A 30-year-old woman with left hand weakness: a case of tumefactive multiple sclerosis

Jillian Moore, Harvard Medical School Year III
Gillian Lieberman, MD

Jillian Moore, MSIII
Gillian Lieberman, MD

Agenda

1) Patient presentation
2) White matter disease
3) Multiple sclerosis
4) Tumefactive multiple sclerosis
5) Patient course

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Gillian Lieberman, MD

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Gillian Lieberman, MD

Our patient

A 30-year-old woman presented with **progressive left hand weakness** she first noticed 3 days earlier while playing the piano.

- No recent trauma or infections.
- No associated symptoms.

Our patient: her history

- Past medical history:
  - Migraines since childhood
  - Ectopic pregnancy
- Single mother from Chile most recently living in a shelter in Somerville.
- No use of tobacco, alcohol, or other drugs

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Our patient: her physical exam

- **Left fingers**: muscle contractions but **no joint motion**
- Left wrist: joint motion with gravity removed
- **Increased reflexes** bilaterally

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Our patient: initial imaging

Due to the **rapid onset of her focal neurological symptoms**, we worried about an acute process in the brain.

We first ordered a **non-contrast head CT** to look for acute hemorrhage.

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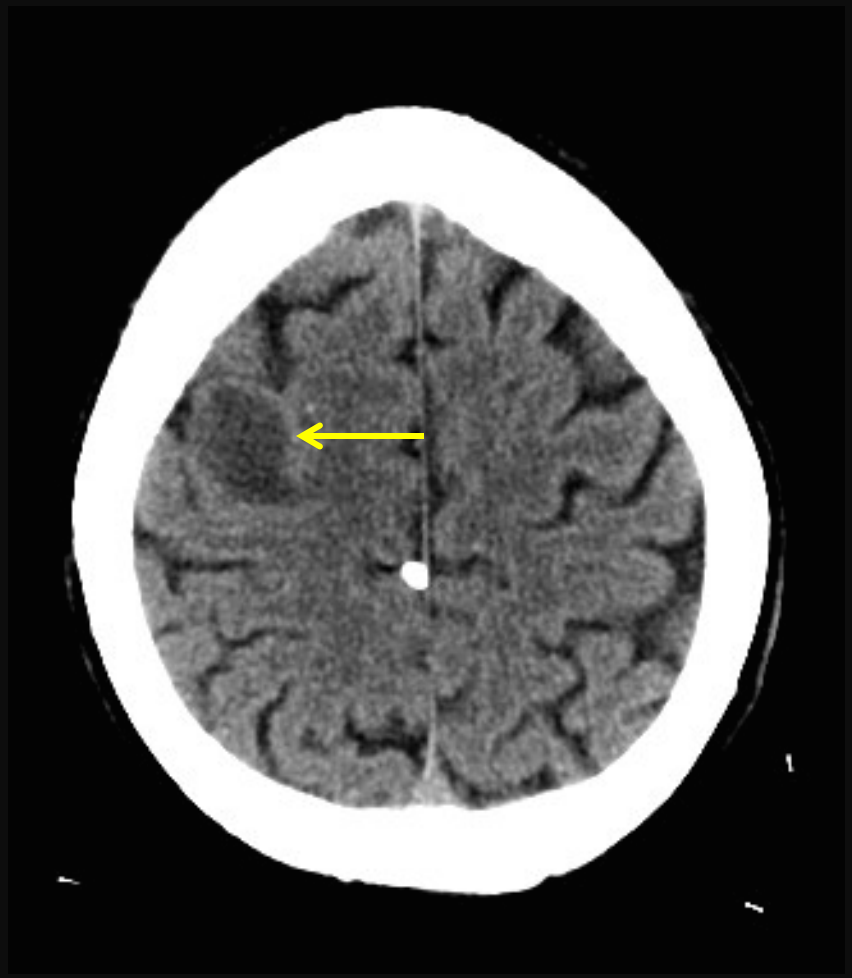
Our patient: lesion on CT



Hypodense lesion in the right precentral frontal lobe not seen on the MRI one year prior.

No acute hemorrhage.

C-, axial head CT

BIDMC PACS

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Our patient: additional imaging

To further characterize the lesion seen on the non-contrast head CT, we ordered a head MRI.

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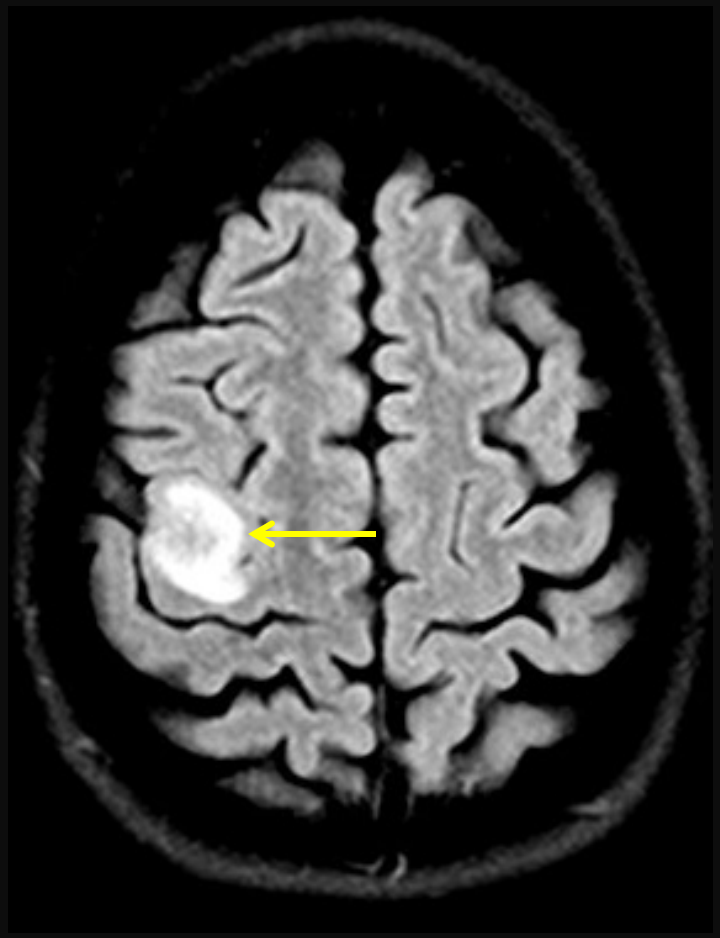
Our patient: lesion on MRI



C-, axial head FLAIR MRI *BIDMC PACS*

Right precentral gyrus lesion measures 1.8 x 1.6 x 1.9 cm and shows peripheral FLAIR hyperintensity.

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FLAIR MRI

- **FLAIR** (fluid-attenuated inversion recovery) is a **T2-weighted** sequence.
- On T2 MRI **fluid is bright**. Cerebrospinal fluid, edema, and inflammation will be bright.
- For FLAIR MRI, the effect of **CSF has been suppressed** in order to bright out the presence of **edema and inflammation**.

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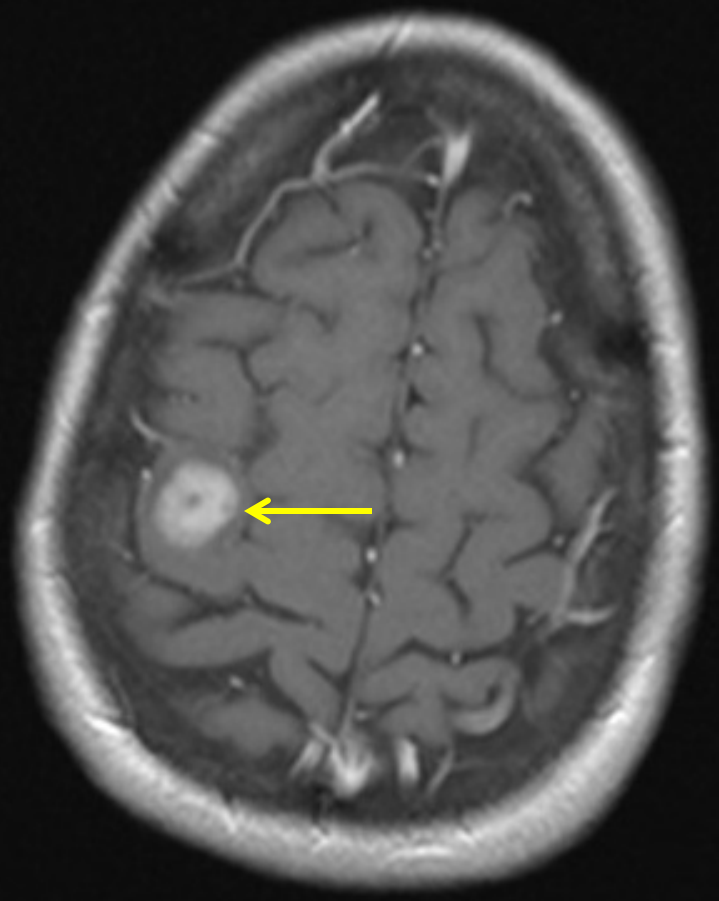
Our patient: lesion on MRI



Lesion shows heterogeneous central enhancement with gadolinium contrast.

C+, axial head T1 MRI post gadolinium *BIDMC PACS*

Gadolinium IV contrast

- Gadolinium is a metal ion that is **paramagnetic**, meaning that it moves differently in a magnetic field. It is chelated to reduce toxicity.

- It crosses the **blood-brain barrier** only where the barrier has been **degraded** by processes like neoplasm or **acute inflammation**. Therefore, these processes will enhance.

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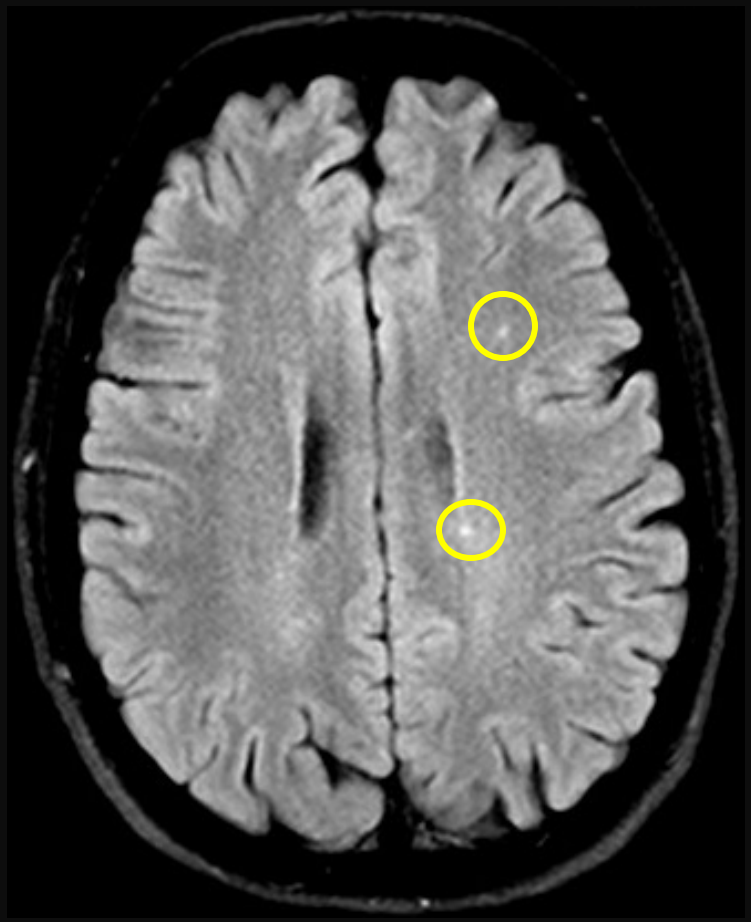
Our patient: other lesions on MRI



C-, axial head FLAIR MRI *BIDMC PACS*

FLAIR hyperintense foci in the periventricular white matter.

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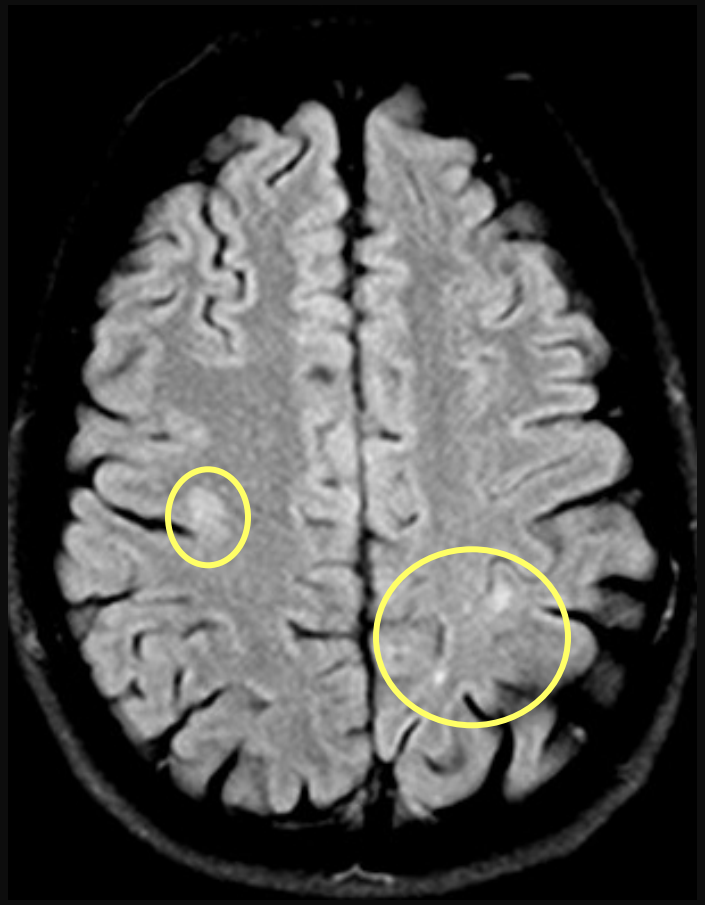
Our patient: other lesions on MRI



C-, axial head FLAIR MRI *BIDMC PACS*

FLAIR hyperintense foci in the subcortical white matter.

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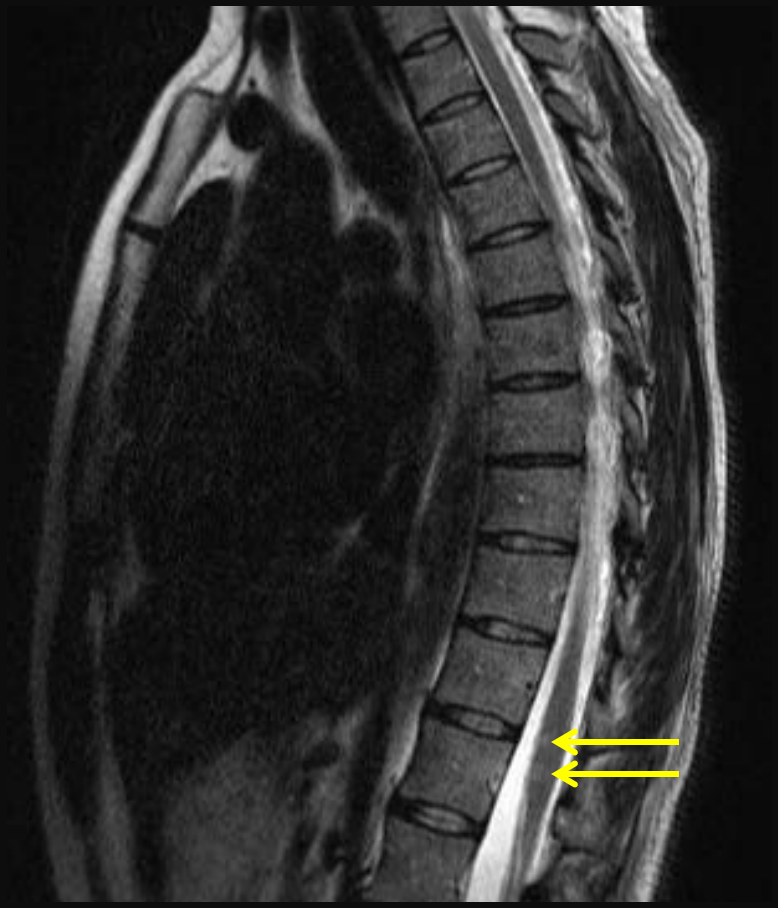
Our patient: spine lesions on MRI



C-, saggittal thoracic T2 MRI *BIDMC PACS*

T2 hyperintense lesions in the thoracic spinal cord.

Our patient: imaging summary

- She has **diffuse white matter disease**.
  - There is a lesion in the right precentral gyrus that is FLAIR-hyperintense and peripherally enhancing.
  - There are small FLAIR-hyperintense lesions in the subcortical and periventricular areas of the brain and T2-hyperintense lesions in the thoracic spinal cord. These do not enhance.

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2) **White matter disease**
3) Multiple sclerosis
4) Tumefactive multiple sclerosis
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Diffuse white matter disease differential diagnosis

- **It can be infectious:**
  - HIV, tuberculosis, Lyme disease

- Inflammatory
  - acute disseminated encephalomyelitis (post-infectious), systemic lupus erythematous (SLE), Sjögren syndrome, sarcoidosis, multiple sclerosis

- Neoplastic
  - metastasis, glioma, CNS lymphoma

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Our patient: other studies

- A CT of her abdomen and pelvis did not show any primary malignancy.
- Her white matter disease was not likely due to metastasis.

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Our patient: other studies

- Her tuberculin skin test was negative.
- The following studies were normal:
  - CBC, ESR, BMP, LFTs, coagulation factors, angiotensin converting enzyme
  - ANA, CRP, HIV antibody, dsDNA antibody, Sjögren-associated antibodies
  - CSF: cultures, cytology, protein and glucose

- Her white matter disease was not likely due to sarcoidosis, SLE, Sjögren syndrome, or infection.

Our patient: other studies

- Her CSF showed increased oligoclonal bands and IgG index.

- These are markers of intrathecal IgG synthesis.
  - Increased CSF oligoclonal bands are seen in 95% of patients with multiple sclerosis (Dobson et al. 2013).
  - Increased IgG index is seen in 90% of patients with multiple sclerosis (McLean et al. 1990).
  - These measures can also be increased due to infections or other inflammatory etiologies.

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Our patient: differential diagnosis

It seemed likely that her lesion was due to multiple sclerosis; however with the large tumor-like lesion in the pre-central gyrus we could not necessarily rule out CNS lymphoma or glioma.

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1) Patient presentation
2) White matter disease differential
3) **Multiple sclerosis**
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Multiple sclerosis (MS)

- MS is a disease of **multifocal inflammatory demyelinating white matter lesions** with variable presenting symptoms depending on where the lesions appear.

- It can be progressive or relapsing and remitting.

- The mean age of onset of 28-31 years (Goodin 2014), and the female-to-male ratio is about 2:1 (Alonso & Hernán 2008).

Diagnosing MS

MS is diagnosed according to the McDonald criteria (Polman et al. 2011) which require clinical or radiological evidence of the **dissemination of CNS lesions in time and space**.

MS: dissemination in **time**

- Clinical
  - A second clinical attack

- Radiological
  - Presence on MRI post gadolinium of **both** enhancing (acute) and non-enhancing (non-acute)
  - New enhancing or T2-hyperintense lesions on a follow-up MRI

From Polman et al. 2011

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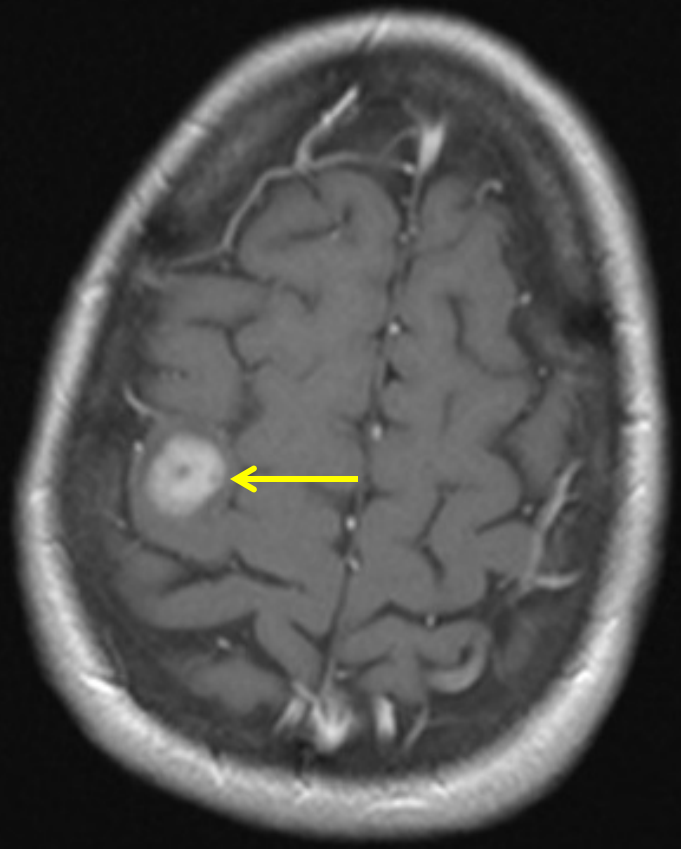
Our patient: dissemination in time



Her T1 MRI showed an enhancing lesion in the pre-central gyrus as well as other non-enhancing lesions in the brain and spinal cord

C+, axial head T1 MRI post gadolinium *BIDMC PACS*

MS: dissemination in **space**

- Clinical
  - A second clinical attack that implicates a lesion in a different region of the CNS

- Radiological
  - One or more lesions on T2 MRI in regions of the CNS typical of MS (periventricular, juxtacortical, infratentorial, spinal cord)

From Polman et al. 2011

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Our patient: dissemination in space

Her FLAIR MRI showed hyperintense lesions in the subcortical and periventricular regions.

Her T2 MRI showed hyperintense lesions in the lower thoracic spinal cord.

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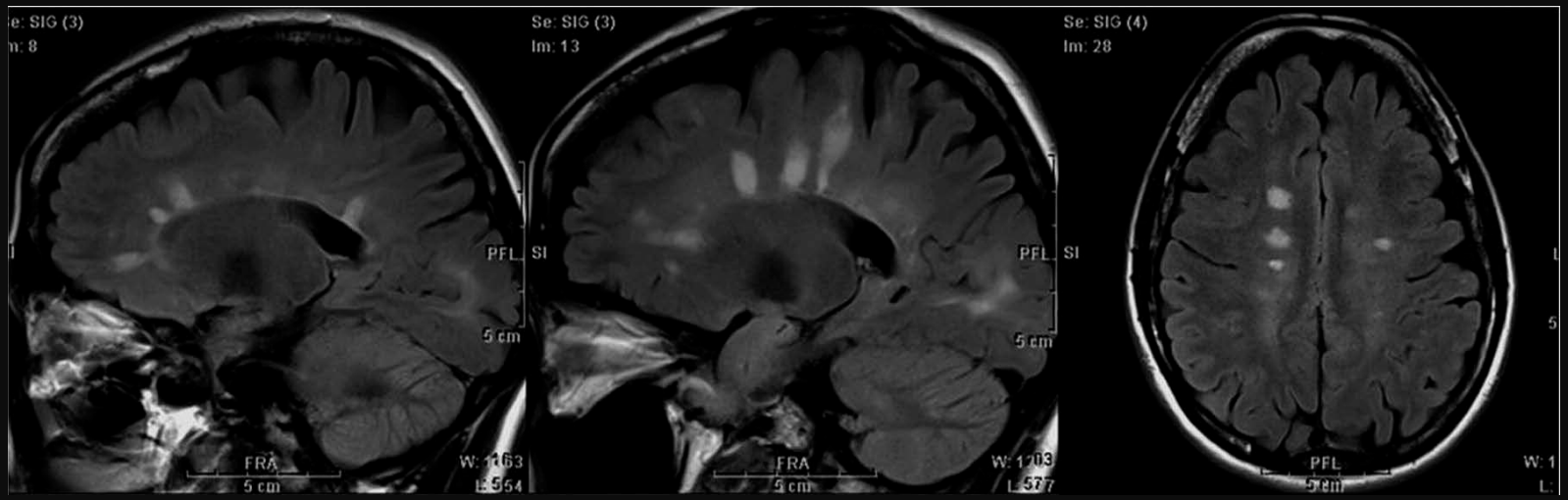
Another patient: MS lesions on MRI

- While our patient meets the McDonald criteria for MS, her **tumor-like lesion** is **not typical of MS**.
- MS plaques are **typically small ovoid lesions** of less than 2 cm, as seen in the MRI below.



C-, saggittal and axial FLAIR head MRI

Modified from Lövblad et al. 2010

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4) **Tumefactive multiple sclerosis**
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Tumefactive MS

Tumefactive MS is an **atypical variant** with **tumor-like lesions** larger than 2 cm in size.

In patients with clinically isolated attacks, tumefactive MS lesions are **difficult to differentiate from neoplasms on MRI** and may require biopsy to confirm a diagnosis of MS (Lucchinetti et al. 2008).

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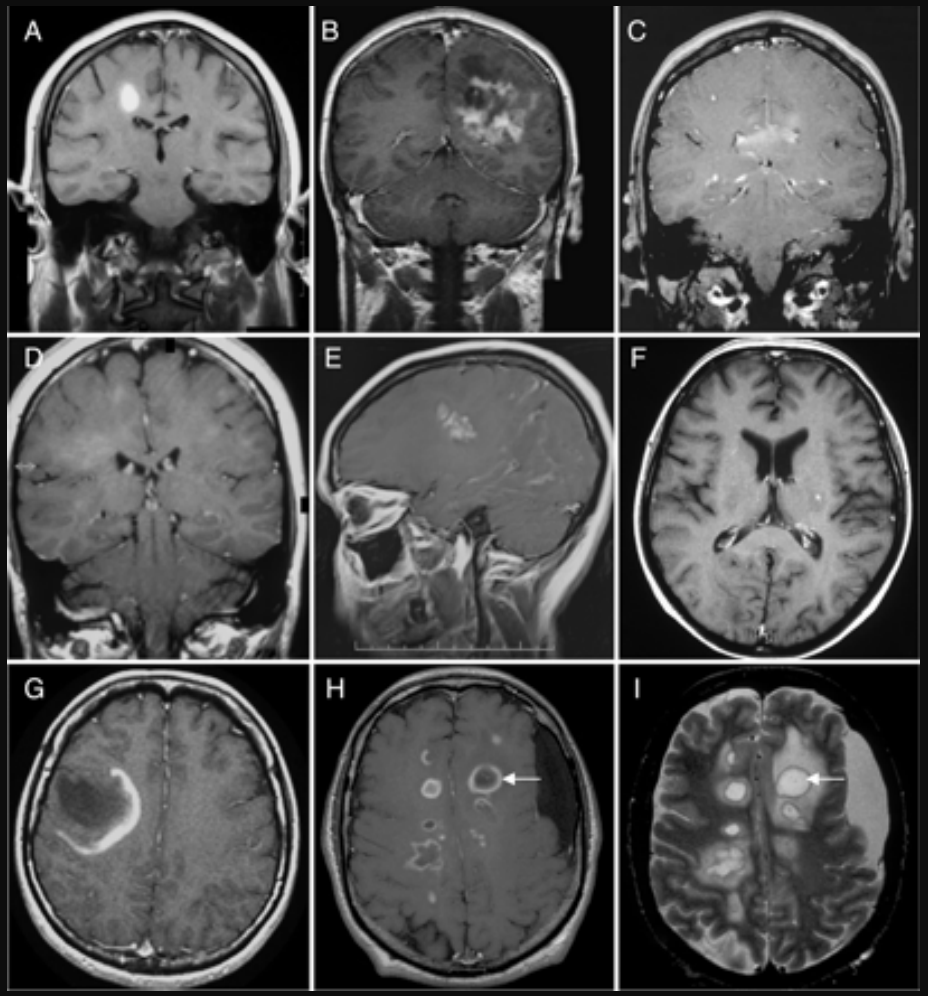
Other patients: tumefactive lesions on MRI



C+, axial T1 MRI post gadolinium *Lucchinetti et al. 2008*

Tumefactive MS plaques have variable appearances.

They can have a **variety of enhancement patterns** including homogenous (A), heterogeneous (B), open ring (G), and closed ring (H).

Tumefactive MS: diagnosis

While tumefactive MS has variable appearance on MRI, some tools have been proposed to differentiate tumefactive MS lesions radiologically and avoid biopsy:

1) Tumefactive MS plaques often have open ring enhancement on T1 MRI post gadolinium with the incomplete portion facing the grey matter (Hardy & Chataway 2013).
2) Tumefactive MS gadolinium-enhancing lesions are more likely to show CT hypodensity than those of CNS lymphoma (Kim et al. 2009).
3) Serial proton MR spectroscopy may be used to differentiate between glioma and tumefactive MS (Butteriss et al. 2003).

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Tumefactive MS: diagnosis

Despite these proposed tools, it continues to be difficult to differentiate tumefactive MS from neoplasms like CNS lymphoma or glioma especially in patients with clinically isolated attacks.

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Our patient: MS diagnosis

She was diagnosed with tumefactive MS.

She met the McDonald criteria of dissemination of CNS lesions in time and space. The increased CSF oligoclonal bands and IgG index supported this diagnosis.

Our patient: MS treatment

While in the hospital, she completed a five-day course of hydroprednisolone. This is the standard treatment for an acute MS attack.

She also met regularly with our physical and occupational therapists.

Our patient: MS treatment

After discharge, she continued to see an occupational therapist. In outpatient clinic three weeks later, she had full strength of all the muscles in her left hand and wrist.

Two months later, she started monthly natalizumab infusions. Patients with relapsing-remitting MS choose from a variety of immunomodulatory treatments including interferon beta. These treatments reduce the relapse rate, but they may not affect long-term outcomes.

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Summary

1) T1 MRI post gadolinium contrast may be used to differentiate acute inflammation from chronic lesions.
2) The differential diagnosis for diffuse white matter disease is broad and includes infectious, inflammatory, and neoplastic etiologies.
3) A diagnosis of multiple sclerosis requires demonstrating dissemination of CNS lesions in time and space. Intrathecal IgG synthesis is a supportive feature.
4) Tumefactive multiple sclerosis is an atypical variant that can be difficult to distinguish from neoplasm, though various radiologic tools have been proposed.
5) The treatment for an acute MS attack is IV steroids. Long-term management of relapsing-remitting MS includes immunomodulatory therapies like natalizumab and interferon-beta.

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