Cerebral toxoplasmosis during mycophenolate mofetil therapy for myasthenia gravis

History

58 year old male

Presented in December 2017 with a 3-day history of: confusion, behavioural changes, vomiting
No other symptoms on systemic enquiry
No recent surgeries, dental work, sinusitis, otogenic infections, nor contact with known TB cases

Background:
Myasthenia gravis (on mycophenolate mofetil for past 3 years)
Type 2 diabetes mellitus (on metformin and insulin)
Brainstem stroke (on clopidogrel and atorvastatin)

Physical examination:
Normal GCS and neurological system
Normal cardiovascular, respiratory, GI systems
No peripheral stigmata of endocarditis

MRI brain:
Two frontal ring-enhancing lesions associated with significant oedema

Blood tests:
WBC 16.7 x10^9 cells/L (neutrophils 13.7 x10^9 cells/L)
CRP <5 mg/L. Normal renal and liver function
HIV Ag/Ab negative

Further elucidation of social history

Lived on a farm for past 14 years
Farm has cattle, sheep, and chickens
Owns 3 dogs and 3 cats

Clinical suspicion of toxoplasmosis

Confirmatory tests
Positive toxoplasma IgG in serum
Brain biopsy samples were sent to Toxoplasma Reference Unit, Swansea:
Positive toxoplasma PCR
Negative Giemsa and immunohistochemical stains for tachyzoites and bradyzoite-containing cysts

Progress
Empirical toxoplasma-specific treatment with pyrimethamine, sulfadiazine, and folic acid for 6 weeks
Withdrawal of mycophenolate and short course of dexamethasone for cerebral oedema
Significant improvement in symptoms with improvement in end-of-treatment MRI scan

Discussion
Recognition of the significant risk of toxoplasmosis in this immunosuppressed toxoplasma-IgG positive patient (despite negative immunohistological stains) led to empirical anti-toxoplasma treatment and a favourable outcome.

Learning points
1. Mycophenolate mofetil used in neuromuscular diseases can increase the risk of cerebral toxoplasmosis.
2. This was a late diagnosis due to low index of suspicion for toxoplasmosis in HIV-negative persons, with the patient ending up with two surgical biopsies.
3. An important risk factor is the number of infected cats and resulting oocyst prevalence in the environment.
4. A positive toxoplasma PCR is expected in serum-positive IgG patients due to brain cells being a site of dormancy. Confirmation of cerebral toxoplasmosis relies on direct histological demonstration of parasites in brain lesions or a positive toxoplasma PCR in CSF. Despite negative tests, empirical treatment should commence in the absence of an alternative diagnosis.

References