Neuropsychological manifestation of lupus(NPSLE) and neuroimaging findings

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- 50% of patients with SLE have neurological involvement

40% is due to disease itself

other causes are 1) infections

2) metabolic disorders

3) side effects of drugs

Headache
Seizure disorders
Cerebrovascular disease
Demyelinating syndrome
Myelopathy
Movement disorder
Aseptic meningitis
Cognitive dysfunction
Mood disorder
Anxiety disorder
Psychosis
Acute confusional state
Peripheral nervous system
Mononeuropathy
Polyneuropathy
Cranial neuropathy
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)
Plexopathy
Autonomic disorder
Myasthenia gravis

- CNS syndromes are more common than PNS
- Diffuse or focal manifestation
- Single or multiple NPSLE event
- Low quality of life
- High morbidity & mortality

Since there are no biomarkers of CNS activity, the DX of NPSLE is often made by ruling out secondarycauses

Pathogenic mechanisims

1) Inflammatory cytokines
2) BBB disruption
3) Accelerated atherosclerosis
4) Thrombotic vasculopathy
5) Neuronal apoptosis

Headache

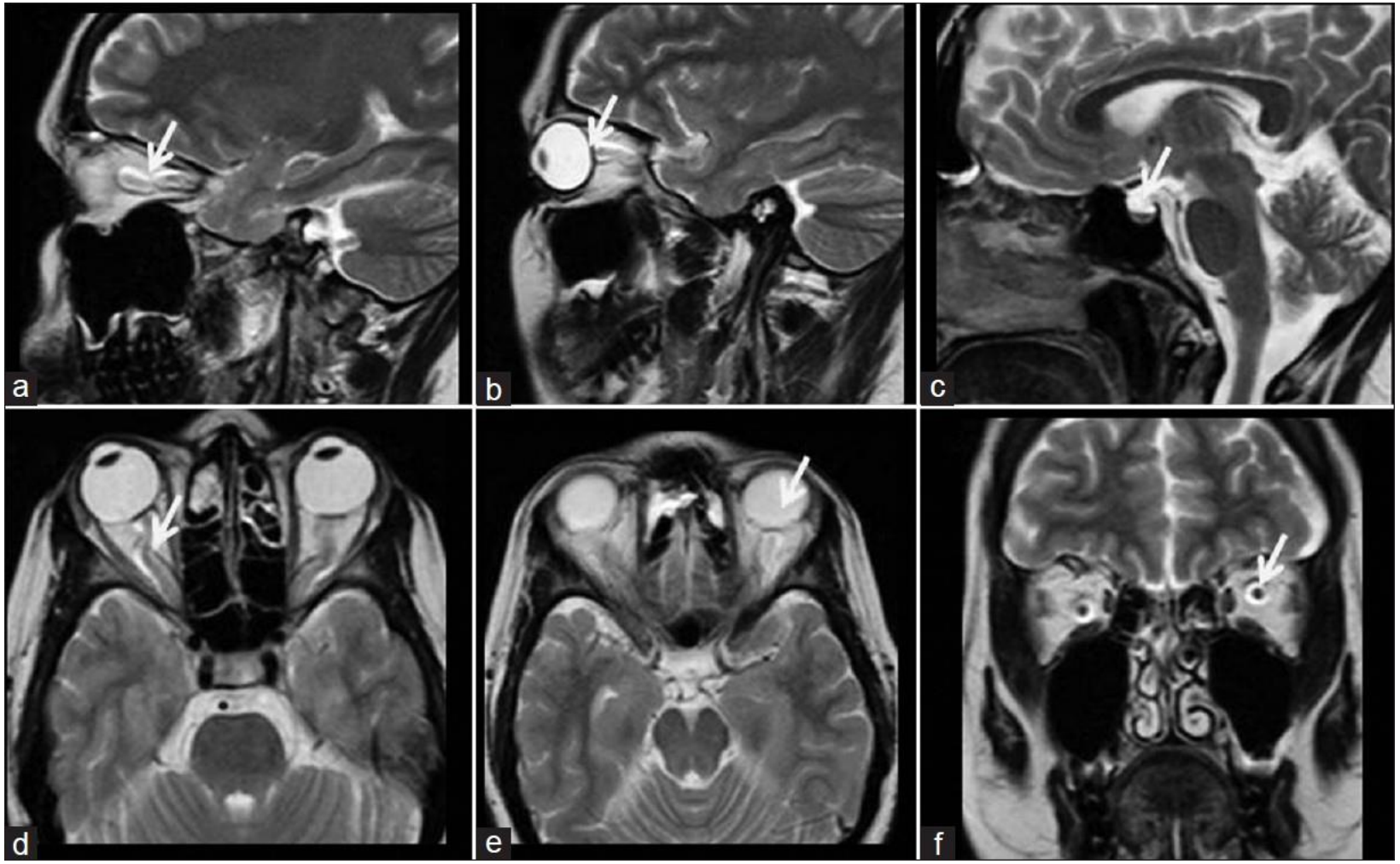
- Common & non-specific
- Migraine has higher perevalance ? (not confirmed)
- Migraine is not associated with
  1) more MRI lesions
  2) disease activity
  3) biomarkers(except aPL)

Always R/O

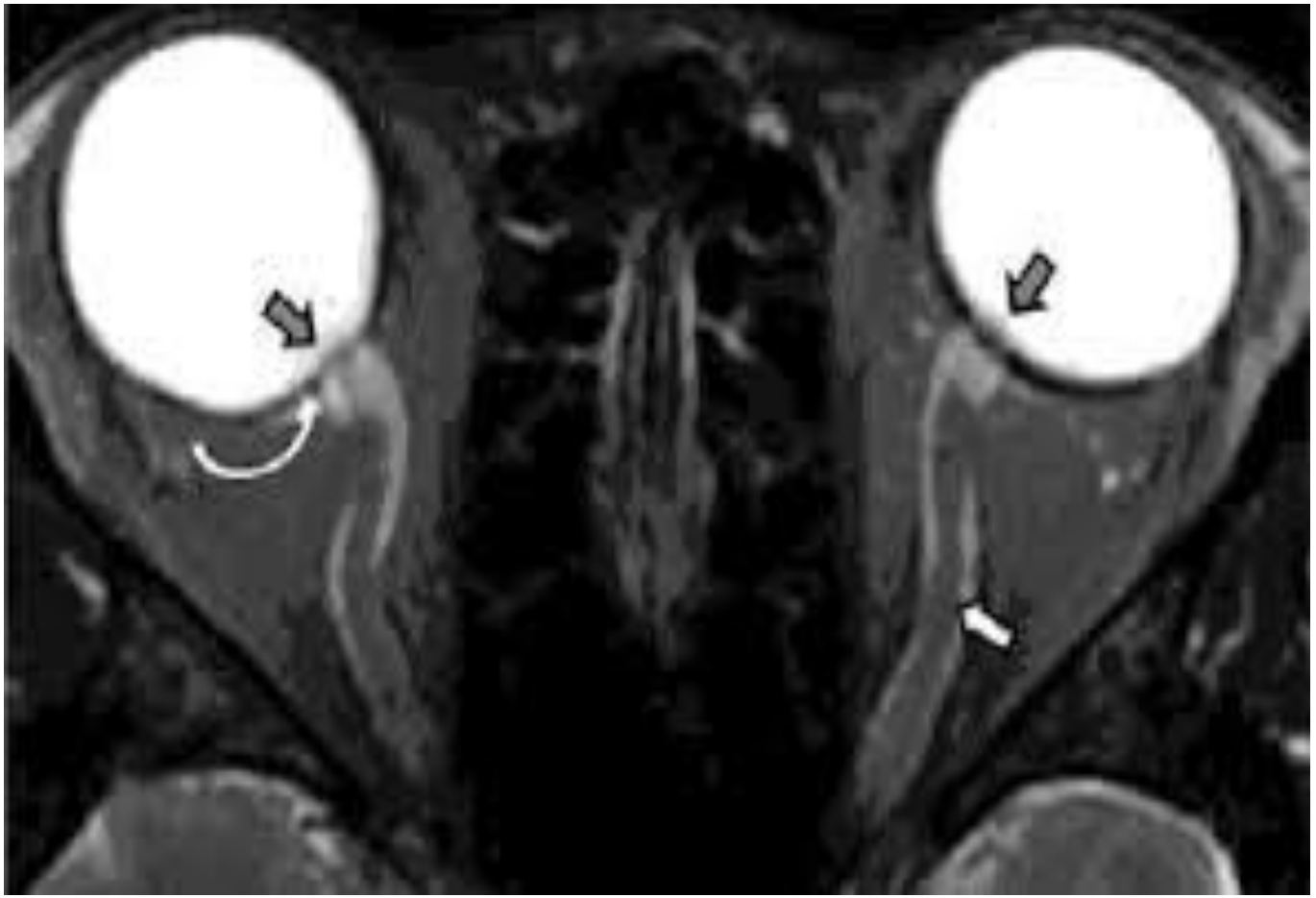
-IIH (idiopathic intracranial hypertension)

- CVT (cerebral venous thrombosis)

IIH



IIH



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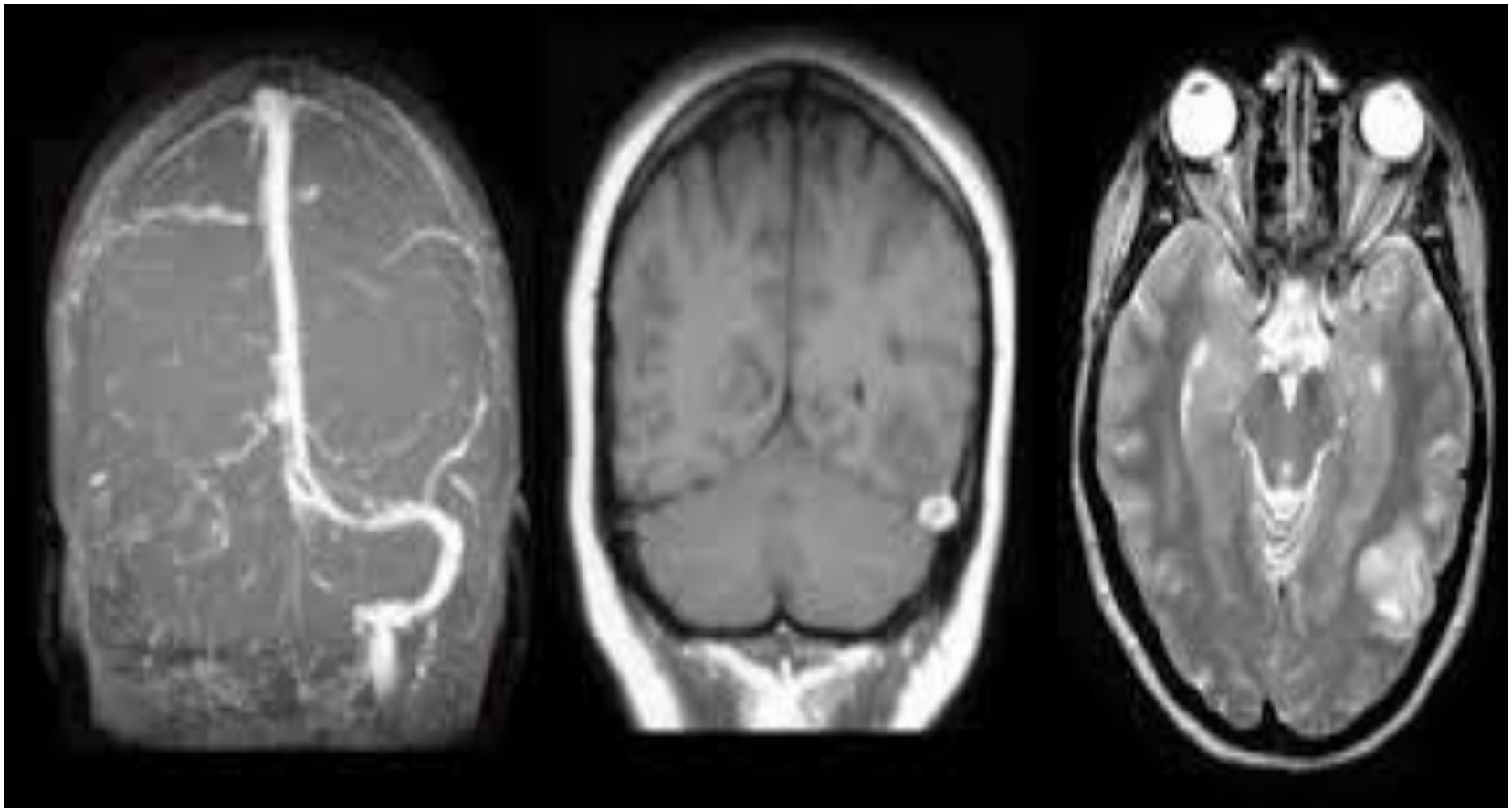

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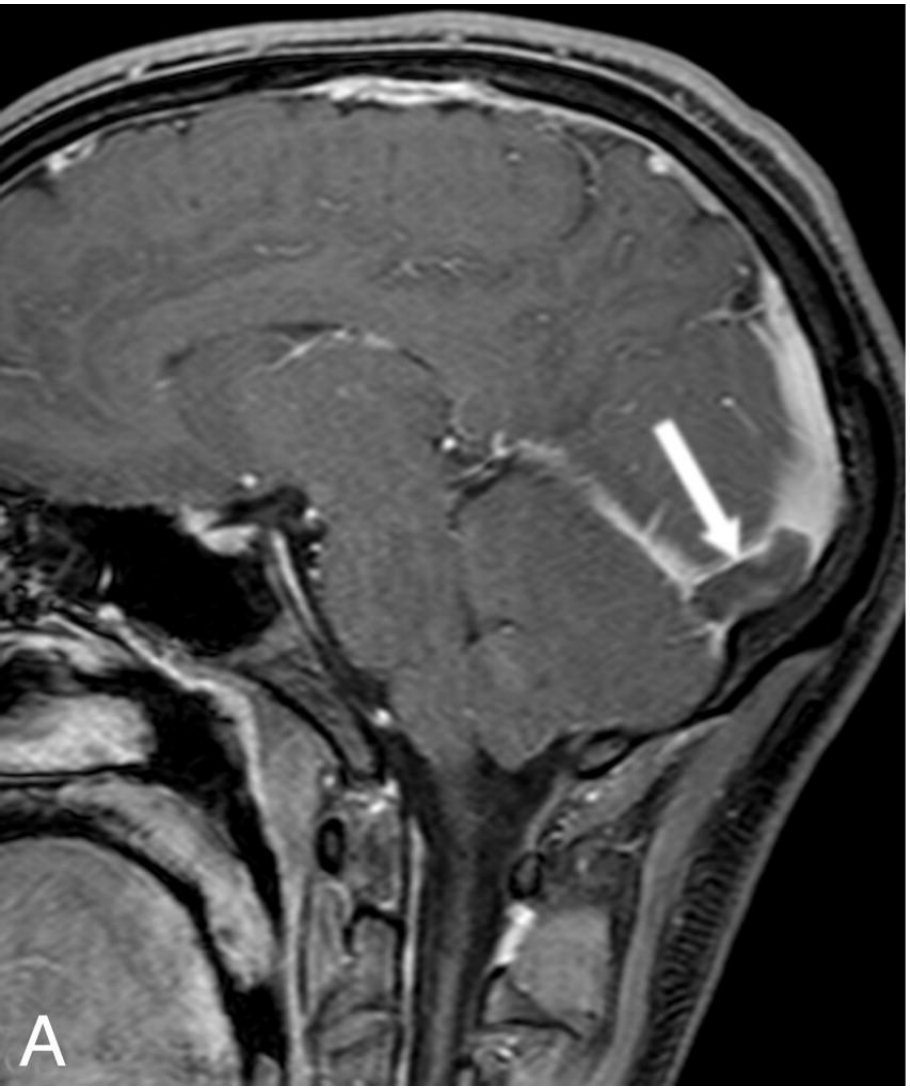
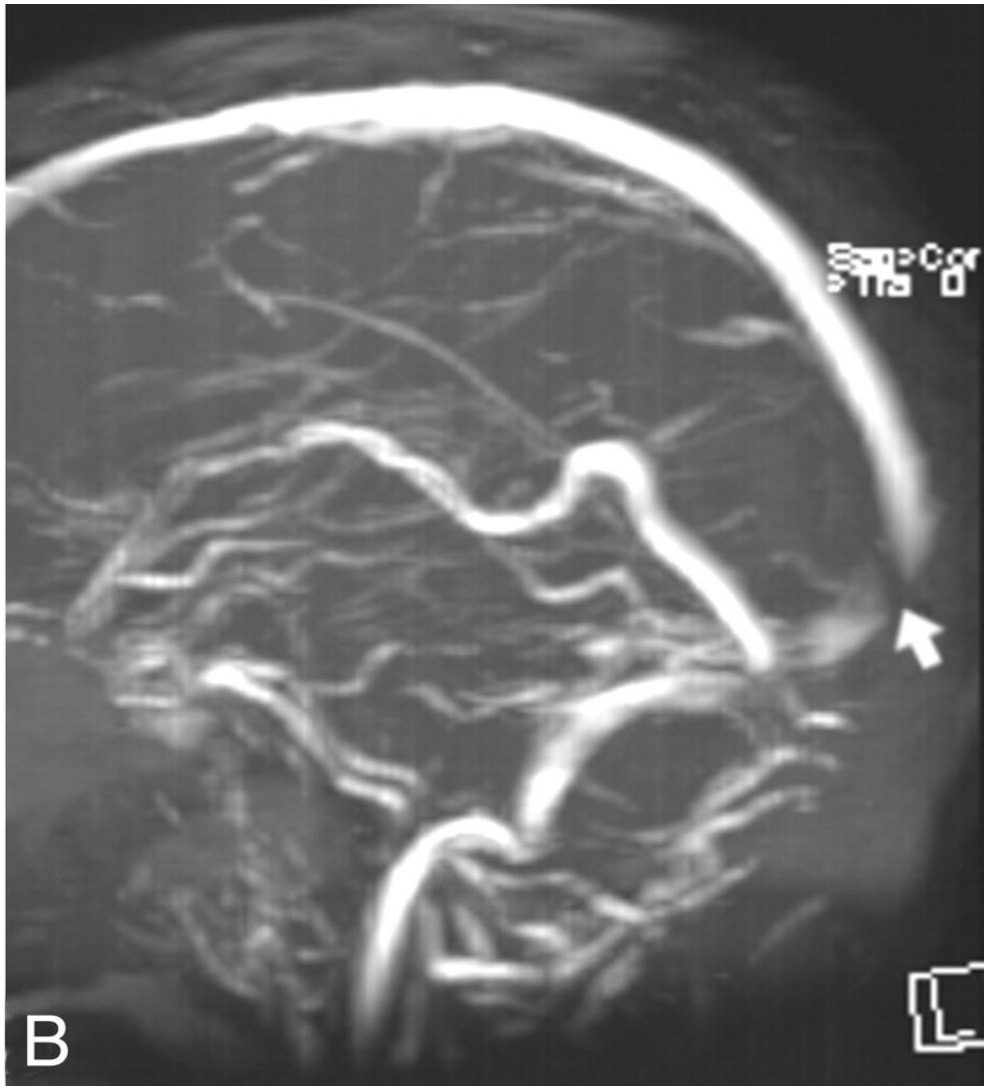
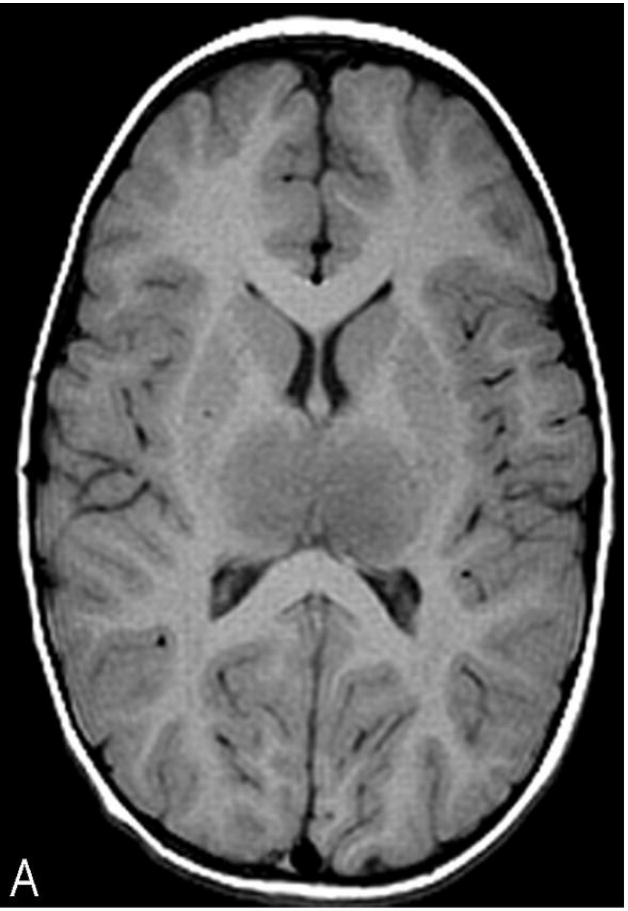
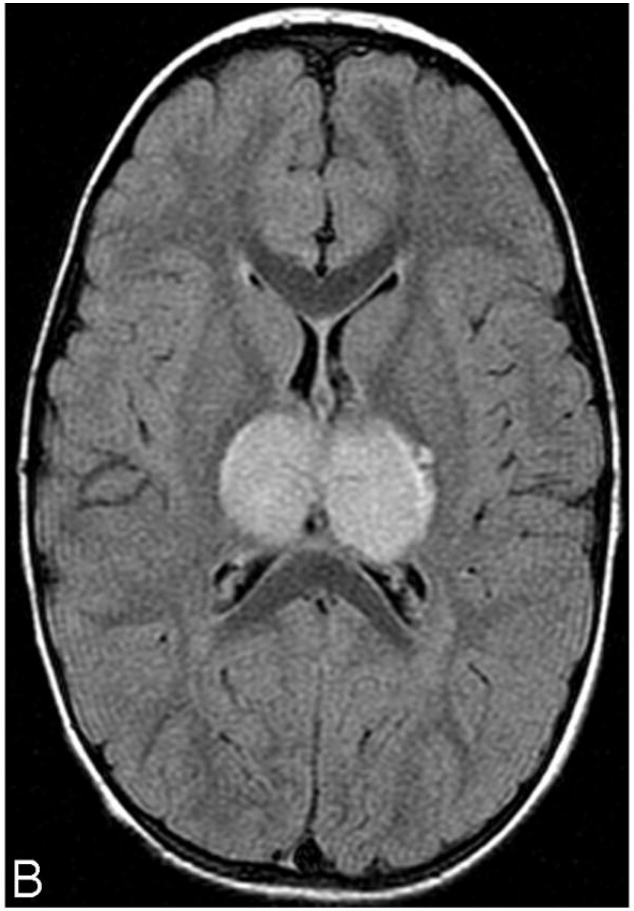
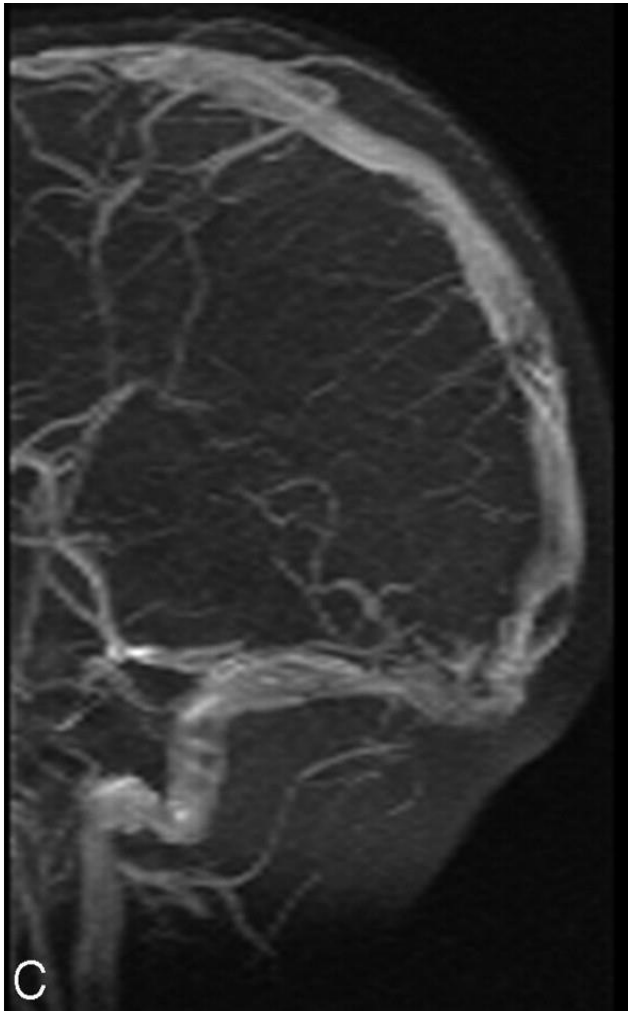




CVT







***Red flag* for simple headache**

- *Focal neurological signs*
- *Fever*
- *Presence of APS*
- *Immunosuppression*
- *Use of anticoagulant*
- *Altered mental status*
- *Meningismus*
- *Generalized SLE activity*
- *ICP rising signs*

Cognitive dysfunction(CD)

- Most affected area are:

1- attention

2- processing speed

3- memory

Cognitive dysfunction in SLE is associated with APL antibodies, steroid use?, low level of education and depression.

-***No relation to active systemic disease***

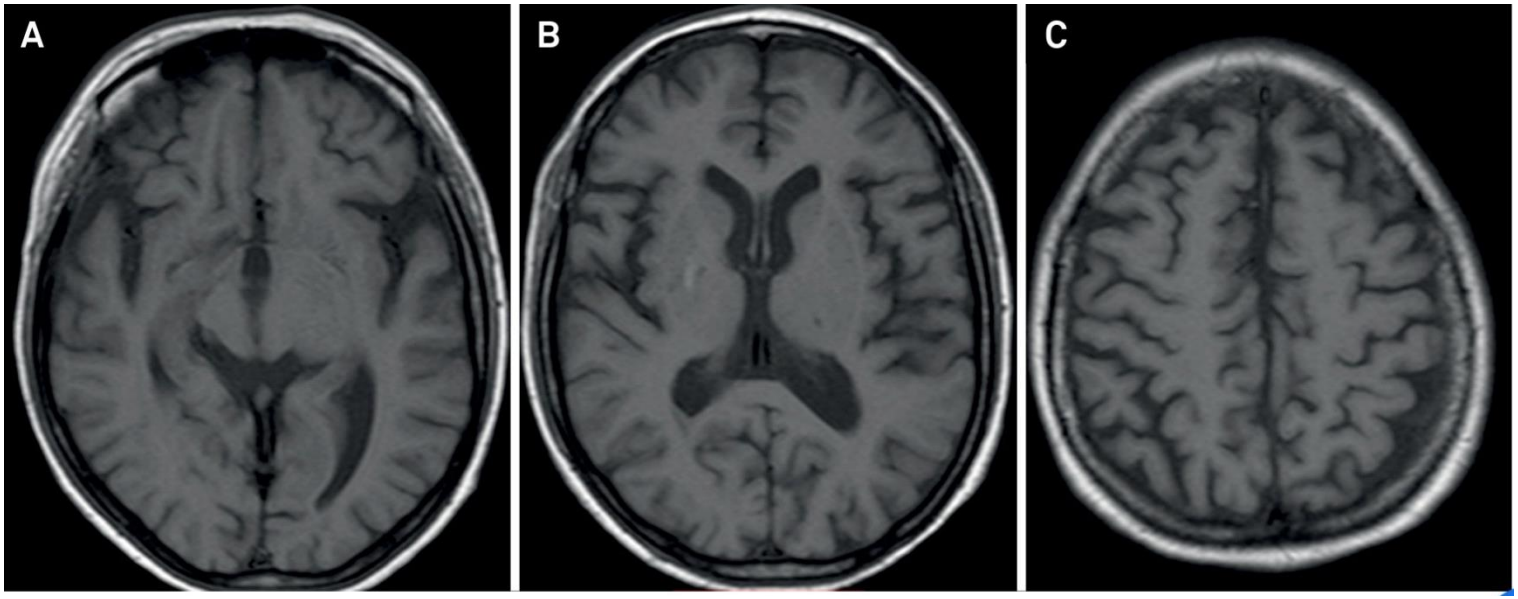
Severity of cognitive disorder are correlated with:

- Cerebral atrophy
- White matter lesions
- Cerebral infarction

If MRI is normal in CD

CD is due to immune-mediated myelinopathy

MRS or DTI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Pathophysiology of CD probably due to

- Vascular abnormality
- Cytokines
- BBB disruption
- Lupus anticoagulant
- Anti-NMDA (murine models)
- Anti-NR2

Treatment of CD

- Remains uncertain
- Management of exacerbating causes
- Methylphenidate
- Prednisone
- Aspirin
- Cognitive rehabilitation
- No efficacy of current dementia drugs

seizures

- 12-22%
- GTC is the most common (60-88%) & they are associated with active disease
- Abnormalities on the EEG are common
- Patient with seizures show:
  - more gray matter hyperintensities
  - may develop brain atrophy

Risk of seizures

- Inflammatory processes(disease activity)
- Ischemic vascular disease
- Antibodies (anticardiolipin & anti-Sm)
- Multiple NPSLE manifestations
- Severe baseline organ damage

For evaluation of SLE patients With seizure:

Brain MRI & CSF/A

(FOR R/O of infection & vasculitis)

Are included

Treatment of seizure

Control of baseline active disease

&

Transient antiepileptic drugs

PRES

-Rapid onset of headache

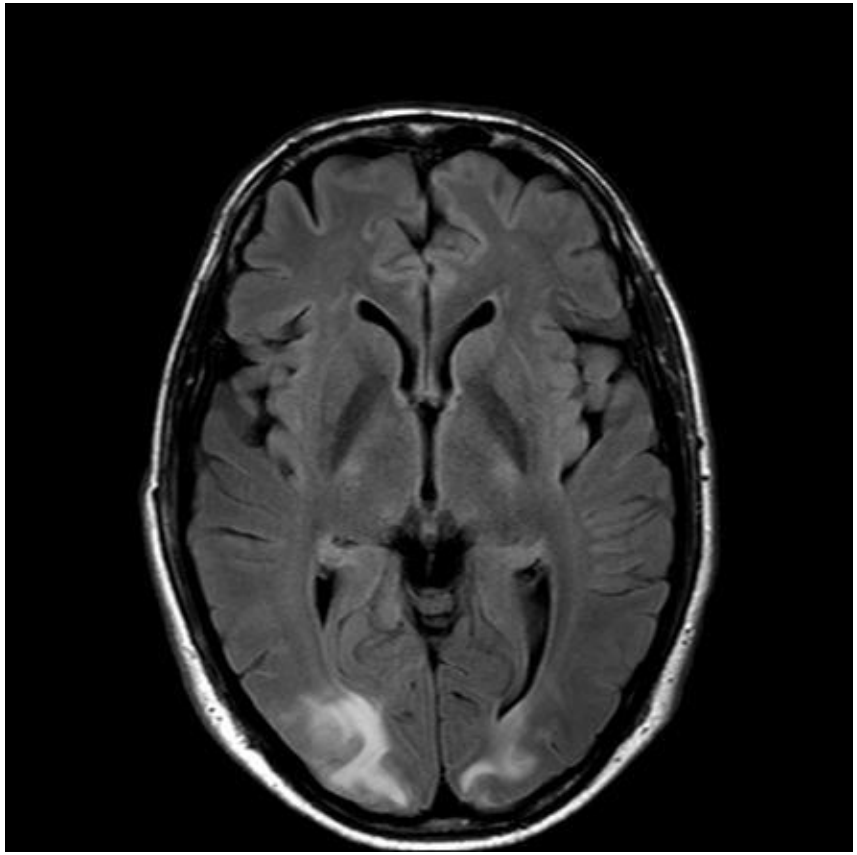
-seizure

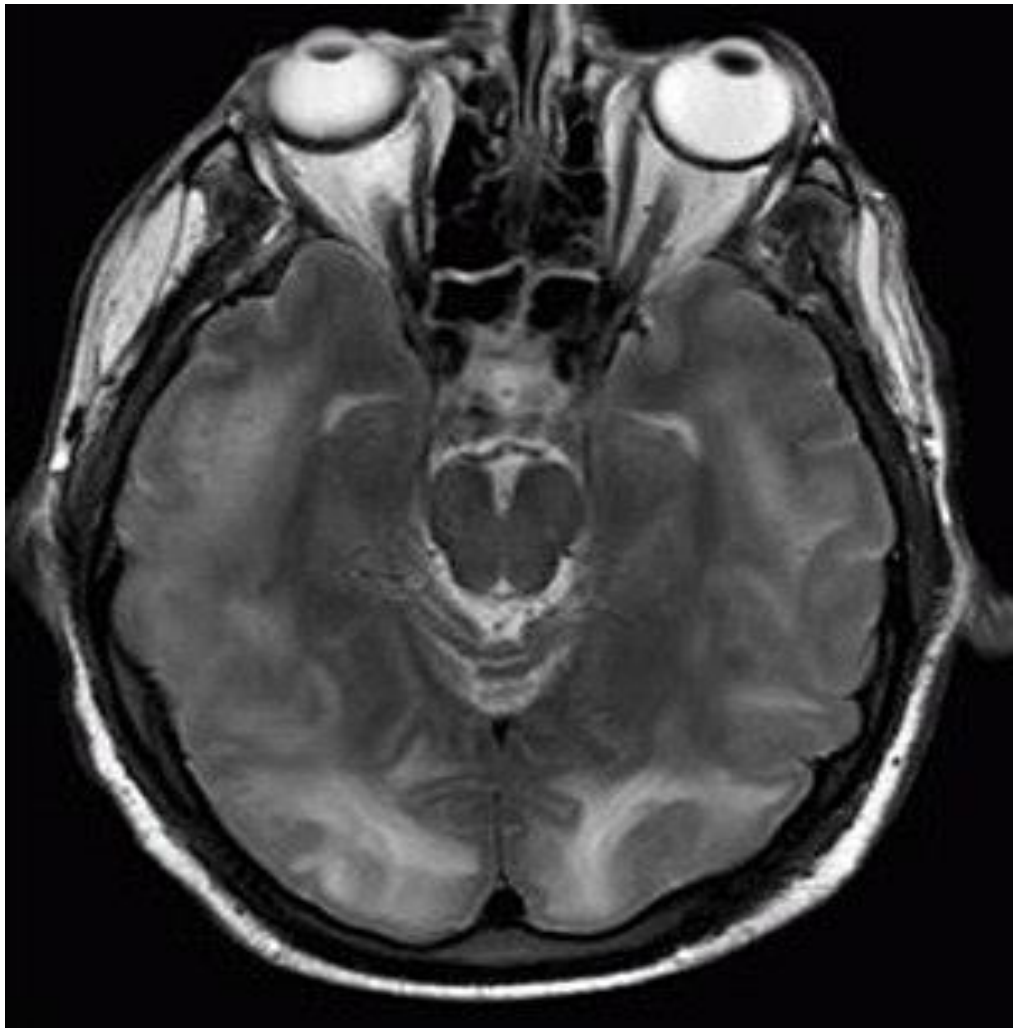
-hypertension

-blindness

-altered mental status

-prognosis is very good





Acute confusional state

- Anti-NR2 ?
- Anti-Sm ?
- *Pathogenic mechanism* → inflammatory

<u>treatment</u>

-Risperidone

-Corticosteroids

-immunosuppression

Psychosis,depression & anxiety

- Mood disorders are associated with :

-- disease activity

--high prednisone doses (> 20mg)

--cutaneous disease

--myelitis

--patients more likely have neurologic abnormality, more ophtalmologic findings

Mood disorder

- *No evidence on the use of neuroimaging or serological marker for dx of depression & anxiety disorders*

- ***Anti-P ?***
- ***Anti-NMDA ?***
- ***TNF ?***

Psychosis occur early in the course of disease and has favorable prognosis.

(*High level of* ***anti-P*** *are associated with* ***psychosis but is not diagnostic.)***

Treatment of psychosis

-glucocorticoids

-immunosuppressive drugs

Cerebrovascular disease

- 10-15% of deaths
- ***Ischemic stroke is more common(lacunar infarct)***
- ICH & SAH are inferequent
- First 5 years after dx of SLE

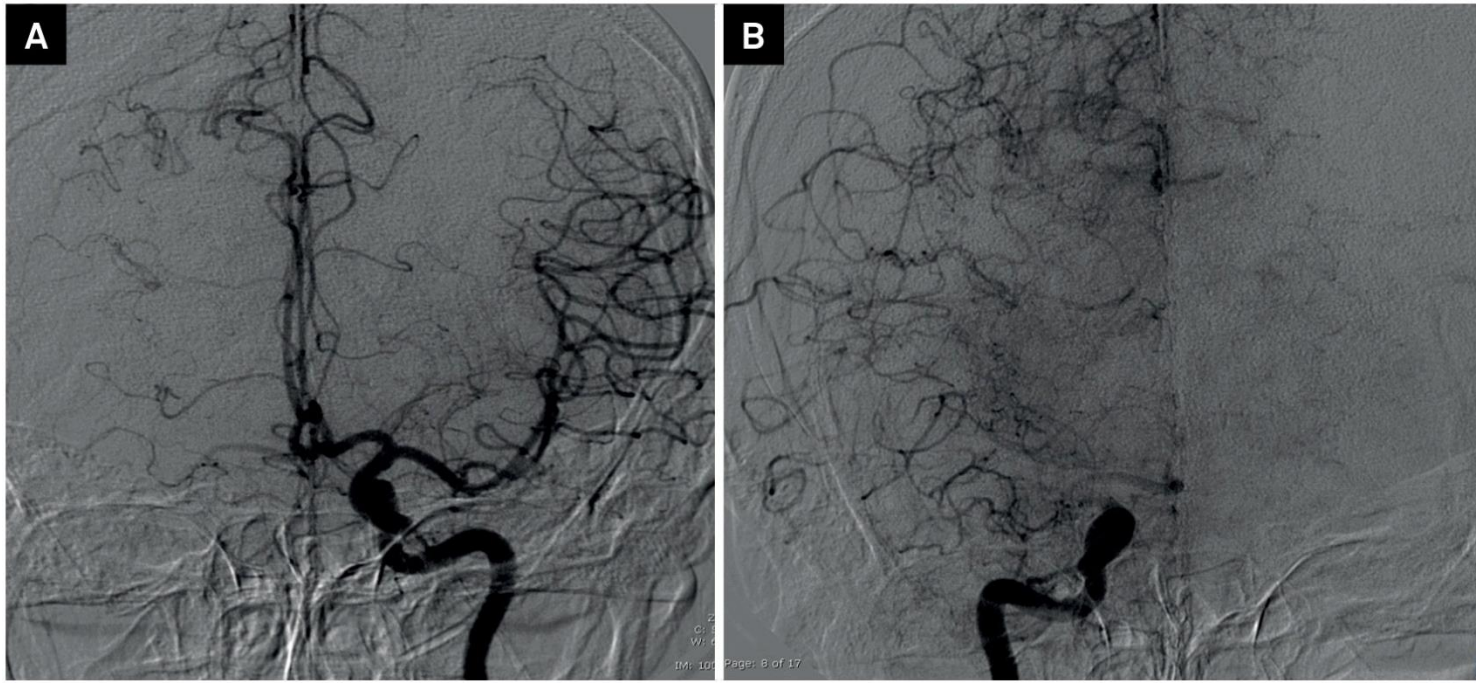
Risk factor for CVA

- Accelerated atherosclerosis & young age
- Previous CVA & TIA
- Apl antibodies
- High cummulative dose of steroids
- ***Vasculitis*** ***a rare cause of stroke(7%)***
- Ischemic stroke in APS is
  - embolic
  - thrombotic

Management of CVA

- Modifiable risk factors
- 0ral anticoagulant(APS)

Glucocorticoids* & *immmunosuppressive do not reduce the risk of Ischemic stroke(EXCEPT in vasculitis cases)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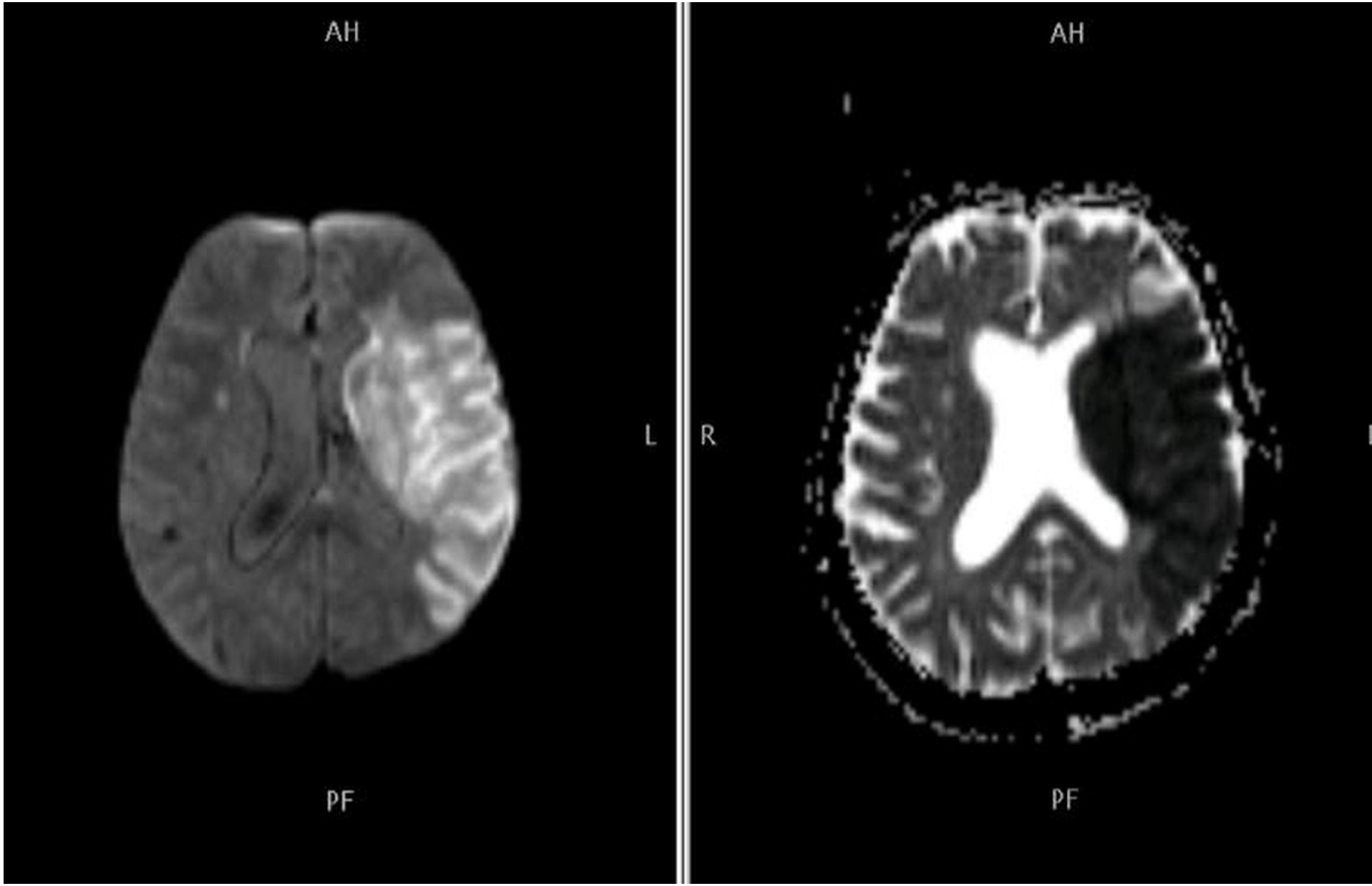
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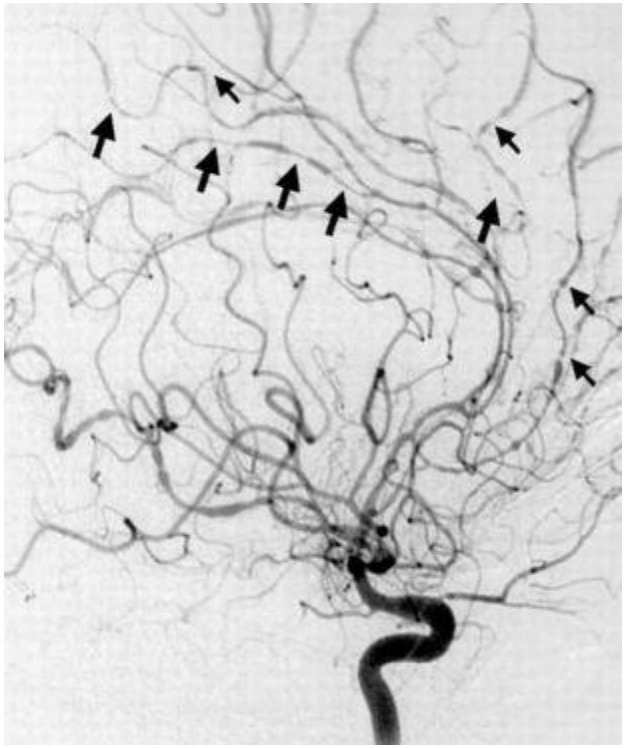

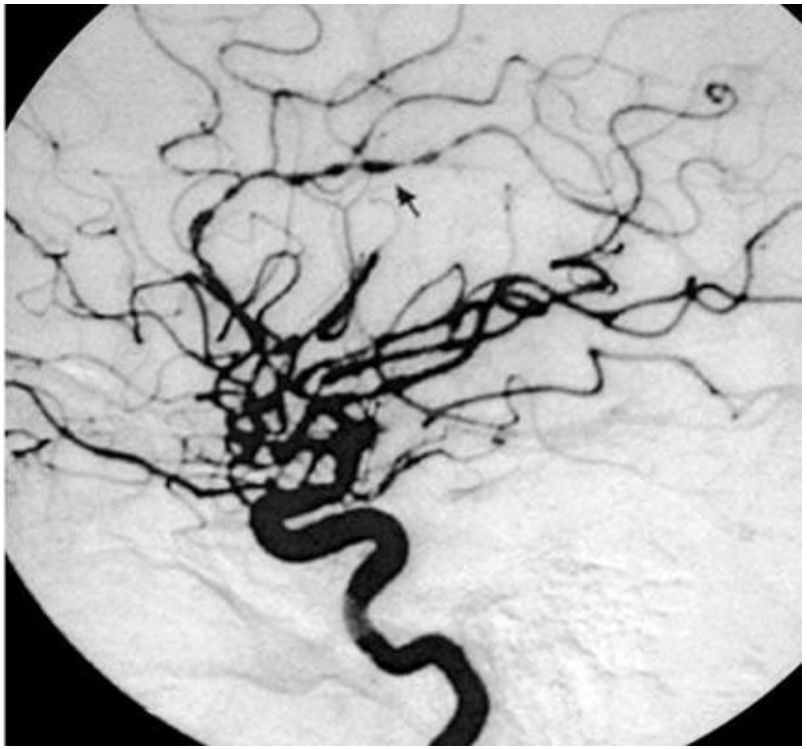

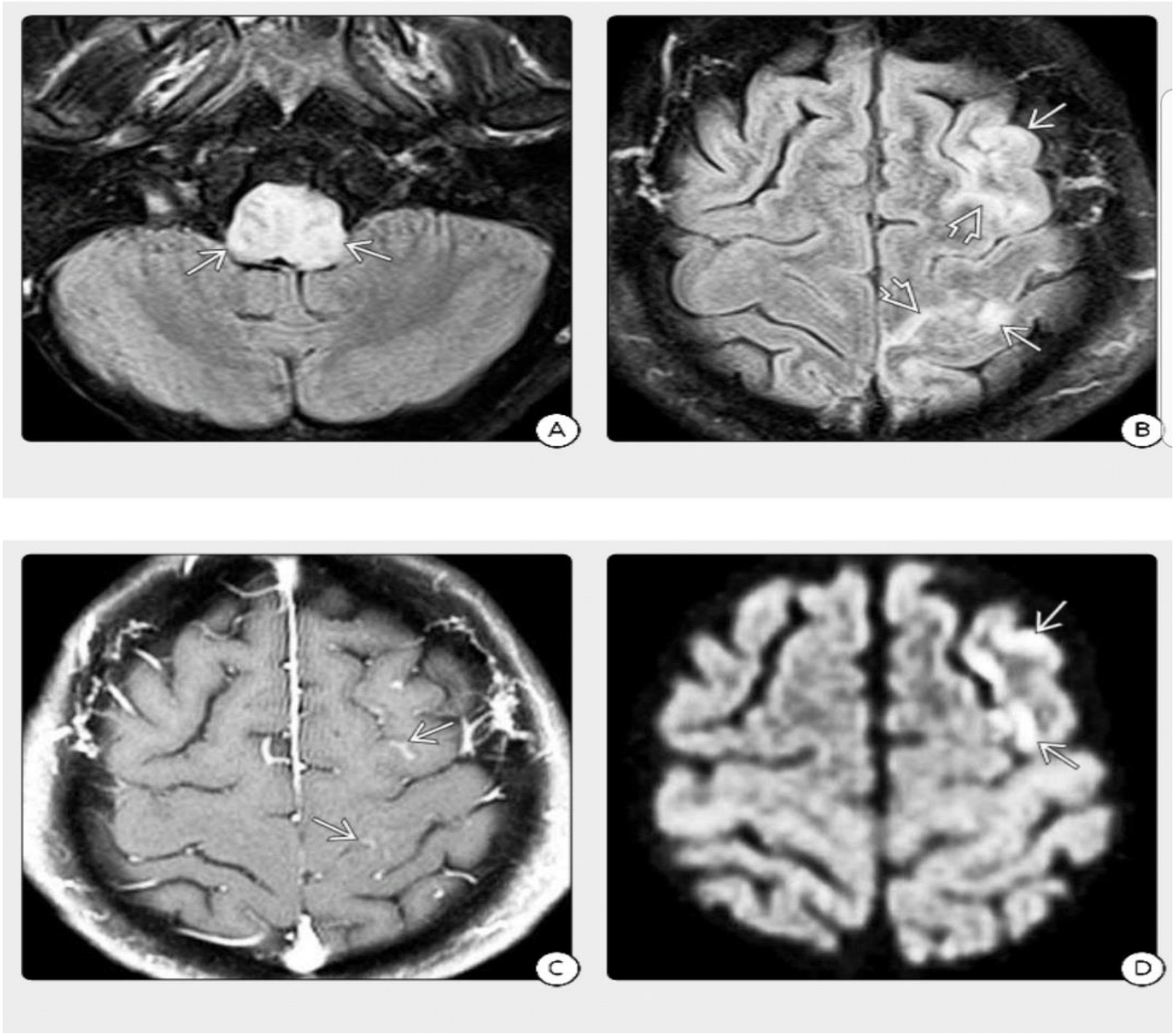
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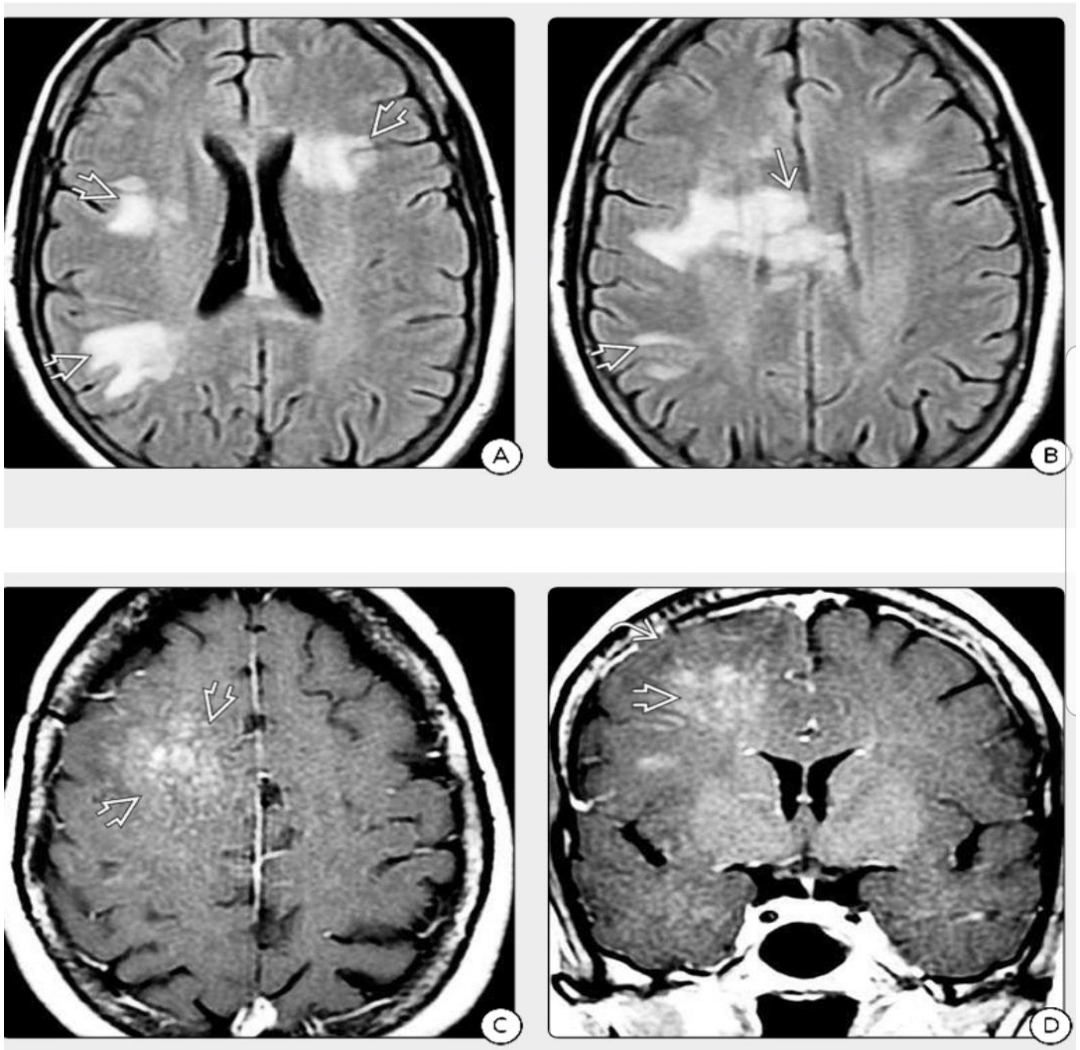
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Movement disorders

- *Uncommon in NPSLE*
- *Chorea most common (early)(good prognosis)(associated with anticardiolipin)*
- *Autoimmune mechanism & cerebral ischemia*
- *Parkinsonism(APS)*
- *Other manifestation: tremor, tic, myoclonus, dystonia*

Aseptic meningitis

- ***1.4-1.6%***
- ***Occurs during flares***
- ***Infections must be ruled out***
- ***Headache & altered mental status***
- ***High titers of anti-dsDNA***
- ***Spontaneous remission***
- ***Steroids & immunosuppressive***

Myelopathy

- ***1-1.5%***
- ***Hemiparesis, tetraparesis, bladder involvement, sensory level***
- ***First 5 years***
- ***Ischemia & inflammation***
- ***Association with antiphospholipid antibodies***
- ***Has two clinical pattern***

Gray matter myelitis

- Prodromal phase of fever
- Urinary retention at onset
- With flacid paraplegia at onset
- MRI show increased signal and swelling

White matter myelitis

- Less severe presentation
- Slower progression
- Spasticity & hyperreflexia

Co-occurrence of SLE &NMO

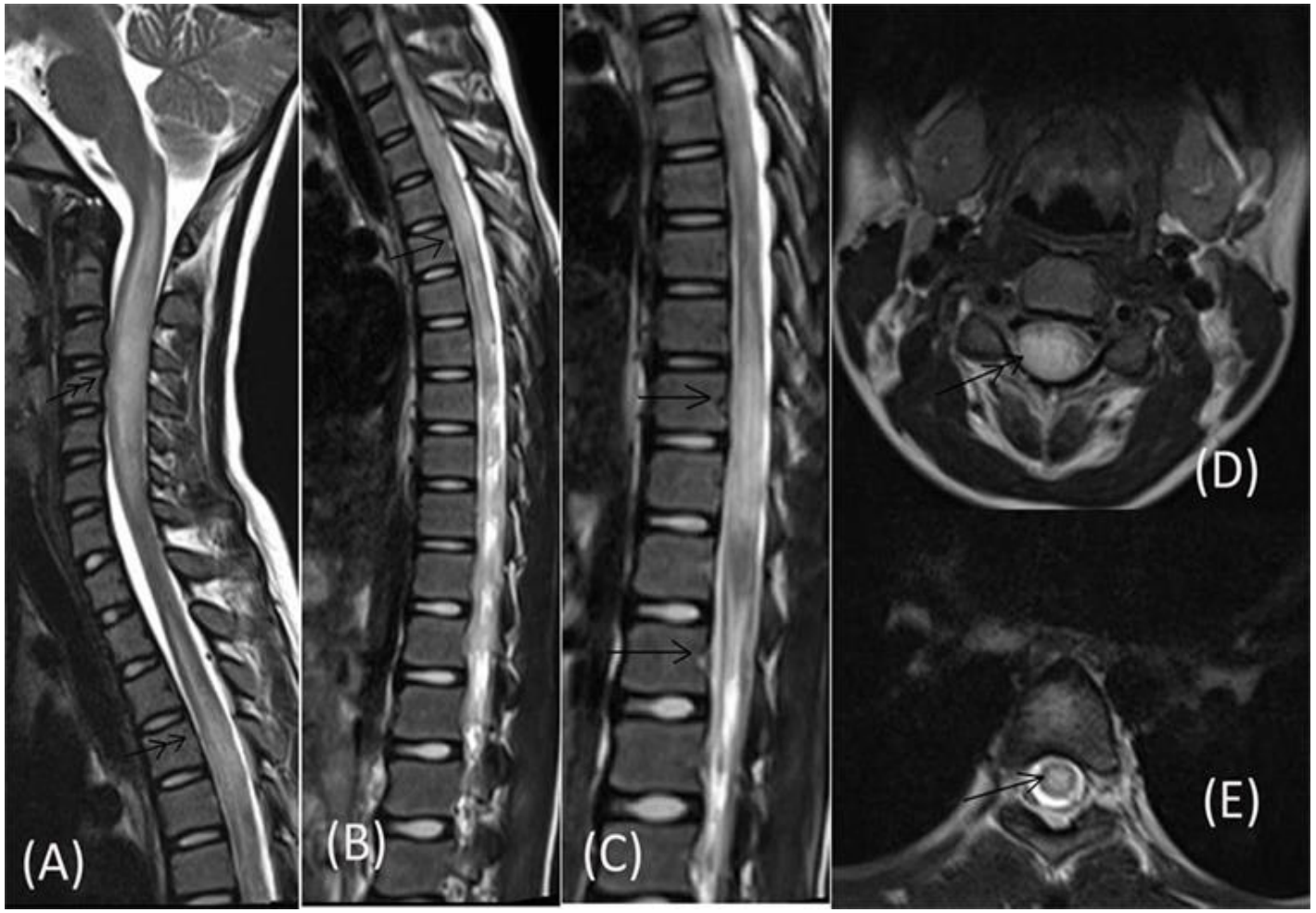
NMO IgG

(cyclophosphamide has a bad outcome in NMO)

In the presence of myelitis

*Overlap of **APS , sjogren & NMO***

SHOULD BE INVESTIGATED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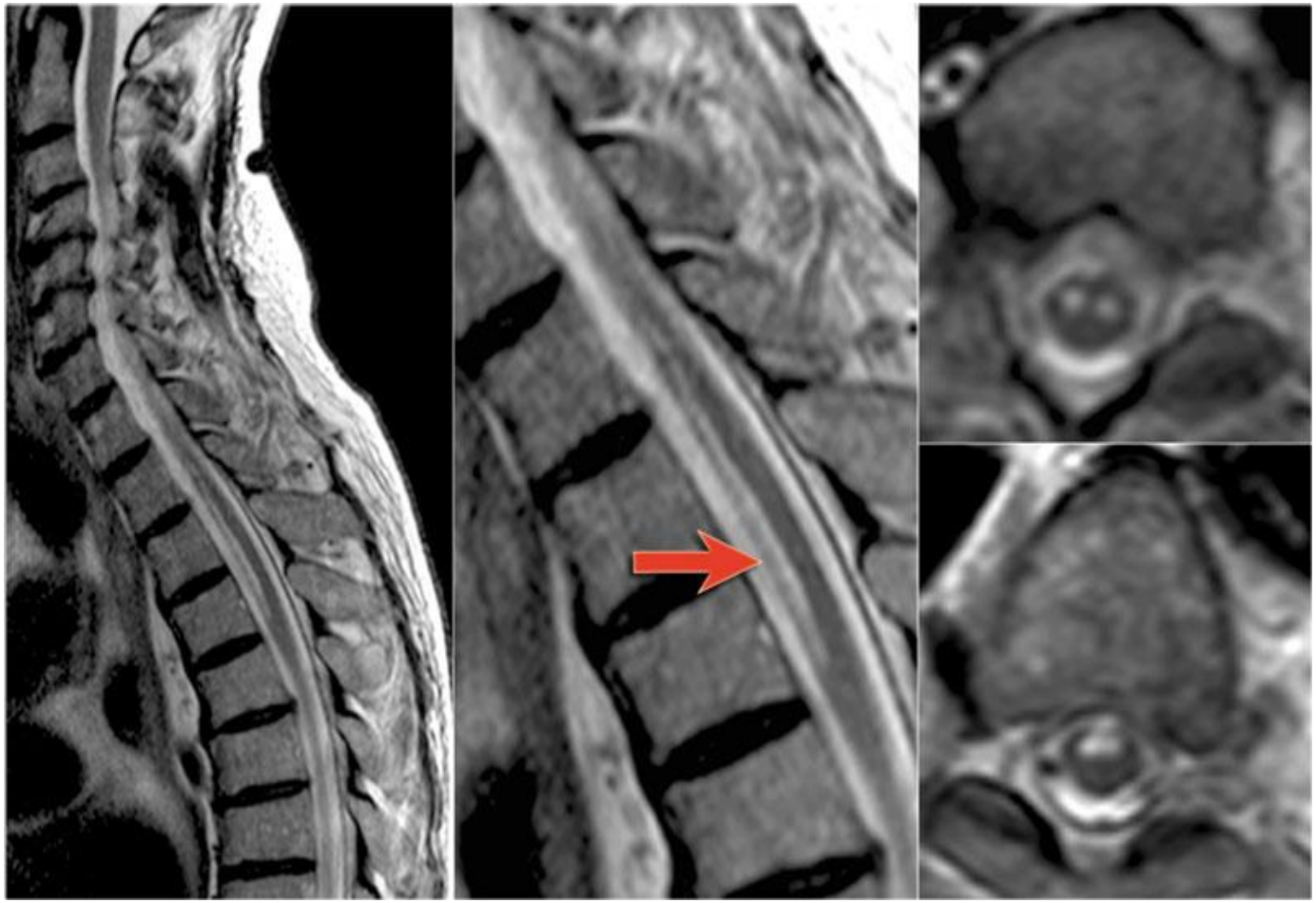
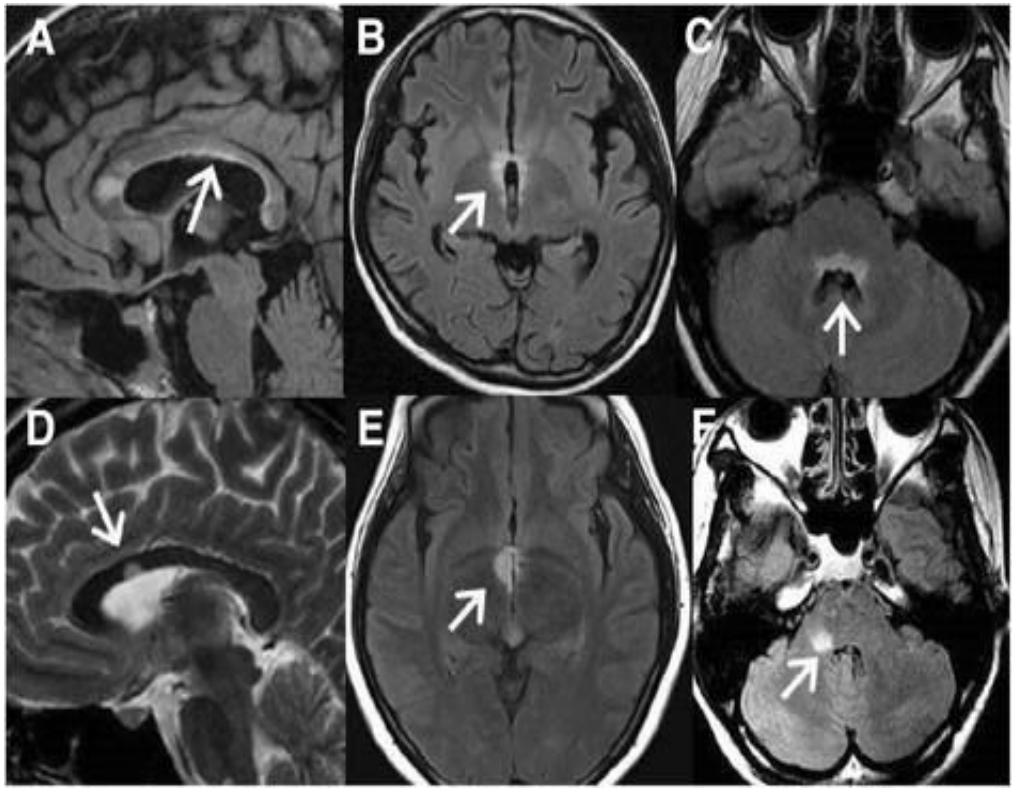
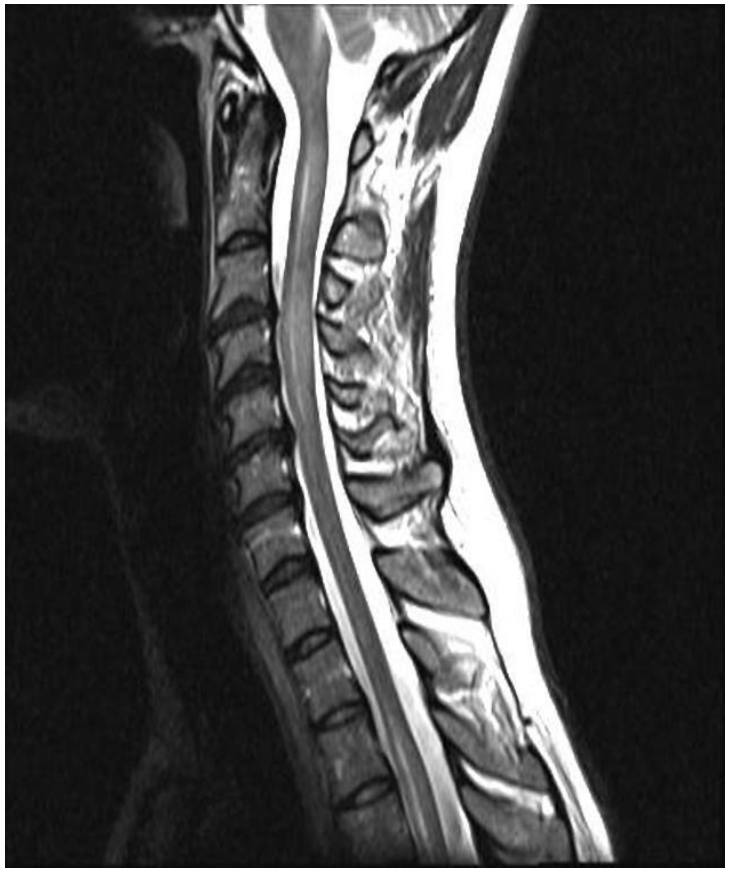


NMO





MYELITIS TREATMENT

- Steroid puls therapy
- IV cyclophosphamide
- Plasmapheresis
- *Consider relapse during steroid tapering(50-60%)*
- Muscle strength<3/5 most important prognostic factor
- Other prognostic factors are *bladder dysfunction and no cyclophophamide thrapy*
- *Good recovery only in 50%*

Peripheral nervous system

- 28%
- Paresthesia, pain, autonomic dysfunction, peripheral ataxia, weakness & atrophy
- Most common in older patients
- And most seen in those with CNS lesions and active systemic disease
- ***Most common subtype is mild distal symmetric axonal sensory or sensorymotor neuropathy***
- Mononeuropathy are the second perevalant manifestation
- GBS & CIDP

Small fiber neuropathy is not included in ACR definition

Prevalence is 17.1%

Skin biopsy for dx

Mononeuritis multiplex

- Sudden weakness
- At any time during disease course
- Has higher disease activity
- More aggressive immunosuppressive therapy

Neuropathy treatment

- **Symptomatic therapy for mild cases w/o motor impairment**
- **Steroids**
- **Immunosuppressive(vasculitic neuropathy)**
- **IVIG**
- **Plasma exchange**
- **Rituximab**
- **Good outcome (60-75%)**

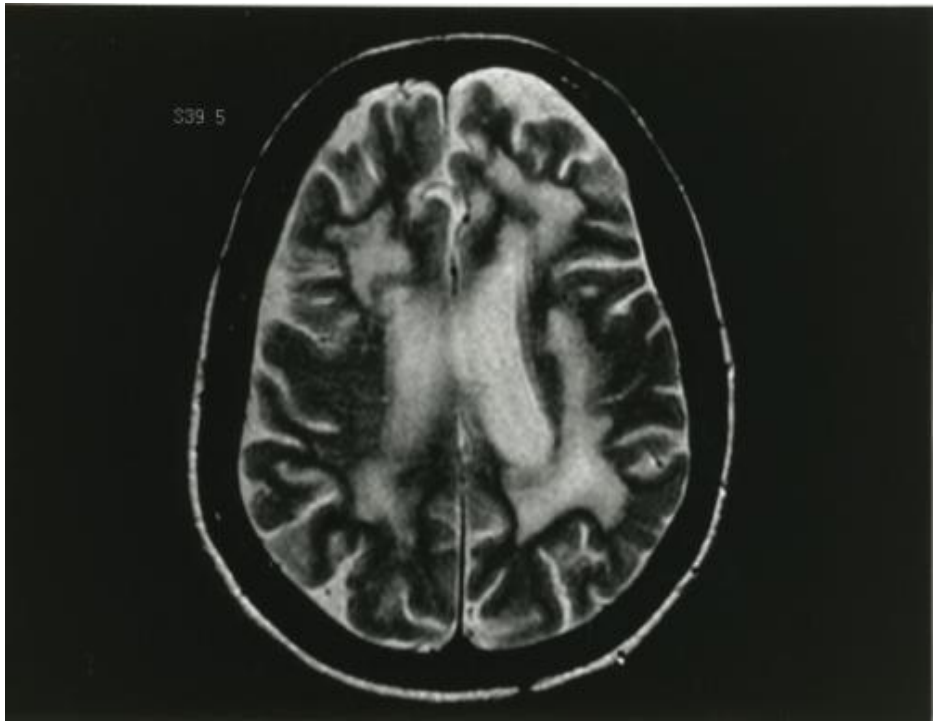
Cranial neuropathy

- Eight , third, fourth, sixth, fifth and seventh nerves
- 5-42%
- Rarely isolated manifestation
- Mainly microvascular
- Patients with SLE may presnt with asymptomatic cranial neuropathies that eighth n. is most commonly affected

Anti-ribosomal P protein & anti-DNA

Optic neuritis

- <1%
- unilateral → Related to Apl(ischemic)
- Bilateral or chiasm involvement → inflammatory
- 50% has good recovery



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