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Acanthamoeba granulomatous amoebic encephalitis mimicking tumefactive demyelination

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Case Report

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Abstract

Background

Acanthamoeba brain infection can cause ring-enhancing lesions that mimic neoplasm, abscess or demyelination on brain imaging. High-dose corticosteroids, the standard treatment for tumefactive demyelination, can be detrimental if infection is not systematically excluded.

Case presentation:

A 42-year-old immunocompetent woman presented with a two-week history of non-fluent aphasia, executive dysfunction, and progressive right hemiparesis. An MRI scan of the brain showed two left frontoparietal lesions with perilesional oedema, open-ring enhancement, and mass effect. Spectroscopy showed elevated choline and reduced N-acetyl aspartate. Based on the radiological differential diagnosis of tumefactive demyelination versus high-grade glioma, intravenous methylprednisolone 1 g daily was initiated at an outside hospital before referral to our centre. Cerebrospinal fluid (CSF) study on day 5 of methylprednisolone showed 6 cells/mm³, sugar 78 mg/dL, protein 79 mg/dL, and no oligoclonal bands. CSF 18S rRNA PCR detected *Acanthamoeba spp.* Combination anti-acanthamoeba therapy (doxycycline, fluconazole, co-trimoxazole, and miltefosine) was administered. The lesions regressed, and deficits improved; however, CSF *Acanthamoeba* PCR remained positive even after four months of treatment, with co-detection of *parvovirus* B19.

Conclusion

Acanthamoeba CNS infection can mimic the clinical, neuroradiological, and spectroscopic features of tumefactive demyelination, including the characteristic open-ring sign. When tumefactive lesions lack definitive features of established demyelinating disease, it is prudent to rule out infective etiologies, such as CNS infections with free-living amoebae, before administering immunomodulators.

Introduction

Acanthamoeba species cause granulomatous amoebic encephalitis (GAE), with an overall mortality of 76%. Space-occupying or ring-enhancing lesions are the most common neuroimaging finding.[1]

When tumefactive demyelinating lesion(TDL) is suspected, acute treatment includes high-dose intravenous corticosteroids. Corticosteroids, however, are a recognised predisposing factor for free-living amoebae (FLA) infection.[1] We describe an immunocompetent woman who had an open-ring sign of demyelination and received pulse methylprednisolone before the diagnosis of *Acanthamoeba* CNS infection was made.

Case Presentation

History. A 42-year-old Indian woman with no known comorbidities, trauma, or freshwater exposure developed nonfluent speech and word-finding difficulty over two weeks. Over the next few days, she had executive dysfunction(forgetting things and planning tasks) with a nocturnal bifrontal headache. In a week, she had difficulty climbing down stairs and developed difficulty lifting her right leg and raising her right arm and became dependent for daily activities. She had no visual, sensory or bladder symptoms

Examination. She was alert and oriented, with no meningeal signs. Speech was nonfluent, with agrammatism and telegraphic output; impaired repetition and naming, literal paraphasias, perseveration, and mild dysarthria were present. Attention was impaired, with frontal executive deficits and impaired praxis. Saccades were slow, particularly to the right, with slowed vertical gaze and oculomotor apraxia. She had right spastic hemiparesis (MRC grade 2 in the lower limb and 3- in the upper), brisk reflexes, an extensor plantar response and right upper motor neuron facial palsy.

Diagnostic Process. Extensive screening was negative. (Table 1)

Visual evoked potentials (VEP) were normal on two occasions. An MR scan of the brain on 4 June showed two lesions: a left posterior parietal lobe lesion (3.6 x 3,5 cm) (Fig. 1) and a left high frontal lobe lesion(2.6 x 2cm) (Fig. 2). Both had significant perilesional oedema, open-ring enhancement, and a peripheral rim of diffusion restriction. MR Spectroscopy (MRS) showed elevated choline, reduced N-acetylaspartate (NAA), and a lipid-lactate peak at the centre. Susceptibility-weighted imaging (SWI), cervical spine MRI, and MR angiography (MRA) were normal. The radiology report suggested TDLs, with high-grade glioma as the differential diagnosis. Intravenous methylprednisolone 1 g daily was started at another hospital on June 4, and she was referred to our centre. As TDL was the working diagnosis, we continued it.

Axial (a) and sagittal (b) T1-weighted images show a well-defined hypointense lesion. Axial T2-weighted (c) and FLAIR (d) images show hyperintensity with extensive perilesional oedema. Post-contrast T1-weighted images (e-h) show open-ring enhancement (e, f axial; g sagittal; h coronal). (i) SWI. DWI (j) and ADC map (k) show a peripheral rim of restricted diffusion. (l) MR spectroscopy shows raised choline, reduced NAA and a central lipid-lactate peak. The lesion measures approximately 3.6 × 3.5 cm.

(a) Axial T1-weighted image shows a well-defined hypointense lesion. (b) Axial T2-weighted image shows hyperintensity with perilesional oedema. Post-contrast T1-weighted images (c-e) show open-ring enhancement (c axial; d coronal; e sagittal). (f) SWI. DWI (g) and ADC map (h) show a peripheral rim of restricted diffusion(red arrow). The lesion measures approximately 2.6 × 2.0 cm.

Case Resolution. CSF obtained on 8 June (Table 1) showed 6 cells/mm³ (occasional lymphocytes), protein 79 mg/dL, glucose 78 mg/dL, CSF-to-blood glucose ratio 0.78, and adenosine deaminase(ADA) 2.6 U/L. The 18S rRNA multiplex FLA PCR returned positive for *Acanthamoeba spp.* on the following day.

On day 6 of methylprednisolone, we tapered methylprednisolone and started anti-amoebic therapy (Table 2).

MRI repeated on 18 September showed a significant reduction in the size of the now non-enhancing lesions (Fig. 3). A paramagnetic rim appeared at the open edge of the larger lesion in the left posterior parietal region. In the smaller lesion in the left high frontal region, the white-matter tract pattern became evident on the T2-FLAIR sequence. FLA PCR remained positive in serial CSF studies (Table 1).

Left posterior parietal lesion (a-h, green arrows): (a) axial T1; (b, c) T2-weighted images (b axial, c sagittal); (d) post-contrast T1 axial ; (e, f) T2-FLAIR (e axial, f coronal); (g, h) SWI sequence. Left high frontal lesion (i-o, yellow arrows): (i) SWI; (j) axial T1; (k, l) T2-weighted images (k axial, l sagittal); (m) post-contrast T1 axial; (n, o) T2-FLAIR (n axial, o coronal). Both lesions are smaller and non-enhancing, with residual FLAIR hyperintensity. SWI shows a hypointense rim at the open edge of the parietal lesion (blue arrow).

Follow-up and outcome. (Table 2) From mid-June, speech and strength improved progressively, and by late June she was ambulant with support. We added rifampicin 600mg orally once daily to the combination anti-amoebic regimen (fluconazole, co-trimoxazole, and doxycycline) when the fourth CSF sample was still PCR-positive for *Acanthamoeba spp*. She now has mild dysarthria and a modified Rankin scale(mRS) score of 1.

Table 1
Serial CSF findings

Parameter	8 June	4 July	25 July	10 oct
Cells/mm³	6	17	46	6
Differential count	100% lymphocytes	100% lymphocytes	100% lymphocytes	100% lymphocytes
Protein (mg/dL)	79	33	50	58
Glucose (mg/dL)	78 (ratio 0.78)	75 (ratio 0.33)	79 (ratio 0.62)	65 (ratio 0.6)
ADA (U/L)	2.6	Not done	1.9	Not done
Wet mount	No trophozoites	No trophozoites	Few sluggishly motile trophozoites	No trophozoites
FLA PCR	*Acanthamoeba* detected	*Acanthamoeba* detected	*Acanthamoeba* detected	*Acanthamoeba* detected
Other	CBNAAT, VDRL negative; Gram, AFB, fungal stains and India ink negative; culture sterile; no oligoclonal bands(OCBs) ; Serum and CSF MOG-IgG, AQP4-IgG, and the autoimmune encephalitis panel negative. HIV, hepatitis C, hepatitis B surface antigen, and VDRL negative. Antinuclear antibody immunofluorescence, rheumatoid factor, tumour markers, and abdominal and breast ultrasound normal	CBNAAT, VDRL negative; Gram, AFB, fungal stains and India ink negative; culture sterile; autoimmune panel negative	CBNAAT, VDRL negative; Gram, AFB, fungal stains and India ink negative; culture sterile	*Parvovirus B19* in multiplex PCR

Table 2
Timeline

Date (2026)	Event
Late May	Onset of non-fluent aphasia and executive dysfunction
29 May	CT scan of head: vasogenic oedema in left frontal and posterior parietal lobes
4 June	MRI/MRA/MRS: two left open-ring enhancing lesions with mass effect; reported as tumefactive demyelination versus glioma: started IV methylprednisolone 1 g once daily, started in peripheral hospital
6 June	Admission at our centre: mRS score of 4, IV methylprednisolone 1 g daily continued
8 June	Lumbar puncture 1 (FLA PCR later positive): day 5 of IV methylprednisolone 1 g daily
9 June	*Acanthamoeba* PCR-positive; combination anti-amoebic therapy started, doxycycline 100 mg intravenously two times a day, fluconazole 600 mg intravenously once daily, co-trimoxazole double-strength tablets three times a day, and miltefosine 50 mg three times a day (for 28 days) and methylprednisolone reduced to 16mg orally two times a day. Ceftriaxone 2 grams intravenously twice a day for 14 days to address possible bacterial co-infection.
23 June	Methylprednisolone reduced to 8mg orally two times a day for two weeks
4 July	Lumbar puncture 2: *Acanthamoeba* PCR positive
25 July	Lumbar puncture 3: *Acanthamoeba* PCR positive
18 september	Follow-up MRI: lesions reduced in size significantly, SWI rim on open aspect
10 October	*Acanthamoeba* PCR-positive, *parvovirus B19*-positive mRS score of 1

Discussion

This case illustrates how closely *Acanthamoeba* CNS infection can mimic TDL. She had two large brain lesions with radiologic features that are typical of TDL.

The open-ring sign has been reported as highly specific for atypical demyelination.[2] However, a 2026 review reported space-occupying or ring-enhancing lesions in 61% of *Acanthamoeba* cases, often leading to misdiagnosis as neoplasm.[1] Infections mimicking TDL can mislead clinicians into reflexively initiating high-dose corticosteroids or monoclonal antibodies, with potentially fatal consequences. Our case highlights that although the open-ring sign strongly supports demyelination, clinicians should also consider infectious etiologies, particularly when other features of demyelinating disease are absent. We

confirmed the diagnosis of *Acanthamoeba* CNS infection by 18S rRNA PCR in CSF, which remained positive even in the 4th month of treatment.

Clues in retrospect. She had a subacute, progressive cortical syndrome (aphasia, executive dysfunction, apraxia) without any earlier demyelinating event. OCBs were absent, and VEP and the cervical cord were normal; therefore, the 2024 McDonald criteria could not be met for dissemination in space and time.[4] The CSF had a borderline cell count with raised protein. Together, these findings should lower the threshold for excluding infectious etiologies and, when doubt persists, for biopsy, especially in endemic areas. Co-detection of *Parvovirus B19* may reflect the Trojan horse role of *Acanthamoeba spp.* as carriers of other microbes.[3]

Corticosteroid exposure. Cell-mediated immunity plays a key role in controlling *Acanthamoeba* in the brain, and immunosuppression is an established predisposing factor.[1] She had 6 days of pulse methylprednisolone followed by a low dose. However, she continued to show molecular evidence of *Acanthamoeba spp.* in CSF even after four months of targeted treatment. After FLA diagnosis, methylprednisolone 16mg/day was administered for two weeks, followed by 8mg once daily(equivalent to a daily prednisolone dose of 20 mg and 10mg). A reduced-dose taper was employed to avoid adrenal insufficiency, and also considering the possibility of coexisting demyelination. We cannot say whether the steroids affected disease course, and the favourable outcome must not be considered as evidence that steroids are safe in this setting.

Treatment. Published survivors have generally received combination therapy, most often including fluconazole, co-trimoxazole, rifampicin and/or miltefosine, sometimes with surgical excision.[5] We used a combination including miltefosine 50 mg orally three times a day for 28 days because of its long half-life and release from body fat stores.

Clinicoradiologic overlap (hypothesis). This overlap with demyelinating lesions likely reflects the subacute-chronic course, predilection for the grey-white junction, and vasculitic pathology observed in *Acanthamoeba* infection.[1] Hematogenous spread can produce multiple non-contiguous white-matter lesions at the corticomedullary junction and deep white-matter regions.[6] *Acanthamoeba* infection also triggers a surge in host matrix metalloproteinases (MMPs), degrading tight junction proteins and the extracellular matrix, worsening blood-brain barrier (BBB) breakdown and resulting in vasogenic oedema.[7]

Molecular mimicry and CNS autoimmunity. Acanthamoeba castellanii has peptide sequences structurally homologous to myelin basic protein (MBP) and proteolipid protein (PLP)and also triggers self-reactive CD4 + T cell clones.[8] Unmasking of cryptic myelin antigens can also expose new epitopes.

Since myelin is densely concentrated in the subcortical and deep white matter [9], the active inflammatory margin may form an arc extending towards the deep white matter. Seeding from a cortical collateral vessel or sparing of a better-perfused cortical ribbon from inflammation may also contribute to this appearance.

SWI rim. Pyogenic abscesses show a double-rim sign, and the rim in abscesses and necrotic tumours varies in completeness and regularity. The paramagnetic rim in multiple sclerosis lesions is complete and reflects chronic active inflammation. In our patient, a SWI-hypointense rim confined to the open edge appeared on the follow-up MRI. This may reflect haemosiderin-laden macrophages or microhaemorrhages within perivascular spaces at the lesion edge or iron deposition along penetrating cortical vessels, consistent with the angioinvasive pathology of GAE. We propose that the two margins represent different stages of a single process: the enhancing arc marks ongoing BBB disruption at the advancing edge. In contrast, the cortical rim marks an older margin that retains blood products from earlier perivascular injury. To our knowledge, a susceptibility rim limited to the open edge of an open ring has not been described in GAE.

Practical suggestion. In patients with a ring-enhancing tumefactive lesion without prior demyelinating disease, particularly when dissemination in space and time cannot be demonstrated, OCBs are absent, or the CSF is abnormal, we suggest CSF FLA PCR and wet-mount microscopy at the initial diagnostic lumbar puncture, before high-dose corticosteroids. This approach need not delay timely treatment of a truly fulminant demyelinating attack. A positive result should prompt anti-amoebic therapy and consideration of biopsy. These suggestions are based on a single case and need testing in larger series.

Limitations. FLA culture or genotyping was unavailable. We did not perform histopathology, iron staining of the cortical margin, or tissue PCR for FLA, as she responded well to anti-amoebic treatment. CD4 count or an immunoglobulin assay were not measured.

Learning points

- *Acanthamoeba* brain infection is an infectious mimic of tumefactive demyelinating lesions (TDLs)
- Consider open-ring lesions a radiological syndrome rather than a radiological signature of multiple sclerosis.
- Before immunosuppressing for presumed tumefactive demyelination, exclude CNS infection. A negative CSF FLA PCR does not exclude infection; consider a biopsy if suspicion persists.

Declarations

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Ethics approval: This study involves human participants, and ethics committee approval is not required for an individual case report.

Data availability statement: Data are available in the article.

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Figures

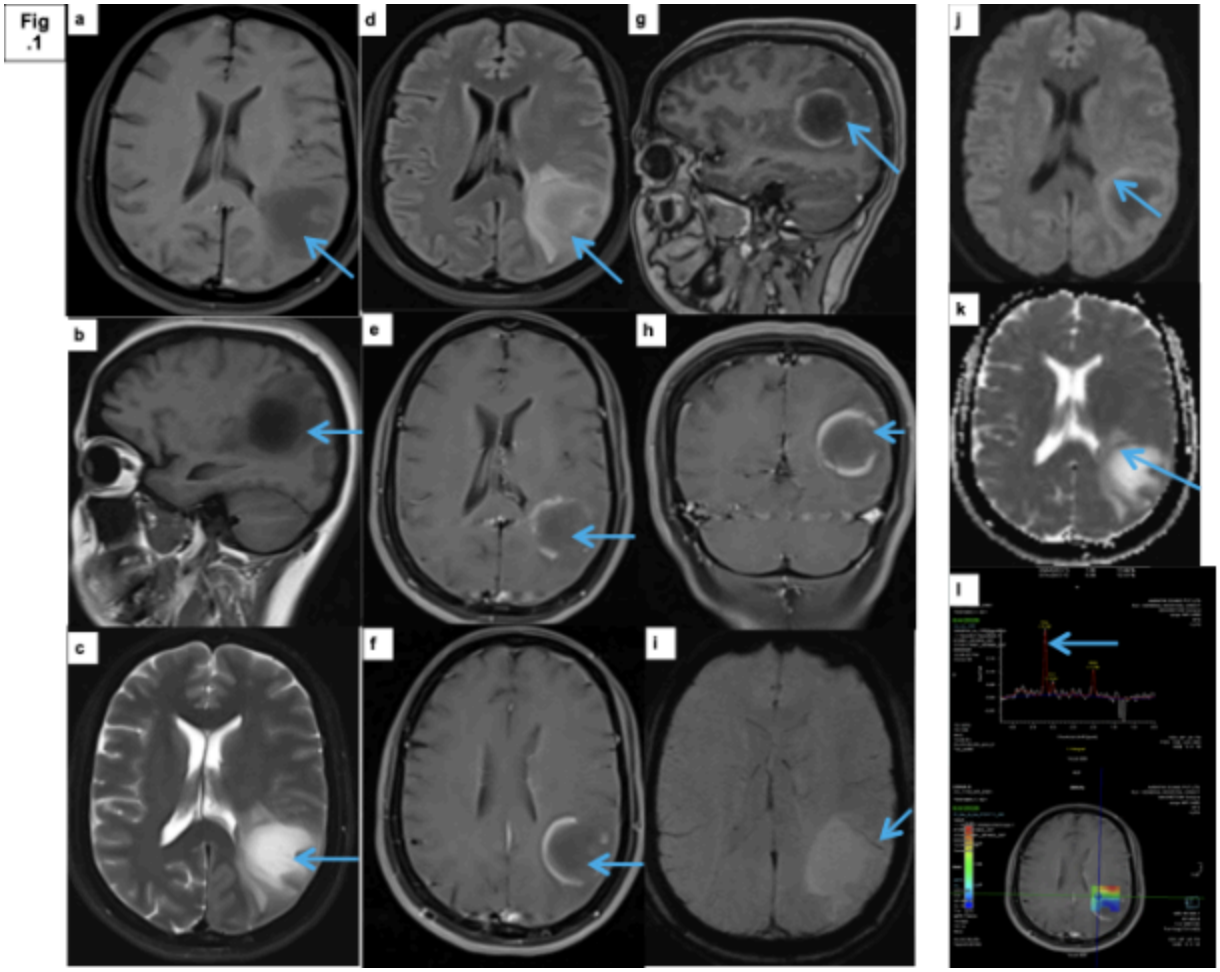


Figure 1

MRI of the left posterior parietal lobe lesion (arrows).

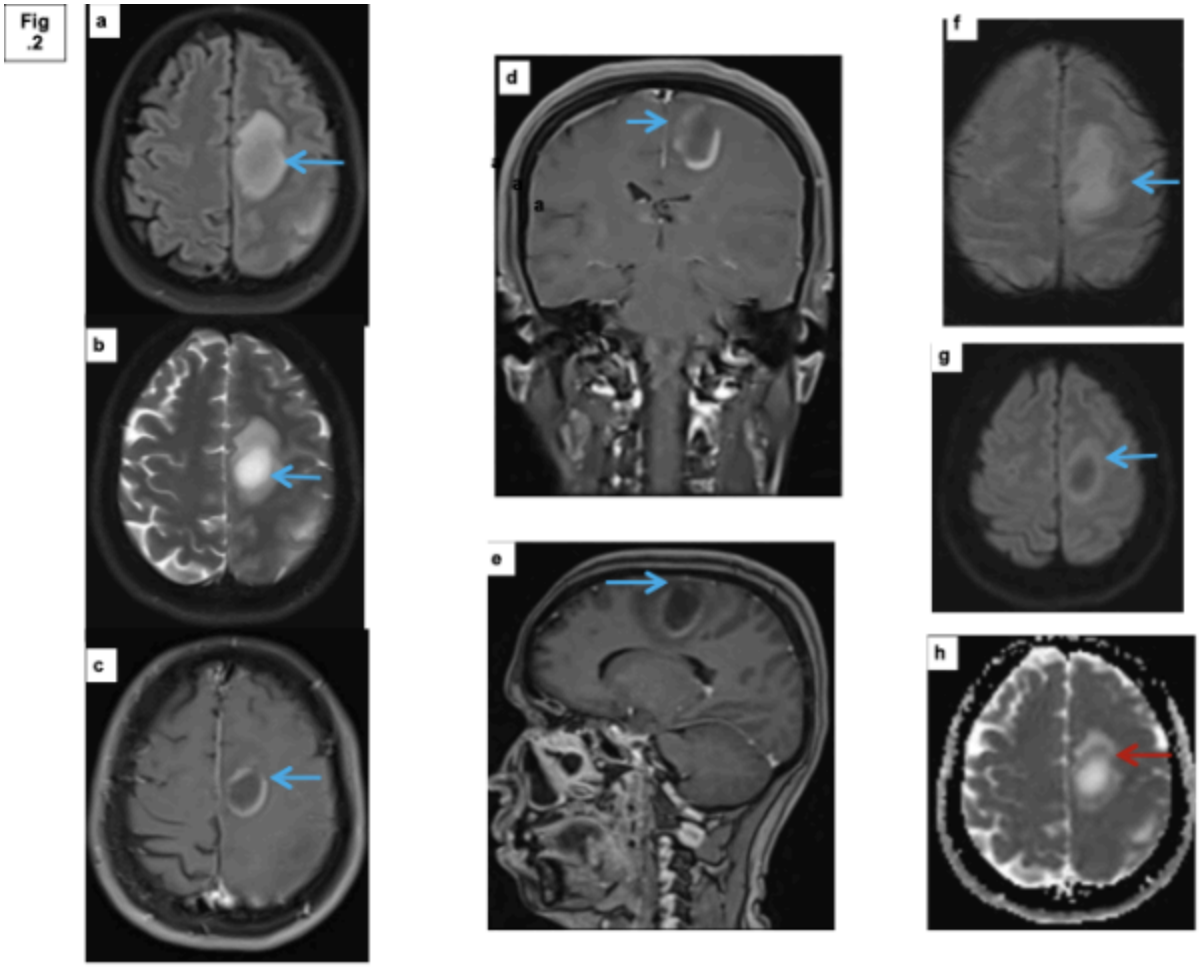


Figure 2

MRI of the left high frontal lobe lesion (arrows).

Fig. 3

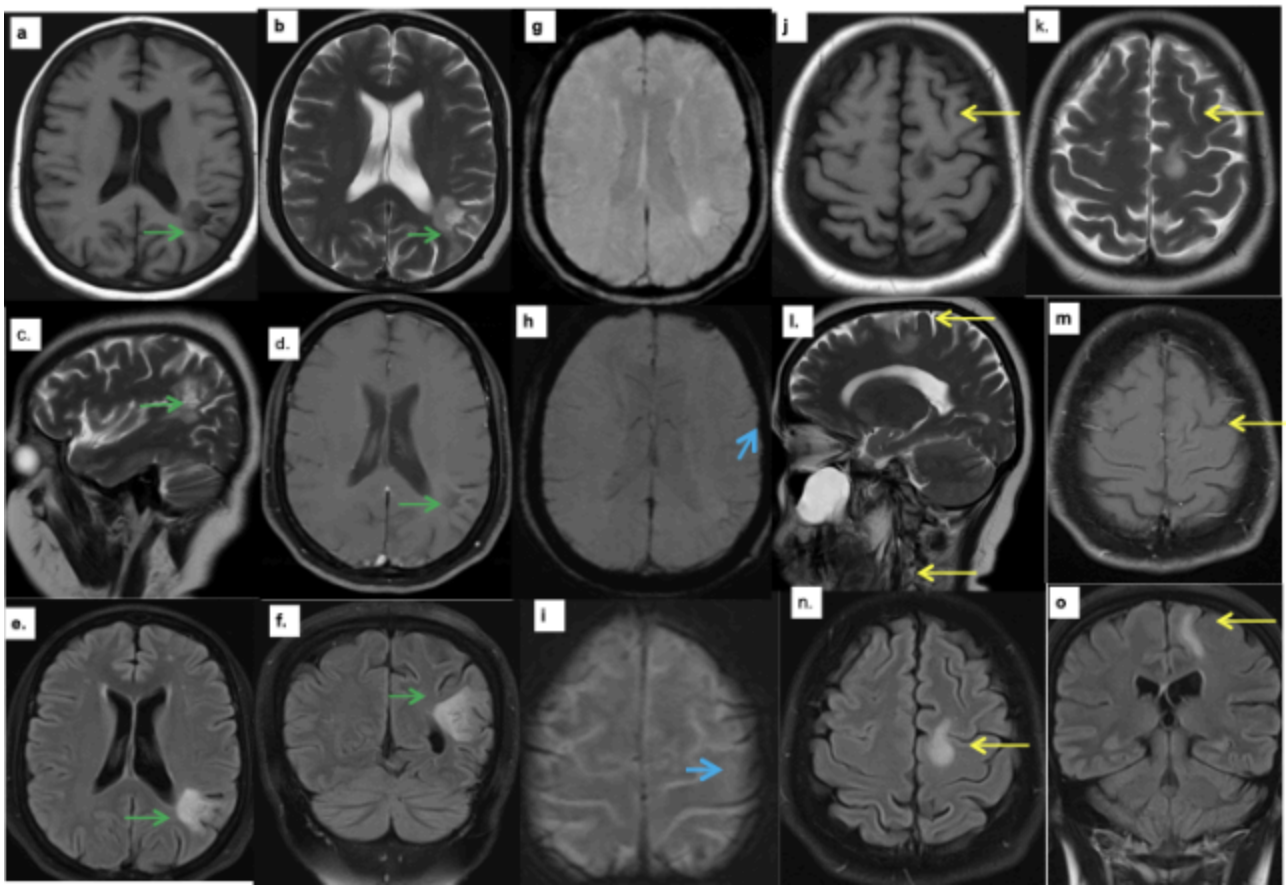


Figure 3

Follow-up MRI on 18 September.