axial T2 MRI of the brain. Images demonstrate improvement in the white matter changes. However, there are residual changes in the cerebral white matter and the pons, almost 18 months after treatment.

suggested an indolent infection, degenerative disease or a progressive malignant process. The MRI and CSF findings quickly pointed to an inflammatory and infectious problem, despite his being persistently afebrile with a normal C reactive protein. Tuberculosis was a possibility, but his travel history provided a critical clue to consider trypanosomiasis.

TREATMENT

The patient was transferred immediately to the Hospital for Tropical Diseases, London, and started on a 14-day course of eflornithine 100 mg/kg 6-hourly. Further investigation of CSF revealed a weekly positive trypanosomal IFAT of 1:32, but PCR and microscopy were negative. CSF IgM was raised at 0.06 g/L. (Normal ranges: CSF IgM <0.046 g/L, serum IgM 0.5–1.9 g/L.) By day four of treatment, the patient was less drowsy, although his AMT was still 1/10. By day 10, improved cognition and alertness were noted. On day 12, he was able to follow two-stage commands, and on day 18 his AMT was 6/10. Continence

began to improve, although he remained unsteady on his feet. His admission was complicated by an arterial thrombus on the right leg.

OUTCOME AND FOLLOW-UP

He was transferred back for rehabilitation 3 weeks later at which time his Mini Mental State Examination (MMSE) was 15/30 and GCS was maintained at 15/15. At the time of discharge home 2 months later, his MMSE was 29/30. He is now independently able to perform activities of daily living and can walk unaided, although he has had a number of falls. He has occasional lapses of memory and some urinary incontinence persists. The patient has declined follow-up lumbar punctures.

Follow-up MRIs were performed after 2 and 18 months. At 2 months, despite clinical improvement, there was no significant change. By 18 months, there had been significant improvement in the white matter hyperintensity in all areas, but background residual changes remained (figure C, D).

DISCUSSION

Human African trypanosomiasis (HAT), or sleeping sickness, is a purely African disease caused by two morphologically identical subspecies of trypanosomes—*Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense*—that are transmitted to humans by tsetse flies (*Glossina spp.*).¹ West-African trypanosomiasis (WAT) is endemic to western and central Africa but now has disappeared from most West-African countries. In a 2004 report, the WHO recorded no cases in Ghana after the year 2000, although the disease was present in neighbouring Cote d'Ivoire to the west.² About 20 cases of WAT are diagnosed annually in Africans who have migrated outside endemic areas.³ WAT is extremely rare as an imported infection in short-term visitors to Africa.⁴

After infection by a tsetse fly, many remain asymptomatic for months or even years. Our patient may have been infected for up to 4 years prior to his presentation. After a prolonged incubation period, patients develop intermittent fevers lasting for a few days and spaced by weeks, accompanied by headache, myalgia, malaise and weight loss. Posterior cervical lymphadenopathy (Winterbottom's sign) and splenomegaly are not infrequent. Gradually over a period of months, neurological symptoms begin to manifest. 80% become somnolent. Five to ten per cent have behavioural changes or psychosis. There may be irritability, language problems and unsteadiness. Focal neurology is unusual. If left untreated, the patient progresses to stupor, coma and death, which is often secondary to aspiration pneumonia.⁵

The clinical features of WAT in travellers not indigenous to endemic areas have been summarised by Lejon *et al*.³ Illness is more likely to start acutely; a trypanosomal chancre at the site of a tsetse fly bite is more likely to be apparent in 25–40% and up to half of the patients develop an evanescent, central papuloerythematous rash. Our patient had initial shivers and may have been feverish. Subsequently, there was no clear history of fevers. Skin lesions and lymphadenopathy were not present by admission and neurological features were the only clinical manifestations present.

The patient did have typical abnormalities on investigation. Anaemia, thrombocytopenia, raised erythrocyte sedimentation rate, hypergammaglobulinaemia and hypoalbuminaemia are frequent but non-specific. A high serum and CSF IgM level is also characteristic. CSF usually has a raised white cell count (WCC) and protein. EEG often reveals slow-wave (δ -wave) oscillations.

Specific diagnosis in this case was made by a serological test (IFAT). Direct visualisation of trypanosomes is possible from a lymph node aspirate, blood and CSF. Visualisation of trypanosomes is more likely in East-African trypanosomiasis (EAT). The sensitivity of direct visualisation is improved in the mini Anion Exchange Centrifugation Test (mAECT) which allows concentration of trypanosomes from larger volumes of blood.⁶ In endemic areas, the most widely used test is a rapid card agglutination test (CATT).⁷

Radiological findings on MRI have been reviewed by Kager *et al*.⁸ In early infection, meningeal enhancement is present, but as infection progresses there is a transition from meningitis to encephalitis. Trypanosomes may pass into perivascular spaces and the resulting inflammatory changes result in a T2 hyperintense signal on MRI in the supratentorial white matter, brainstem and cerebellum. The appearances are non-specific and may occur in other causes of leukoencephalitis, such as progressive multifocal leukoencephalopathy and acute demyelinating encephalomyelitis. Radiological change may persist for a long time, despite clinical improvement. Cerebral atrophy may also

become apparent. In EAT, MRI can delineate specific changes in patients who suffer toxic, and potentially fatal, reactions to melarsoprol treatment as haemorrhagic encephalitis and oedema develop.⁹

Our patient was treated with eflornithine, a selective and irreversible inhibitor of ornithine decarboxylase. A 14-day regimen results in a 95% cure rate. Drug toxicity is significant, but less than with melarsoprol. A shorter 7 day course of eflornithine combined with nifurtimox is associated with less eflornithine toxicity and is non-inferior in efficacy.¹⁰ Combination treatment with nifurtimox–eflornithine is now the recommended choice for WAT. Follow-up is recommended with lumbar puncture twice a year. Relapse is defined by a rise in the CSF WCC count and/or the presence of trypanosomes together with a recurrence of symptoms. The presence of recurrent symptoms alone is insufficient to secure a diagnosis of relapse as symptoms can be non-specific. It is likely that CSF IgM levels will also rise in relapse.

Conclusion

This case highlights the importance of considering HAT as a diagnosis in those patients presenting with a progressive cognitive decline, neurological symptoms and a relevant travel history. This case is particularly unusual in view of the extremely low incidence believed to be present in Ghana and the fact that infection occurred in a short-term traveller. Untreated HAT is invariably fatal, but as this case illustrates, timely appropriate treatment results in good cure rates.

Learning points

- ▶ Trypanosomiasis can be acquired through the bite of the tsetse fly even in short-term travellers to endemic regions.
- ▶ West-African trypanosomiasis should be included in the differential diagnosis of progressive cognitive decline.
- ▶ Trypanosomiasis can be diagnosed using serology, PCR or direct visualisation of the parasite.
- ▶ Untreated trypanosomiasis is invariably fatal, but as this case illustrates, timely appropriate treatment results in good cure rates.

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Competing interests None.

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