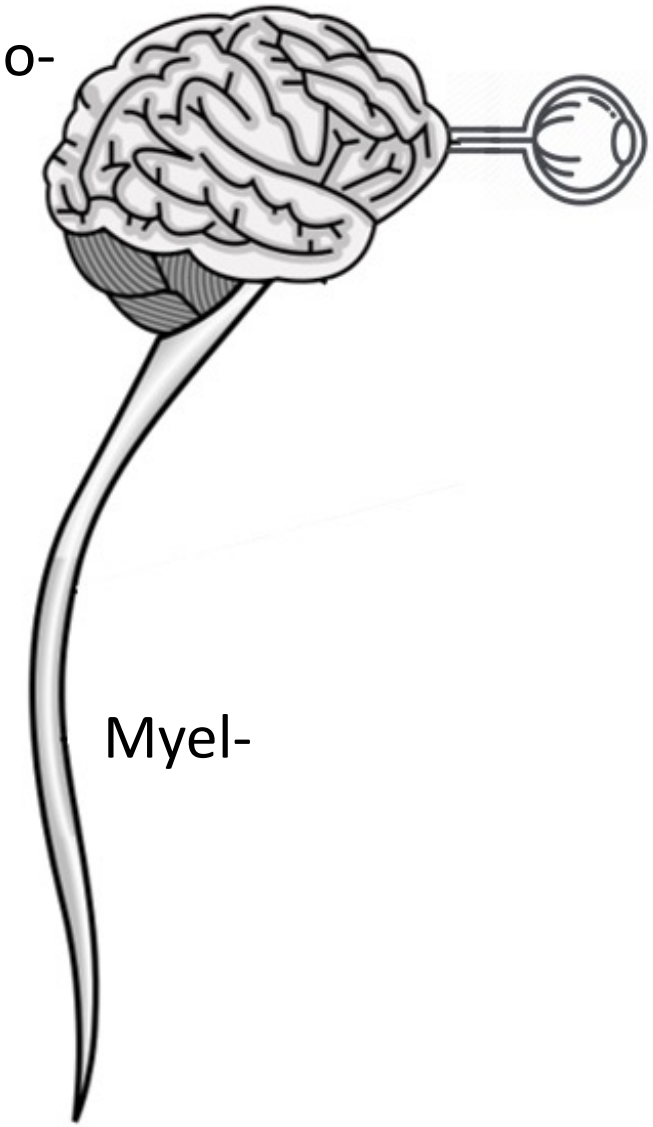
How do you get a diagnosis of ADEM, AFM, MOGAD, NMOSD, ON and TM

KYLE BLACKBURN AND BEN GREENBERG

10/8/2021

Learning the lingo

Encephalo-



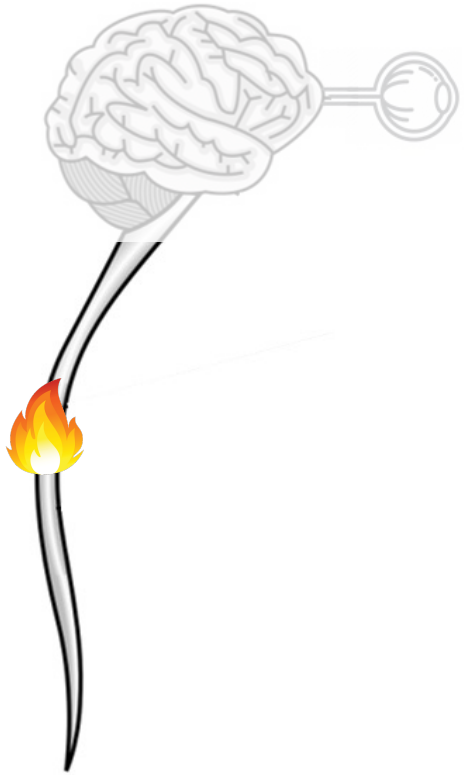
Optic neur-

Myel-

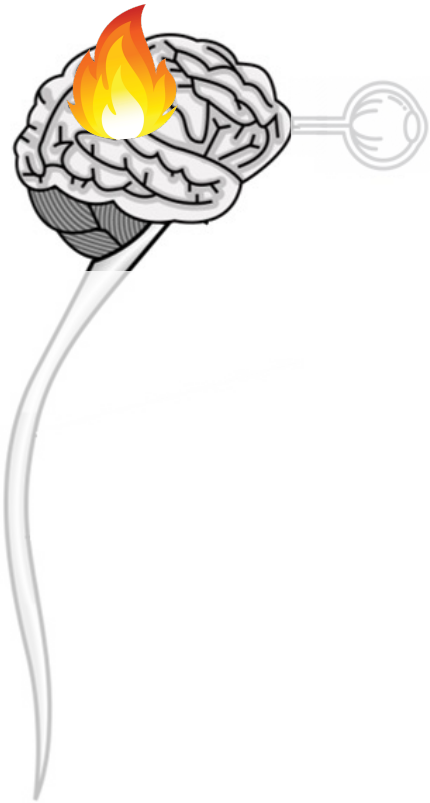
-itis

Learning the lingo

Optic Neuritis



Myelitis



Encephalitis

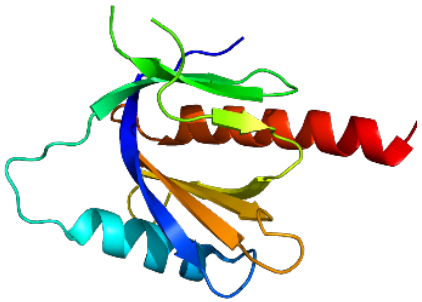
* These terms are descriptive. They do not explain WHY the inflammation occurs.

The list of causes for nervous system injury is extensive

Infections

Toxins

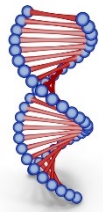
Inflammation



Degeneration

Stroke

Bleed



Genetic

TABLE 1-3 Causes of Chronic Progressive Myelopathy

Cause	Suggestive Diagnostic Clues
Multiple sclerosis	Progressive forms of multiple sclerosis particularly in older adults, oligoclonal bands in CSF, suggestive lesions on MRI of brain, short-segment cord lesion located peripherally, history of progressive cognitive decline
Nutritional	Vitamin B_{12} deficiency: posterolateral syndrome, macrocytic anemia, low serum vitamin B_{12}, elevated homocysteine and methylmalonic acid Copper deficiency: posterolateral syndrome, exposure to excess zinc, peripheral neuropathy, low serum copper levels Vitamin E deficiency: spinocerebellar syndrome, retinopathy, low serum α-tocopherol levels
Toxic	Exposure to IV or intrathecal methotrexate (produces posterolateral syndrome), cytarabine, and other possible chemotherapeutic associations including cisplatin and cladribine
Spinal dural arteriovenous fistula	Usually in older men with slowly progressive myelopathy; MRI with cord T2 hyperintensity, peripheral T2 hypointensity, and perimedullary flow voids; spinal angiogram with vascular malformation
Infectious	Human immunodeficiency virus (vacuolar myelopathy appears similar to vitamin B_{12} deficiency), human T-cell lymphotropic virus type I (HTLV-I)-associated myelopathy, syphilis (causes dorsal column syndrome with peripheral neuropathy)
Neoplastic	More common to have compressive lesions (meningiomas, metastases, or other mass lesions); intramedullary tumors usually ependymoma (central cord lesion often with associated syrinx, persistent enhancement on MRI), myxopapillary ependymoma (lumbosacral cord and filum terminale propensity), or astrocytoma; rare to have intramedullary metastases
Motor neuron disease	Selective degeneration of ventral motor neurons including amyotrophic lateral sclerosis (usually with upper motor neuron findings and sparing bowel/bladder function), Kennedy disease (spinal and bulbar muscular atrophy), monomelic amyotrophy
Genetic disorders	Hereditary spastic paraplegia: expanding group of disorders causing spastic paraparesis usually with dorsal column involvement, presence of family history, evaluated by genetic sequencing Adrenoleukodystrophy: progressive spastic paraparesis with sensory loss, adrenal insufficiency may not be overt, elevated levels of very long chain fatty acids, *ABCD1* mutation analysis Friedreich ataxia: early prominent sensory ataxia with progressive corticospinal tract weakness and cerebellar signs, associated with cardiomyopathy and diabetes mellitus, autosomal recessive disorder with loss of function of frataxin protein Spinocerebellar ataxia: autosomal dominant disorder with ataxia as core feature with other neurologic signs and symptoms including myelopathy
Delayed radiation myelopathy	History of more than 45 Gy of radiation particularly with combination chemotherapy, onset months to years after radiation; paraparesis with sensory involvement; MRI in early phase with T2 hyperintensity, cord swelling, and variable enhancement

Cho and Bhattacharrya. Continuum 2018.

Review symptoms and perform examination

Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

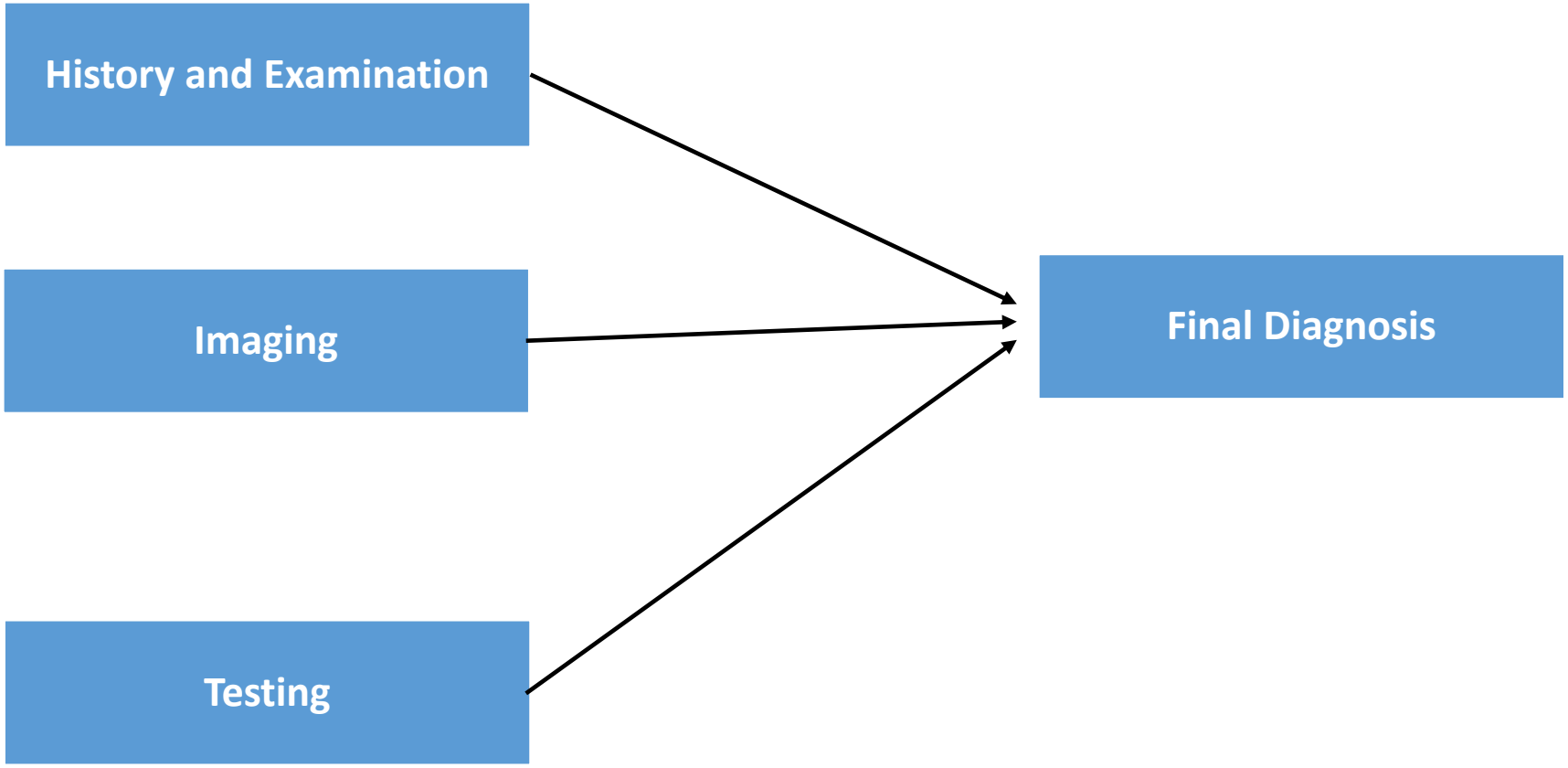
Formulate list of possibilities (“Differential Diagnosis”)

Collect evidence to narrow down possibilities

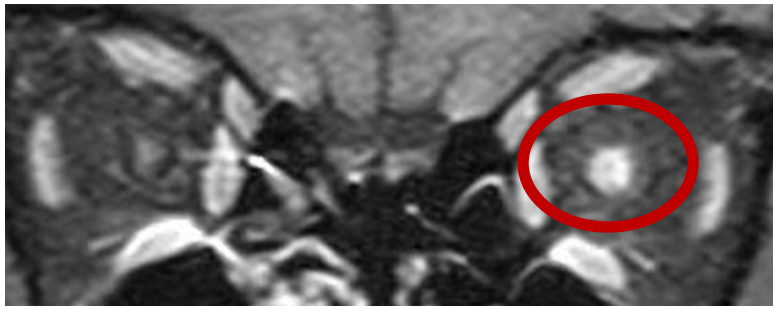
Obtain imaging	CSF analysis (lumbar puncture)	Obtain appropriate supportive tests

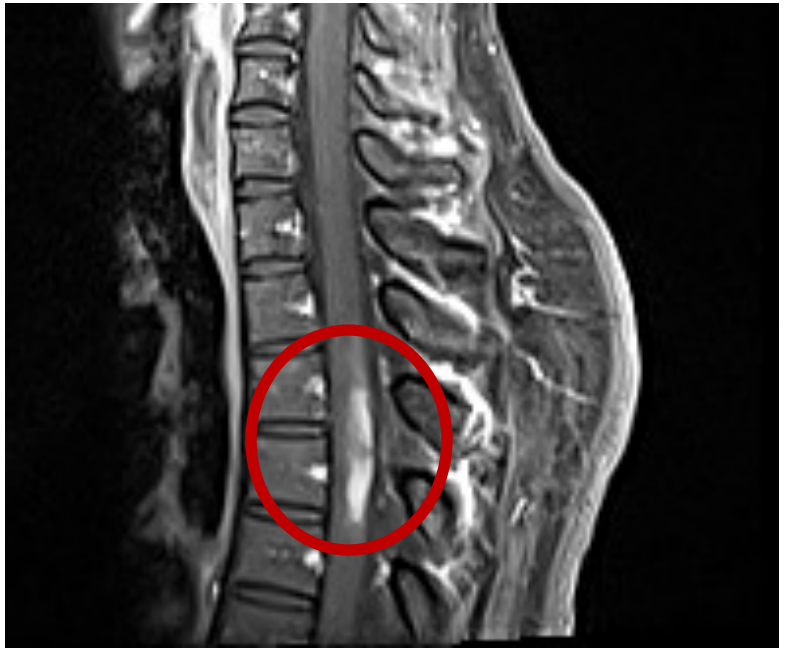
Formalize Diagnosis (or establish a “working diagnosis”)

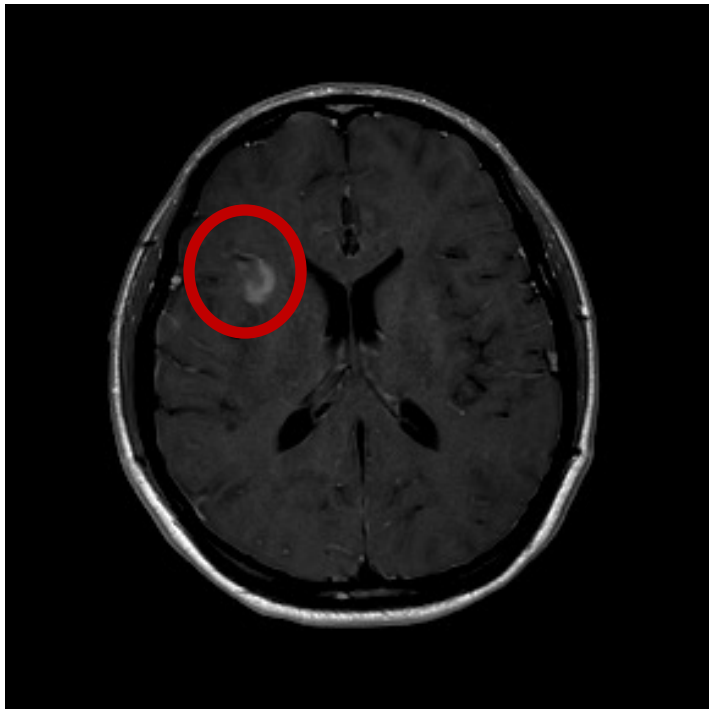
Ways to reach the final diagnosis



Clues for inflammation in the nervous system: MRI scans

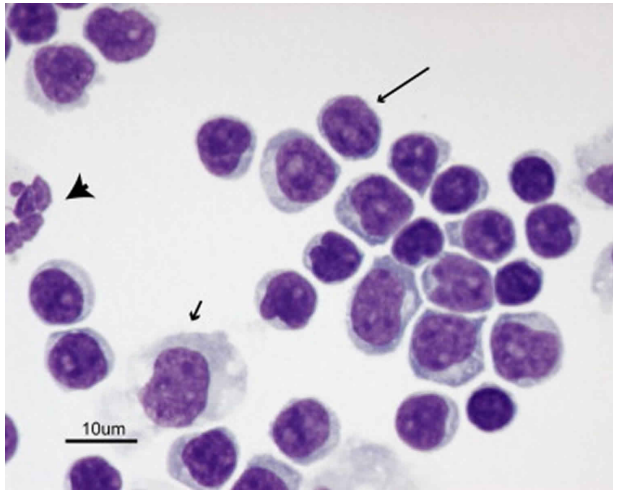






Contrast enhancement is a marker of recent inflammation.

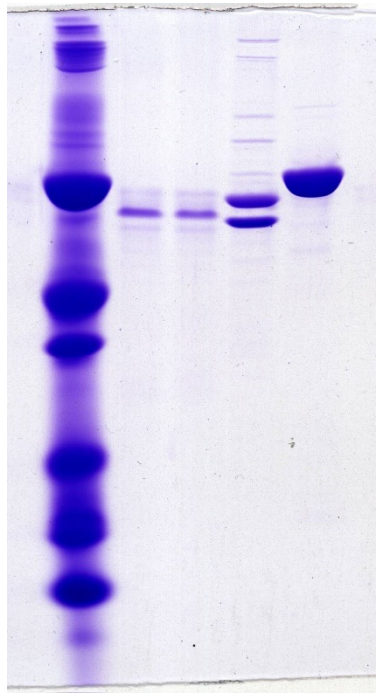
Clues for inflammation in the nervous system: MRI scans



Elevated white blood cells

Elevated protein levels

Normal sugar (glucose) level



Antibody production in CSF (oligoclonal bnads)

How we make a diagnosis of:

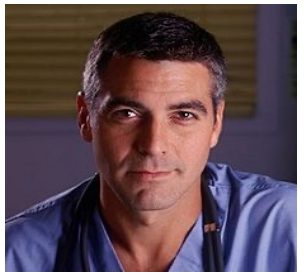
myelitis

33 year-old woman presents with leg weakness, sensory changes, and urinary incontinence that started 4 days ago.

Review symptoms and perform examination

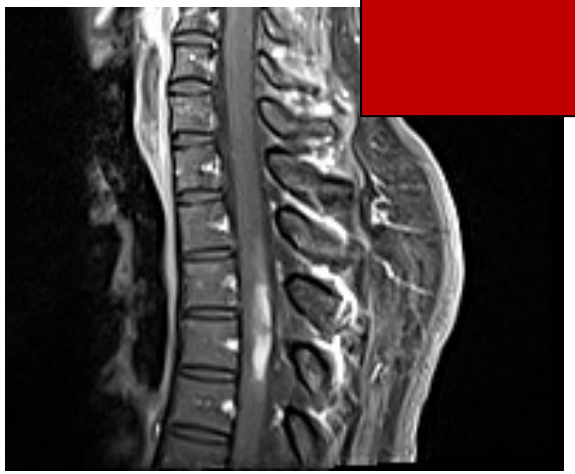
Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

Obta



“Spinal Cord”

More testing is needed to determine why the spinal cord inflammation has occurred.

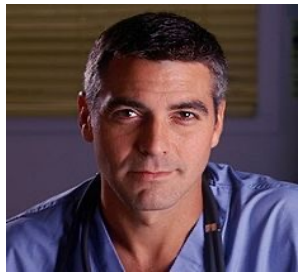


ng Diagnosis: “Transverse myelitis”

Review symptoms and perform examination

Determine ‘where’ in the nervous system damage is occu

Obtai



nal Cord”

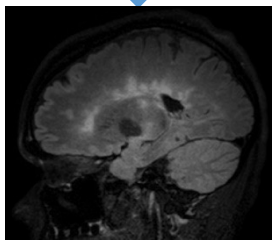
g Diagnosis:
erse myelitis”

Diagnosis:
ple Sclerosis

Treatment with Immunotherapies

In certain cases, a person that has had myelitis should undergo close monitoring to see if they develop signs of multiple sclerosis.

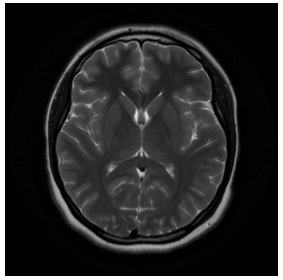
Brain imaging

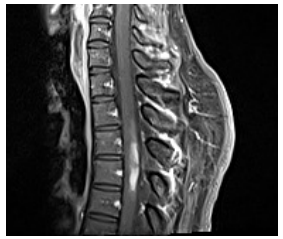


Review symptoms and perform examination

Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

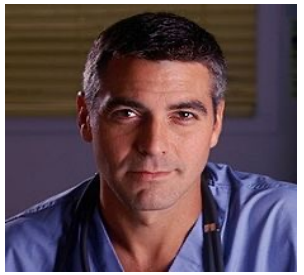
Obtains imaging and CSF analysis





Confirmatory Testing (~1 week later)

Aquaporin-4 antibodies



“Spinal Cord”

Working Diagnosis: “Transverse myelitis”

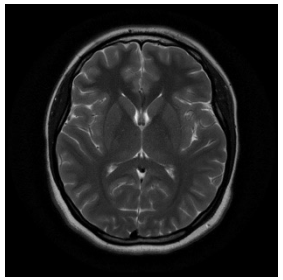
Final Diagnosis: AQP4 + Neuromyelitis Optica

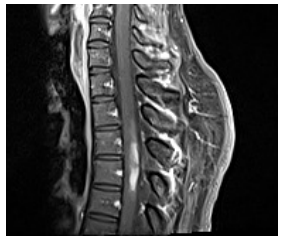
Treatment with Immunotherapies

Review symptoms and perform examination

Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

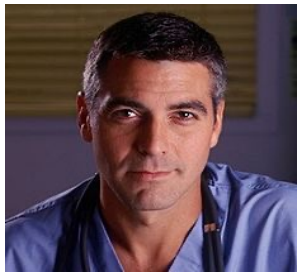
Obtains imaging and CSF analysis





Confirmatory Testing (~1 week later)

Myelin Oligodendrocyte Glycoprotein antibodies



“Spinal Cord”

Working Diagnosis: “Transverse myelitis”

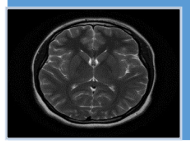
Final Diagnosis: MOG Associated Disorder

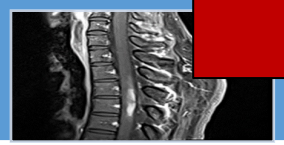
Close monitoring

Review sy

Determine ‘where’

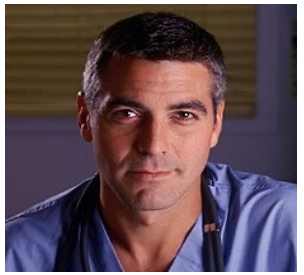
Negati





After a comprehensive evaluation for infections and autoimmune disorders, a person may receive a diagnosis of an ‘idiopathic’ disorder.

This implies no known cause was identified.



“Spinal Cord”

Working Diagnosis: Transverse myelitis”

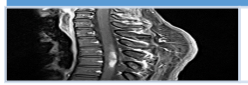
Diagnosis: iopathic Transverse Myelitis

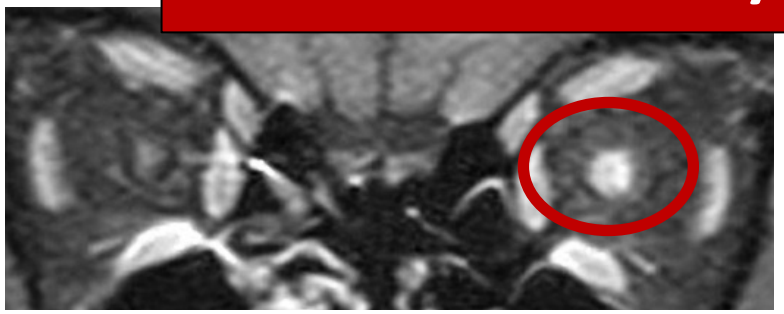
Monitoring and symptomatic management

Review symptoms and perform examination

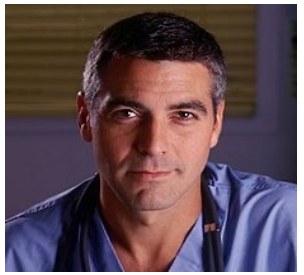
Determine 'whe

Collect e





A diagnosis of seronegative NMOSD can be given if someone has multiple episodes of inflammation in different parts of the nervous system.



"Spinal Cord"

Working Diagnosis:
"Transverse myelitis"

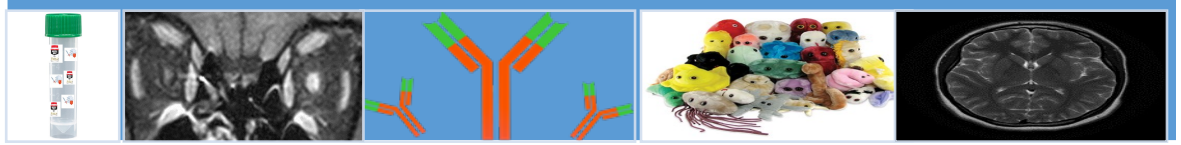
Diagnosis:
Seronegative NMOSD

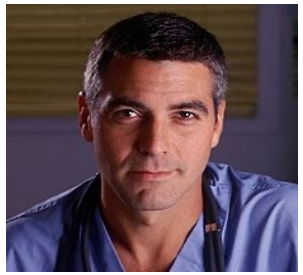
33 year-old woman presents with vision loss and pain that started 4 days ago.

Review symptoms and perform examination

Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

Collect evidence to narrow down possibilities





~~“Spinal cord”~~
“Optic Nerve”

Working Diagnosis:
~~“Transverse Myelitis”~~
“Optic Neuritis”

Diagnosis:
Idiopathic ~~Transverse Myelitis~~ Optic Neuritis

Monitoring and symptomatic management

How we make a diagnosis of:

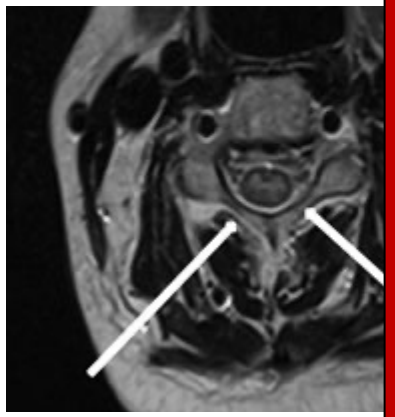
Acute Flaccid Myelitis

8 year-old boy presents with fevers, runny nose, followed by left arm weakness.

Review sym

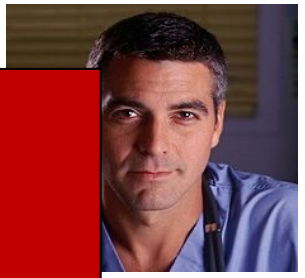
Determine ‘where’ ir
(

Obtain



AFM often presents with:

- Recent signs of a respiratory infection (fever, sore throat, runny nose).
- This is followed by weakness (often in one or both arms), with decreased muscle tone.
- Changes in the motor nerves in the spinal cord on imaging.
- In some cases, the enterovirus testing will return positive.



al Cord”

e Flaccid
yelitis

How we make a diagnosis of:

Acute	Fast onset
Disseminated	Dispersed
Encephalo-	Brain and
Myelitis	Spinal cord inflammation

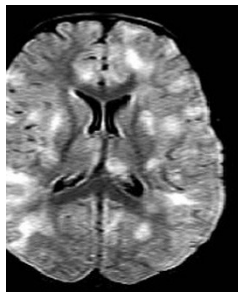
6 year-old boy presents with confusion, weakness, and a seizure starting 3 days ago. Last week, he had a 2 days of diarrhea and fevers.

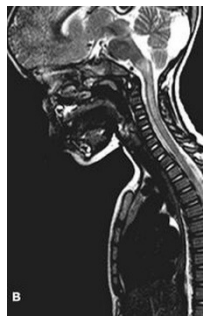
Review symptoms and perform examination

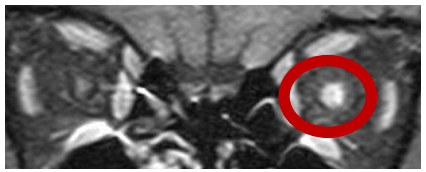
Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

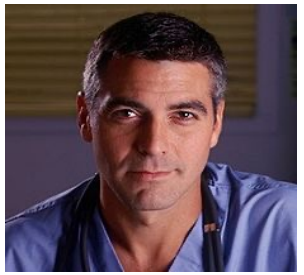
CSF analysis

Imaging









“Brain”

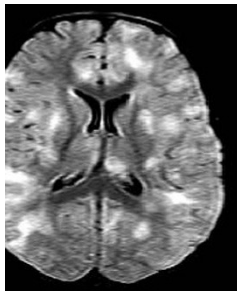
Working Diagnosis:
“Possible meningitis”

Final Diagnosis:
ADEM

Review symptoms and perform examination

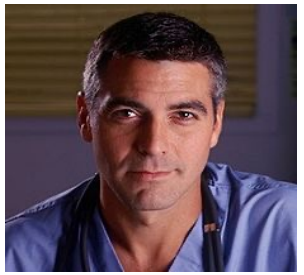
Determine ‘where’ in the nervous system damage is occurring (“localize the lesion”)

CSF analysis and imaging



Testing returns

Myelin Oligodendrocyte Glycoprotein (MOG) Antibodies



“Brain”

Working Diagnosis: “ADEM”

Final Diagnosis: MOG Associated Disorder

Key points

1. Terms such as ‘Transverse Myelitis’ and ‘ADEM’ are purely descriptive– more investigation is needed to determine ‘why’.

2. People with inflammation in the nervous system may receive a more refined diagnosis based on the results of imaging and laboratory testing.

3. If, after a comprehensive evaluation, a clear cause for inflammation is not identified, the cause is labeled as ‘idiopathic’ (example: idiopathic transverse myelitis).

4. In cases where a recurrent episode of inflammation occurs, an ‘idiopathic’ diagnosis should be re-evaluated.