CASE REPORT

An unusual cause of isolated secondary ovarian failure due to cerebral toxoplasmosis in an African woman with AIDS

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SUMMARY

Primary ovarian failure is common. However, isolated secondary ovarian failure due to gonadotrophin deficiency is rare. A few cases of isolated gonadotrophin deficiency, due to congenital cerebral toxoplasmosis, have been described in children. We report the case of a 34-year-old African woman positive for HIV, who developed secondary amenorrhoea following the successful treatment of cerebral toxoplasmosis. Investigations revealed that she developed an isolated gonadotrophin deficiency due to pituitary lesion. The rest of the pituitary function dynamic tests were normal.

BACKGROUND

Cerebral toxoplasmosis is usually caused by the reactivation of a latent infection and is commonly seen in patients positive for HIV with a CD4 count of less than 100 cells/mL. The common clinical features of cerebral toxoplasmosis include headache, speech impediment, hemiparesis, cerebellar dysfunction and cranial nerve palsy. Our patient presented with symptoms of raised intracranial pressure, though without any focal neurological signs but later developed secondary ovarian failure due to isolated gonadotrophin deficiency as a result of pituitary lesion. To the best of our knowledge, no similar case has been reported in an adult with cerebral toxoplasmosis.

CASE PRESENTATION

A 34-year-old African woman was admitted in February 2010 with a 3-week history of fever, headache and rigours. She had returned from a holiday in the Gambia 3 weeks prior to her presentation. Examination revealed that she was feverish at 39.0°C. She was alert, with a Glasgow Coma Score of 15/15. There were no focal neurological signs, nor was neck stiffness evident. Fundi were normal. Blood pressure was 130/85 mm Hg. The rest of the examination was unremarkable.

INVESTIGATIONS

Investigations showed that her haemoglobin was of 101 g/L, white cell count was 5.0×10^9 /L, lymphocyte count was 1.0×10^9 /L, mean corpuscular volume was 88 fL and platelet count was 432×10^9 /L. Serum vitamin B₁₂ was 399 pg/mL (191–663), folate was 20 ng/mL (4.6–18.7) and serum ferritin was 526 ng/mL (13–150).

Blood film showed no malarial parasites. Blood biochemistry showed that Na⁺ was 141 mmol/L, K⁺ was 3.6 mmol/L, creatinine was 51 µmol/L and estimated glomerular filtration rate was >90. Fasting plasma glucose was 4.6 mmol/L. C reactive protein was <1 mg/L (0–10). HIV test was positive. CD4 counts were 54 cells/mm³ (4%), HIV RNA level was 1.2 million copies/mL and HIV genotype showed subtype C with no mutations. Serological test for toxoplasma revealed that ELISA IgM was negative, dye test was 4000 IU/mL, toxoplasma IgM (immunosorbent agglutination assay) was negative and toxoplasma IgG was positive. Syphilis test was negative, and hepatitis B core antibody was positive; hepatitis B surface and e-antigens were negative. Hepatitis C antibodies were negative. MRI scan showed a focal ring enhancing lesion in the occipital lobe (figure 1) and normal pituitary stalk and gland (figure 2).

TREATMENT

She was empirically treated for cerebral toxoplasmosis with sulfadiazine, pyrimethamine and folinic acid, along with a tapering dose of dexamethasone. She was also commenced with tenofovir, emtricitabine and efavirenz. Her headaches subsided, and she remained afebrile a week later.

OUTCOME AND FOLLOW-UP

One month after her initial presentation, she developed secondary amenorrhoea. Her pregnancy test was negative. She had regular periods prior to her current illness and had two healthy children aged 14 and 16 years. Her sense of smell was normal.

Endocrine tests showed that thyroid-stimulating hormone was 0.43 mU/L (0.27–4.2), free T₄ was 12.2 pmol/L (12–22), free T₃ was 5.6 (3.1–6.8), antiperoxidase antibodies were 18 IU/mL (<34.0), serum cortisol was 303 nmol/L at 09.00 hours, prolactin was 144 mU/L, follicle-stimulating hormone (FSH) was 0.36 IU/L, luteinising hormone (LH) was 0.10 IU/L and serum oestradiol was <50 pmol/L. Luteinising hormone releasing hormone (LHRH) test showed that basal FSH was 1.5 and LH was 0.40; 20 min later, FSH was 3.0 and LH was 4.40; 60 min later, FSH was 4.50 and LH was 5.70. Insulin-like growth factor was 13.8 nmol/L (14.2–36.9).

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Figure 1 T1 postcontrast axial sequence shows a focal ring enhancing lesion in the right occipital lobe in keeping with an underlying abscess.

She was prescribed loestrin 20mg (ethinylestradiol and norethisterone) cyclically. She took it for 3 months, stopping on her own accord. She remained amenorrhoeic for 5 years. She was last reviewed in September 2016. Over the previous 3 months, she had started having scanty monthly periods. The repeat blood tests showed that FSH was 7.9 IU/L, LH was 5.2 IU/L, oestradiol was <50 pmol/L and progesterone was <1 nmol/L. Insulin-like growth factor was 15.6 nmol/L. HIV RNA level was less than 70 IU/mL. The CD4 count was 815 cells/L (32%).

DISCUSSION

Cerebral toxoplasmosis is usually caused by the reactivation of a latent infection and is commonly seen in patients positive for HIV with a CD4 count of less than 100 cells/mL, as in our case. The common clinical features of cerebral toxoplasmosis include headache, speech impediment, hemiparesis, cerebellar dysfunction and cranial nerve palsy.¹ Our patient presented with symptoms of raised intracranial pressure, though without any focal neurological signs. A high toxoplasma antibody titre, along with

multiple abscesses in the brain, strongly suggested cerebral toxoplasmosis. The response to antitoxoplasma therapy confirmed the diagnosis of cerebral toxoplasmosis.

The neurological signs of cerebral toxoplasmosis depend on the site of the brain lesions. A few cases of isolated gonadotrophin deficiency, due to congenital toxoplasmosis, have been reported in children.² Our patient developed secondary amenorrhoea a month after developing cerebral toxoplasmosis. The low oestradiol level, combined with very low FSH and LH, indicates secondary ovarian failure due to a defect in the hypothalamic pituitary axis. However, the LHRH test confirmed pituitary lesion (rather than hypothalamic lesion), as LH and FSH failed to rise.

Isolated gonadotrophin deficiency, secondary to glioma in septum pellucidum, has been reported in a 21-year-old man.³ A case of reversible isolated hypogonadotropic hypogonadism has been published, following a head injury in a 26-year-old man.⁴ Isolated gonadotrope failure has been documented in two men due to a selective pituitary gonadotrope failure, as a result of polyglandular autoimmune syndrome.⁵ Tuberculosis of the central nervous system is rare in developed world; the most common form is tuberculous meningitis. However, tuberculoma due to solid granulomatous lesion can present as focal neurological signs. Hypothalamic tuberculoma causing secondary panhypopituitary dysfunction had been reported in a man.⁶ The combination of isolated hypogonadotropic hypogonadism with anosmia is known as Kallmann syndrome. It is five times more common in men. Our patient did not have anosmia; furthermore, her ovarian function was normal, as evidenced by her two normal pregnancies. Isolated congenital idiopathic hypogonadotropic hypogonadism without anosmia is a different entity.⁷ Adult onset idiopathic hypogonadotropic hypogonadism due to pituitary gonadotrophin deficiency has been reported in a 25-year-old man. He had a normal MRI scan of the pituitary, and he failed to increase LH and FSH following a loading dose of gonadotrophin releasing hormone.⁸

In conclusion, clinicians should be made aware of this potential complication of pituitary dysfunction in patients with cerebral toxoplasmosis, or with any other central nervous system complications of HIV infection (such as primary brain lymphoma or progressive multifocal leucoencephalopathy).⁹

Figure 2 T1 sagittal postcontrast scan through pituitary stalk and gland was normal.

Learning points

- ▶ Cerebral toxoplasmosis is usually caused by the reactivation of a latent infection and is commonly seen in patients positive for HIV with a CD4 count of less than 100 cells/mL.
- ▶ Secondary ovarian failure due to isolated gonadotrophin deficiency is a rare complication of cerebral toxoplasmosis in an adult.
- ▶ The combination of isolated hypogonadotropic hypogonadism with anosmia is known as Kallmann syndrome.

Contributors KTY undertook student-selected module on neurological complications of HIV when she was a final year medical student, selected five cases of neurological complications of HIV (this case was one of them) and wrote a case report. SS reported MRI scan and provided this patient's images. KGY, Consultant, was in charge of clinical management of this patient.

Competing interests None declared.

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