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A clinically challenging diagnosis in a returning traveller with pyrexia of unknown origin

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INTRODUCTION

Pyrexia of unknown origin (PUO) is accepted to be one of the most difficult diagnostic challenges in medicine. PUO in a returning traveller poses particular challenges based on a greater breadth of potential causes as a consequence of travel related exposures. We report the case of an unusual diagnosis in a returning traveller.

CASE

A 52 year old Guyanan woman presented with a 2 week history of fever, headache and lethargy.

Travel
Her symptoms began ***2 days after returning*** from Guyana where she had been staying with her mother and sister in Georgetown.

Exposures
Whilst in Guyana she ate home cooked foods and drunk bottled water. She had no freshwater exposure and no new sexual partners. She denied any other symptoms.

On examination
She was febrile at 40 degrees Celsius, tachycardic and had palpable cervical lymphadenopathy.

Initial blood tests are shown in Table 1. Initial infective investigations are shown in Table 2.
An electrocardiogram showed ***T-Wave inversion in the anterior leads.***

Table 1: Routine admission bloods

Haemoglobin	118
MCV	78.8
White cell count	8.08
Platelet count	230
Neutrophils	67.5% 5.45
Lymphocytes	23.5% 1.90
Urea	5.3
Creatinine	108
Estimated GFR	48
Sodium	133
Potassium	4.4
Bilirubin (total)	8
Alanine transaminase	489
Alkaline phosphatase	128
Albumin	35
C-reactive protein	61.2
Creatine kinase	466
Troponin	93

Table 2: Initial infective investigations

Investigation	Result
HIV p24 antigen	Negative
Malaria film	Negative
HCV Antibodies	Negative
HBV	Immune/Vaccinated
HAV	Negative
HEV	Negative
CMV Antibodies	IgG+; IgM-
EBV Antibodies	IgG+; IgM-
Leptospira antibodies	Negative
Blood cultures	8 x Negative

PROGRESS AND MANAGEMENT

Empirical treatment with ***Ceftriaxone and Doxycycline*** for suspected Enteric Fever and suspected Leptospirosis was commenced. There was ***no improvement*** following 7 days of antibiotics so they were stopped.

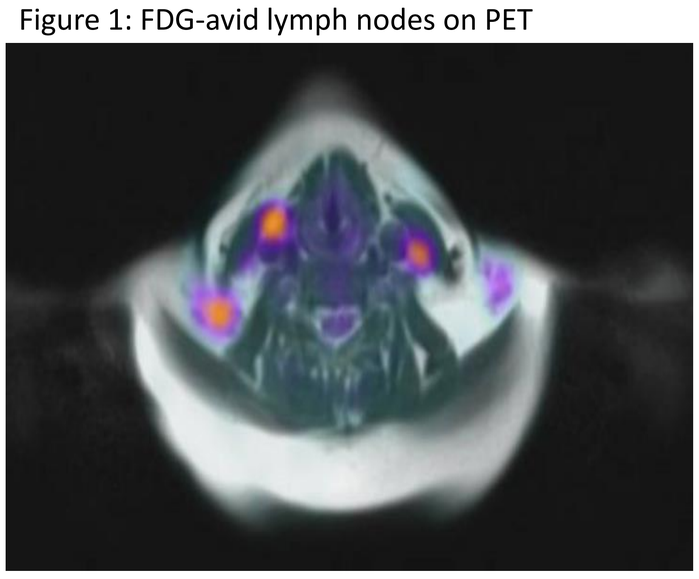
The patient was investigated further with a CT Positron emission tomography (PET-CT) which showed ***small volume FDG-avid nodal disease*** (Figure 1) above and below the diaphragm and ***FDG-avid spleen*** suspicious for lymphoproliferative disorder. A biopsy of the lymph node showed a reactive process only.

4 weeks into her illness the patient had ***persistent fevers*** with biochemical evidence of ***myositis and myocarditis***.

Toxoplasma serology was diagnostic for acute toxoplasmosis based on a strongly positive IgM.

On further questioning the patient reported her mother had a new kitten at the time of her visit. This is the likely route of transmission. The patient was treated with 4 weeks of Azithromycin with resolution of fevers and biochemical abnormalities. Ophthalmoscopy confirmed no ocular involvement.

Figure 1: FDG-avid lymph nodes on PET



DISCUSSION

Toxoplasmosis is caused by the protozoan parasite ***Toxoplasma Gondii***. It infects up to a third of the world's population (1) *T. gondii* seroprevalence is high in South America (2). Transmission routes are usually foodborne, zoonotic or congenital. ***Kittens and cats*** play an important role in transmission of toxoplasma to humans as they shed millions of oocysts in their faeces for as long as 3 weeks after infection. Humans can become infected through either ingesting these oocytes accidentally after handling cat litter or through accidental ingestion of soil contaminated by cat litter.

Toxoplasmosis is ***asymptomatic in 80-90% of immunocompetent adults*** (3); when symptomatic it often causes a 'mono-nucleosis-like' or 'flu-like' syndrome (4). Treatment of immunocompetent adults with lymphadenopathic toxoplasmosis is rarely indicated as it is usually self-limited. The presence of ***end organ injury or marked systemic symptoms*** is an indication for treatment.

Acute toxoplasmosis in ***immunocompromised*** adults is known to cause ***significant morbidity*** and can be fatal. In humans, tissue cysts can affect skeletal muscle, myocardium, brain and eyes. Our patient, although not immunocompromised, had suggestion of involvement of skeletal muscle (myalgia and raised CK) and myocardium (raised troponin, BNP and ECG findings) although biopsies were not done to confirm this. These severe manifestations of acute toxoplasmosis in immunocompetent returning travellers are less commonly described. Painless cervical lymphadenopathy is a common and key clinical finding (5) however widespread lymphadenopathy is not as commonly reported.

Our case highlights that diagnosis of acute toxoplasmosis in returning travellers poses a ***clinical challenge*** due to its atypical manifestations.

Acute toxoplasmosis should always be considered in patients with prolonged fever and headache with multi-organ involvement alongside EBV, CMV and HIV.

LEARNING POINTS

- Always consider acute toxoplasmosis as a cause for prolonged headache, fever and malaise alongside CMV, EBV and HIV
- Serological testing is diagnostic
- Although acute toxoplasmosis is most commonly self-limiting, if there is evidence of visceral involvement or symptoms are severe or prolonged, treatment is indicated for 2-4 weeks.

REFERENCES
1. Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet. 2004;363(9425):1965-76.
2. Furtado JM, Smith JR, Belfort R et al. Toxoplasmosis: A Global Threat. Glob Infect Dis. 2011; 3(3): 281–284
3. Remington JS. Toxoplasmosis in the adult. Bull N Y Acad Med 1974; 50:211–27
4. Bottieau E, Clerinx J, Van den Enden E et al. Infectious mononucleosis-like syndromes in febrile travelers returning from the tropics. J Travel Med 2006; 13:191–7
5. Anand R, Jones CW, Ricks JH, Sofarelli TA, Hale DC. Acute primary toxoplasmosis in travelers returning from endemic countries. J Travel Med. 2012 Jan-Feb;19(1):57–60.