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TOXOPLASMOSIS INFECTION IN AN HIV-NEGATIVE PATIENT PRESENTING WITH CLINICAL AND MRI FINDINGS SIMILAR TO THOSE OF MULTIPLE SCLEROSIS

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ABSTRACT

Toxoplasmosis is a parasitic infection that can present in various clinical forms, ranging from asymptomatic to severe neurological manifestations. The primary sources of infection include undercooked meat, unwashed produce and contact with cat faeces. Toxoplasmosis can lead to encephalitis, particularly in immunocompromised patients, and is often misdiagnosed as other neurological conditions such as multiple sclerosis (MS). We report the case of a 44-year-old male from Almaty, Kazakhstan, who presented with neurological symptoms including headaches, dizziness, diplopia, leg weakness and elevated blood pressure. The patient had a history of consuming undercooked meat, but no prior neurological conditions. Initial magnetic resonance imaging (MRI) revealed demyelinating lesions, leading to a diagnosis of MS. However, high levels of IgG antibodies against *Toxoplasma gondii* were detected, prompting further testing. A polymerase chain reaction test for toxoplasmosis was negative, but the patient was treated empirically with trimethoprim and sulfamethoxazole for six months. A follow-up MRI showed a significant reduction in brain lesions, and the patient's symptoms improved.

KEYWORDS

Toxoplasmosis, central nervous system, MRI

LEARNING POINTS

- This case aids in the differential diagnosis between multiple sclerosis and cerebral toxoplasmosis. It highlights the necessity of conducting ELISA tests for parasitic infections when multiple sclerosis is suspected.

INTRODUCTION

Toxoplasmosis is a parasitic disease of animals and humans caused by *Toxoplasma gondii* and in most cases it is latent[1]. Toxoplasmosis is a global problem, currently up to 50% of the world's population is infected[2]. In the United States, up to 20% of the population is infected, mainly in families with low socioeconomic status, in ethnic minority groups[3,4]. As reported by Torgerson et al.[5], incidents of toxoplasmosis infection increase with age in Kazakhstan. Their study found that 16% of 504 inhabitants in East

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Kazakhstan tested positive for toxoplasmosis via enzyme-linked immunosorbent assay (ELISA)[5]. According to the CDC), the primary routes of infection include consumption of undercooked pork, lamb, beef, venison, crustaceans and molluscs, and infection can spread through unwashed hands, contaminated utensils or poorly pasteurised milk[3,4]. Cats also play a significant role, as they excrete toxoplasma cysts in faeces after eating infected rodents or birds. Humans can become infected by cleaning cat litter, contacting contaminated soil or consuming unwashed produce. Transplacental infection is possible, which can cause nervous system and eye damage. Rare cases of transmission via organ transplantation or blood transfusion have also been reported[6-9]. Clinically, acute toxoplasmosis can present with fever, hepatosplenomegaly and neurological symptoms such as headaches and seizures. A latent form may also persist without symptoms, but reactivation can occur in cases of immunosuppression. Pregnant women are particularly at risk, with possible outcomes including miscarriages, stillbirths, foetal hydrocephalus or microcephaly[6]. In patients with acquired immunodeficiency syndrome (AIDS), toxoplasmosis becomes a major opportunistic infection, leading to encephalitis when toxoplasma cysts rupture, releasing bradyzoites that become tachyzoites[9,10].

CASE DESCRIPTION

A 44-year-old male patient, a commercial representative from Almaty, presented at HAK Medical Centre in May 2017 with complaints of headaches, dizziness, diplopia, leg weakness, hoarseness and elevated blood pressure (140/80 mm Hg). Clinical history revealed that the disease had an insidious onset in early May following an episode of acute respiratory viral infection, self-treated with paracetamol. For the previous seven days, the patient experienced episodic dizziness and diplopia prompting a visit to an ophthalmologist, who found no abnormalities. The patient was referred to a neurologist, who recommended an MRI.

The patient had no significant medical or family history, denied surgical interventions or blood transfusions, and had a positive allergic history to aminophylline. Epidemiological history included frequent consumption of shashlik, with potential ingestion of undercooked meat, and no pets. He occasionally smokes electronic cigarettes and does not consume alcohol. Physical examination revealed moderate neurological symptoms but no osseous-articular deformities. The patient's overall condition was moderately severe; blood pressure was 140/80 mm Hg, and pulse rate was 78 bpm. Neurological evaluation showed that palpebral fissures were equal, but diplopia was present with downward and leftward gaze. Other findings included decreased muscle tone in the left limbs, brisk reflexes and instability in the Romberg test. The patient was referred for an MRI *(Fig. 1)*. In the MRI, focal lesions were identified in the cerebral hemispheres, the left middle cerebral peduncle and the medulla oblongata, more specifically associated with a demyelinating process. Additionally, signs of sinusitis and ethmoiditis were observed. It was recommended to perform a contrast-enhanced brain MRI, which confirmed the presence of

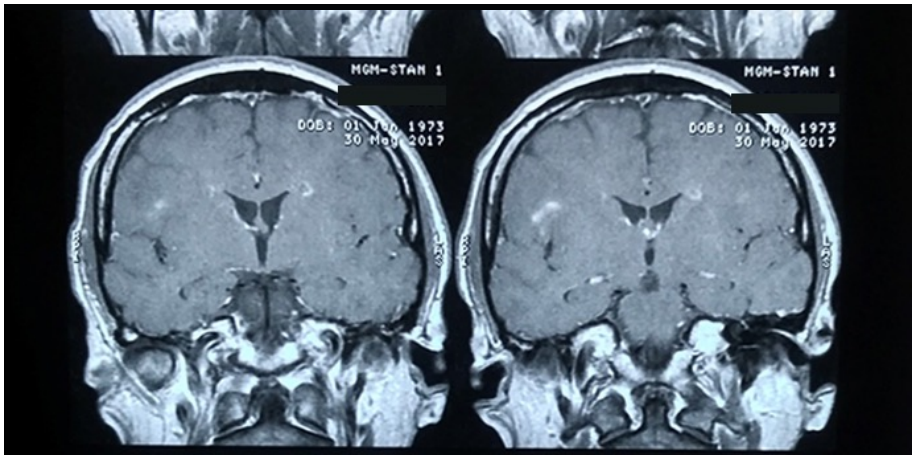

Figure 1. MRI of the brain (30 May 2017).

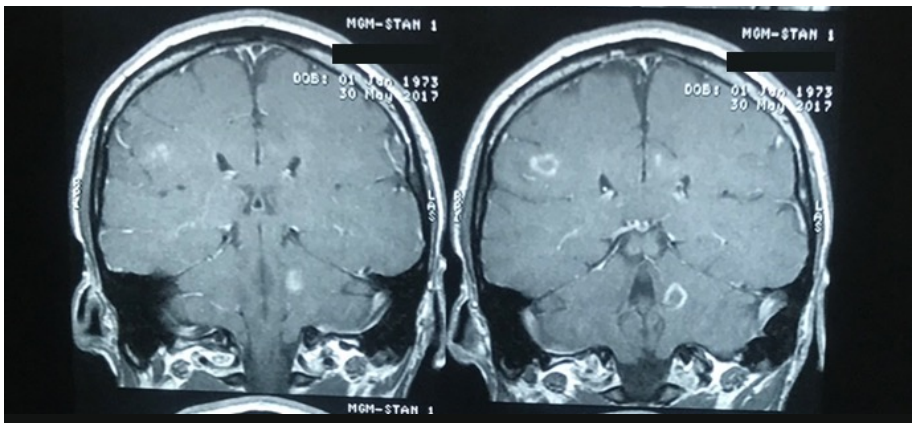

Figure 2. Contrast-enhanced MRI of the brain (30 May 2017).

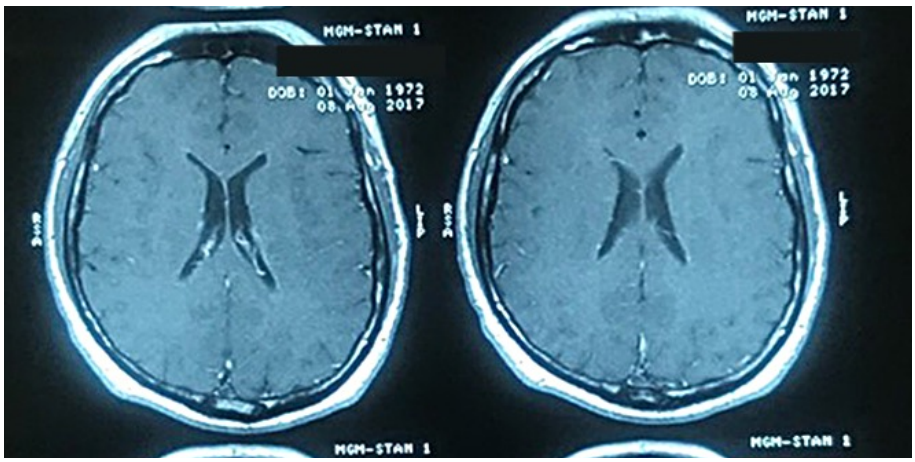

Figure 3. Brain MRI performed on 1 August 2017, four weeks after antibacterial treatment.

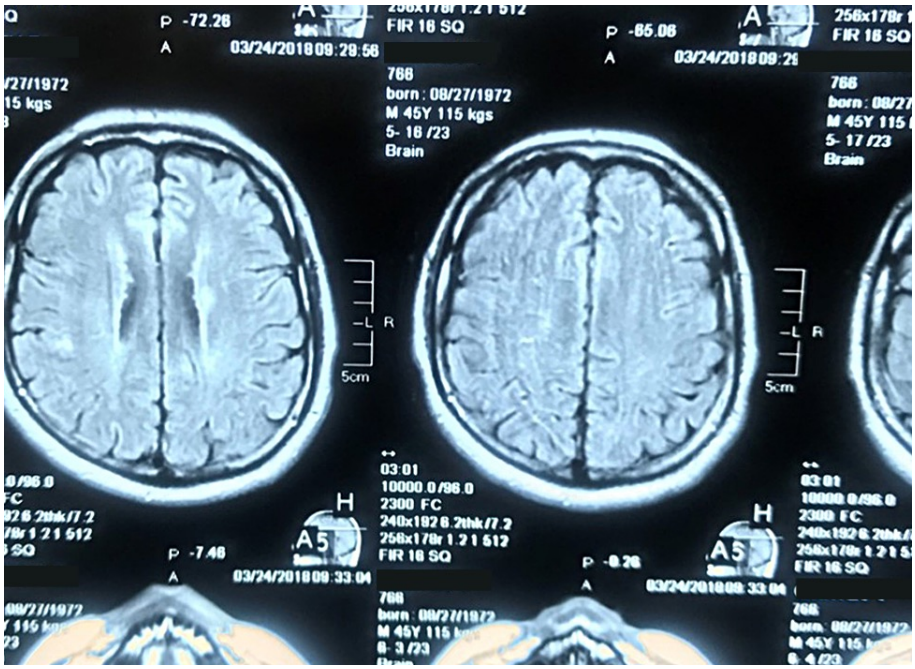

Figure 4. MRI of the brain after treatment completed (22 April 2019).

demyelinating processes in both hemispheres, along with sinusitis and ethmoiditis *(Fig. 2)*. Following this, the patient was re-examined by the neurologist and diagnosed with multiple sclerosis (MS). He was urgently hospitalised in the neurology department of a general hospital in Almaty, where a comprehensive physical examination and symptomatic therapy were administered. The complete blood count revealed no abnormalities: leukocytes 8 $\times 10^9$, red blood cells 5.2 $\times 10^{12}$, haemoglobin 156 g/l, platelets – 332 $\times 10^9$. Biochemical analysis showed glucose at 6.9 mmol/l, total bilirubin at 10.3 mmol/l, creatinine at 89 mmol/l and a negative microprecipitation test.

Further tests, including the Huddleson's and Wright's reaction (for brucellosis) and HIV testing, were negative. In most reported cases, cerebral toxoplasmosis is found in HIV-positive patients. ELISA tests for hepatitis B and C virus markers were also negative. However, Epstein-Barr virus antibodies were detected, with IgG positive at 11.8. A high IgG titre against *T. gondii* was detected (IgG positive at 229.7), while IgM was absent. Antibodies to cytomegalovirus were also present (IgG positive at 9.5, IgM negative), and blood glucose reached 5.8 mmol/l. An ECG revealed sinus rhythm, horizontal heart and left ventricular hypertrophy; a chest X-ray showed signs of chronic bronchitis and left ventricular hypertrophy. On ophthalmological examination, signs of retinal angiopathy were observed. The neurologist diagnosed the patient with MS, left-sided hemiparesis and hemianopia. Symptomatic therapy was administered, but no significant improvement was noted.

DISCUSSION

The initial diagnosis of MS raised doubts at the clinic, particularly after noting the high IgG anti-*Toxoplasma gondii* titre of 229.7 U/ml (a value above 12 U/ml is considered positive). However, polymerase chain reaction testing for *T. gondii* in blood samples was negative.

Serological methods remain the gold standard for diagnosing toxoplasmosis. The ELISA test established the patient's infection through the presence of elevated IgG antibodies. These antibodies peak 1–2 months post-infection and persist for an indefinite period. Despite the high seroconversion, IgM levels specific for acute infection remained unchanged, indicating a chronic infection. The patient's epidemiological history revealed a preference for undercooked meat,

particularly shashlik, which supported the possibility of parasitic infection.

On MRI, clearly outlined hyperintense foci ranging from 0.7 to 1.67 cm in the white matter of both hemispheres were observed. These were considered demyelinating foci, without perifocal oedema. Peripheral contrast uptake was noted. Similar MRI findings were reported by Benson et al.[11], where neurotoxoplasmosis was associated with haemorrhagic foci and described as multifocal abscesses containing tachyzoites and bradyzoites within necrotic areas[12]. Microscopic examination showed damage to arteriole walls, thrombosis and immune vasculitis caused by the parasite.

Given the neurological symptoms, MRI findings and positive ELISA results, the patient underwent a 6-month course of trimethoprim 400 mg and sulfamethoxazole 80 mg twice a day, with folic acid supplementation at 10 mg/day. Four weeks post-treatment, the patient reported improvements in diplopia, dizziness, headaches and walking stability. A control brain MRI performed in August 2017 revealed a reduction in the size of the foci *(Fig. 3)*. Follow-up MRI images showed that in the sagittal, axial and coronal planes, the foci were reduced in size to 1.2 cm (from 1.67 cm) without perifocal oedema. No contrast uptake was detected. These findings indicated a positive therapeutic response to the antibacterial treatment.

In April 2019, a final MRI confirmed the complete disappearance of the foci *(Fig. 4)*. The MRI images revealed signs of dyscirculatory encephalopathy and microangiopathy foci in the frontal and parietal regions, but no signs of demyelination. While neurotoxoplasmosis is typically associated with HIV-infected patients[13], individuals presenting with severe new-onset neurological symptoms and brain lesions should also be tested for toxoplasmosis. If high titres are detected, appropriate antibacterial therapy should be administered.

CONCLUSION

This case highlights the importance of considering cerebral toxoplasmosis in patients with new-onset neurological symptoms, even in the absence of HIV infection. The overlap in imaging findings between MS and toxoplasmosis necessitates serological testing for accurate diagnosis. Early recognition and appropriate antibacterial therapy can lead to a significant improvement in patient outcomes, as demonstrated in this case. Regular follow-up with MRI is essential to confirm the resolution of lesions and prevent recurrence.

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