CASE REPORT

Pseudomonas meningoenkephalitis masquerading as a stroke in a patient on tocilizumab

Cameron J Williams,¹ Andrew Foote,² Philip Choi³

¹Royal Melbourne Hospital, Parkville, Victoria, Australia
²Austin Health, Heidelberg, Victoria, Australia
³Box Hill Hospital, Box Hill, Victoria, Australia

Correspondence to

Dr Cameron J Williams,
cameron.williams8@mh.org.au,
cam_williams00@hotmail.com

Accepted 23 December 2018

SUMMARY

A previously high-functioning woman presents with clinical and CT features of a subacute ischaemic stroke. Her medical history is relevant for refractory giant cell arteritis on long-term high-dose prednisolone and recent commencement of tocilizumab (interleukin-6 monoclonal antibody). The potential for stroke mimic is considered and a magnetic resonance brain scan is requested. She rapidly deteriorates within 24 hours of admission and unexpectedly dies. An autopsy reveals that she has bilateral pulmonary emboli with lower limb deep vein thrombosis and *Pseudomonas* meningoenkephalitis with frank pus on the brain. We discuss the potential risks of immunosuppression and the role of imaging in the diagnosis of stroke.

BACKGROUND

This case highlights the diagnostic pitfalls in the modern era of biologics such as tocilizumab, where immunosuppressive agents may mask the typical symptoms, signs and laboratory tests that clinicians generally rely on to formulate a working diagnosis.

Given the limited availability of MRI slots in most hospitals, there is much debate when, who and why this should be performed urgently. In the case we describe, we propose that an urgent

diffusion-weighted MRI (DWI-MRI) of the brain is indicated to both confirm ischaemia and exclude masquerading medical emergencies that may otherwise go undiagnosed.

CASE PRESENTATION

An 81-year-old woman presents to the hospital at midnight with a dense left hemiparesis. She had awoken with milder symptoms earlier that morning but delayed seeking medical attention. By the time she is assessed by a doctor, it is >24 hours from when she was last seen well.

Her medical history is relevant for biopsy-proven giant cell arteritis (GCA) and polymyalgia rheumatica. She had been on a prolonged course of high-dose prednisolone over the preceding 7 months complicated by fatigue and persistently elevated erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) levels. Three weeks prior to her admission, a whole-body positron emission tomography scan was performed excluding vasculitis or occult malignancy and she was commenced on tocilizumab under the care of a rheumatologist for suspected refractory disease. Her other medical history includes hypertension complicated by stage 4 chronic kidney disease (estimated glomerular filtration rate 20), hypercholesterolaemia and asthma.

Medications on admission are aspirin, candesartan/hydrochlorothiazide, simvastatin, budesonide/formoterol, prednisolone 42.5 mg/day and tocilizumab 162 mcg weekly. She is not on sulfamethoxazole/trimethoprim due to an allergy.

Socially, she is high functioning and living at home with her husband. Her preadmission modified Rankin score is zero.

On examination, she is orientated and able to give a good account of her presenting complaint. Pertinent signs include left visual and tactile inattention, left conjugate gaze palsy, left arm and leg paralysis and an upgoing left plantar response. She is afebrile, normotensive and mildly hypoxic (93% room air) without respiratory distress.

INVESTIGATIONS

The initial non-contrast CT (NCCT) brain is unremarkable (figure 1). Both CT angiogram and CT perfusion are not performed due to her pre-existing severe renal disease and the fact that her symptom duration is >24 hours. A repeat NCCT brain performed 8 hours after the initial scan is thought to show subtle interval hypoattenuation of the

Figure 1 Initial NCCT brain (single axial slice) performed on arrival is unremarkable. NCCT, non-contrast CT.

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Williams CJ, Foote A, Choi P. *BMJ Case Rep* 2019;**12**:e227296. doi:10.1136/bcr-2018-227296

Figure 2 Repeat NCCT brain (single axial slice) performed 8 hours after arrival showing subtle interval hypoattenuation over the right parietal region. NCCT, non-contrast CT.

right parietal region (white arrow in [figure 2](#)). Her ECG shows sinus rhythm and her chest X-ray was clear. On admission, her blood counts are as follow: white cell $16.9 \times 10^9/L$ (4–10), the blood film shows a neutrophilia with mild toxic granulation, ESR is 11 mm/h (1–15) and CRP of 10 mg/L (<5).

DIFFERENTIAL DIAGNOSIS

The patient presents with symptoms of acute left hemiparesis, left gaze palsy, visual/tactile inattention and upgoing left plantar response. These upper motor neuron features localise to the right hemisphere of the brain with cortical involvement; they do not localise to the subcortical region (ie, lacunar infarct which is common in hypertensive patients) or the brainstem. In the setting of acute symptom onset and evolving hypoattenuation over the right parietal cortex, the likely diagnosis is thought to be a subacute ischaemic infarct involving the right middle cerebral artery.

The lack of established changes on the NCCT brain for up to >24 hours of suspected cerebral ischaemia is unusual and raises the possibility of a stroke mimic. In the setting of her immunosuppression, a differential diagnosis of meningoencephalitis is considered but less likely given it is usually associated with fevers, raised inflammatory markers and often confusion or seizures; however, an absence of these in our patient does not exclude the diagnosis.

TREATMENT

She is reviewed by the consultant neurologist and admitted under the stroke team for conservative treatment. Cerebrospinal fluid (CSF) analysis to investigate and exclude masquerading pathologies such as CNS infection was not performed as the working diagnosis of a stroke was supported by changes on interval NCCT. A DWI-MRI of the brain is requested, triaged

and arranged for the following morning with the view that it will confirm with more certainty our diagnosis of stroke.

OUTCOME AND FOLLOW-UP

Later that night, she is witnessed to have a left-sided focal motor seizure and is commenced on empirical treatment to cover infective meningoencephalitis. She then rapidly deteriorates with a cardiorespiratory arrest requiring emergency resuscitation and dies after withdrawal of treatment—in keeping with the patient's pre-existing wishes. A postmortem examination reveals multiple pulmonary emboli with lower limb deep vein thrombosis and *Pseudomonas aeruginosa* meningoencephalitis with frank pus on the brain.

DISCUSSION

The purpose of this case report is (1) to increase awareness of newer immunosuppressive agents and their potential to cause overwhelming bacterial meningoencephalitis which has not been previously described, and (2) to highlight the importance of DWI-MRI in selected patients with suspected stroke, particularly those who are immunosuppressed.

Tocilizumab is a humanised monoclonal antibody that targets the interleukin (IL)-6 receptor and is widely used as an effective steroid-sparing agent for the treatment of rheumatoid arthritis. High levels of IL-6 have also been shown in the serum of patients with GCA and there is emerging high-quality evidence to support the use of tocilizumab in GCA.¹ Several case series have demonstrated some serious adverse events (none of the overwhelming bacterial meningoencephalitis) and further research is underway with larger trials to determine long-term efficacy and safety.²

Diffusion-weighted MRI changes appear as early as 3–30 min of brain ischaemia. In large territorial stroke, CT is usually positive after 6 hours when the net increase of water in the tissue exceeds 3%.³ MRI is more sensitive in detecting stroke mimics, particularly infections and neoplasms⁴; however, routine access is often limited, even in most large tertiary hospitals and confirming the diagnosis of ischaemic stroke on MRI is rarely time critical.

NCCT, CT angiogram and CT perfusion of the brain are the first-line acute stroke imaging in most stroke centres. Our patient presented >24 hours from symptoms onset and hence no advanced CT imaging was performed. In clinical practice, when the initial CT imaging is negative for stroke a delayed NCCT is performed allowing interim evolution of the infarct. Usually, DWI-MRI is reserved only if the repeat NCCT remains negative or if a posterior circulation stroke is suspected where NCCT has limited accuracy irrespective of time. In the appropriate setting, a negative scan should immediately prompt further investigation.⁵

Learning points

- ▶ Tocilizumab is an immunosuppressant that inhibits interleukin-6, preventing a C reactive protein rise, even in the setting of overwhelming sepsis.
- ▶ Tocilizumab may be associated with the adverse event of bacterial meningoencephalitis which has previously not been described; however, the role of concomitant prednisolone use contributing to this is unclear.
- ▶ Immunosuppression should be considered a red flag in all clinical presentations, particularly in patients presenting with stroke-like symptoms. Prompt, definitive imaging diagnosis is required for these patients.

We acknowledge that an urgent MRI scan in our patient may not have necessarily altered the clinical outcome. This is particularly so given the patient died within 24 hours of presentation to hospital with concurrent pulmonary embolism. In another situation, however, a timely antemortem diagnosis by an urgent DWI-MRI and CSF analysis might avert such a fatal outcome.

In conclusion, biologic immunosuppressive therapies are increasingly being used in modern medicine and should be considered a ‘red flag’ in patients presenting with acute neurological deficits. They may mask the typical symptoms, signs and laboratory tests that clinicians generally rely on to make an accurate diagnosis. In such circumstances, an urgent DWI-MRI +/- CSF analysis should be performed to differentiate other serious pathologies masquerading as a stroke that may go undiagnosed with conventional CT imaging.

Contributors Primary and corresponding author is CJW. Concurrent clinical care during patient management and edits to manuscript provided by PC and AF.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Stone JH, Tuckwell K, Dimonaco S, *et al.* Trial of tocilizumab in giant-cell arteritis. *N Engl J Med* 2017;377:317–28.
- 2 Ninan JV, Lester S, Hill CL. Giant cell arteritis: beyond temporal artery biopsy and steroids. *Intern Med J* 2017;47:1228–40.
- 3 Li F, Han S, Tatlisumak T, *et al.* A new method to improve in-bore middle cerebral artery occlusion in rats: demonstration with diffusion- and perfusion-weighted imaging. *Stroke* 1998;29:1715.
- 4 Schellinger PD, Bryan RN, Caplan LR, *et al.* Evidence-based guideline: the role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2010;75:177–85.
- 5 Brunser AM, Hoppe A, Illanes S, *et al.* Accuracy of diffusion-weighted imaging in the diagnosis of stroke in patients with suspected cerebral infarct. *Stroke* 2013;44:1169–71.

Copyright 2019 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow