Neurology and Rheumatology

(what happened to Monday?)

Eslam Shosha, MD FEBN
Neuroscience clinical department
Western University, ON, Canada
Eslam.shosha@lhsc.on.ca

Western

Disclosure

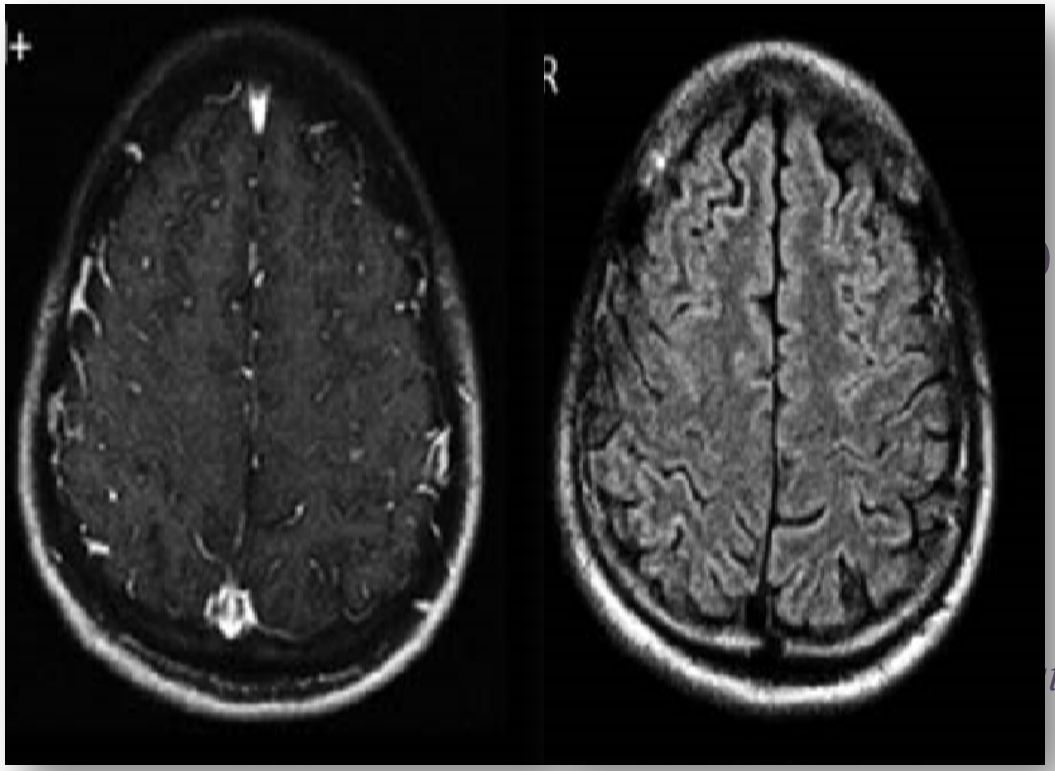
Relevant Financial Relationship(s)

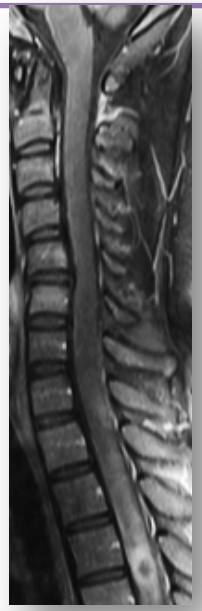
None

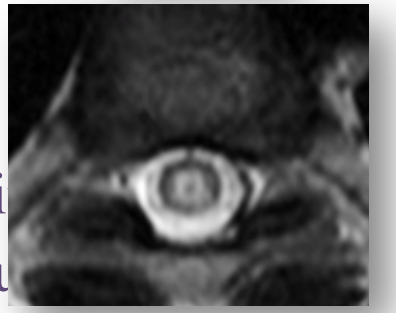
Off-label therapy discussion

Methylprednisolone, plasma exchange,azathioprine, mycophenolate mofetil, mitoxantrone, rituximab, intravenous immune globulin, cyclophosphamide, and other immunological therapies

Case 1





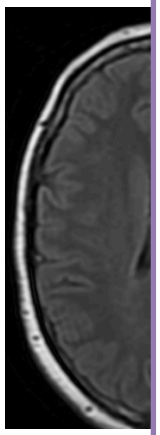


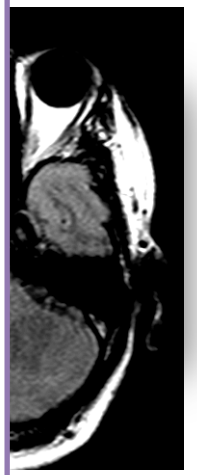
days

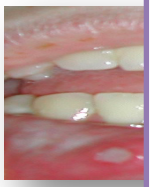
tations

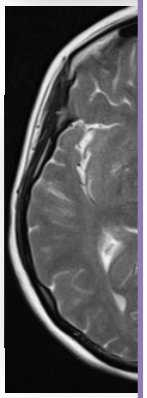
- CSF: 50 cells/ul (65% PMNL), ptn 60mg/dl, posi
- Ne MO, MOG, autoimmu

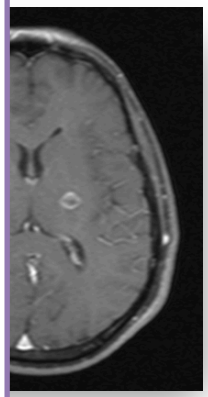
Positive pathergy test











Acute parenchymal CNS involvement in Behçet's disease
(acute intra-axial neuro-Behçet disease)

↓

5–10 days of IVMP (1000 mg/day)

↓

Oral MP (60–80 mg/day)
+
Add azathioprine (2.5 mg/kg per day)
↓
Taper oral MP by 8 mg/week (to 32 mg/day)
↓
Continue 32 mg/day for 3 months,
then further taper down to 8 mg/day
over 3 months

Weekly IVMP (1000 mg) for 4 weeks
+
32 mg/day oral MP between pulses
+
Add azathioprine (2.5 mg/kg per day)
↓
Monthly IVMP (1000 mg)
for up to 6 months
+
Taper oral MP over 3 months to 8 mg/day

↓

No progression,
No recurrences.
↓
Azathioprine (years)

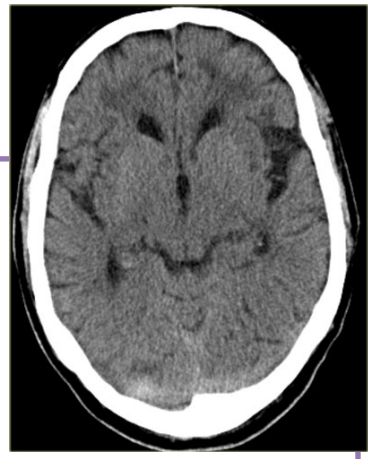
→

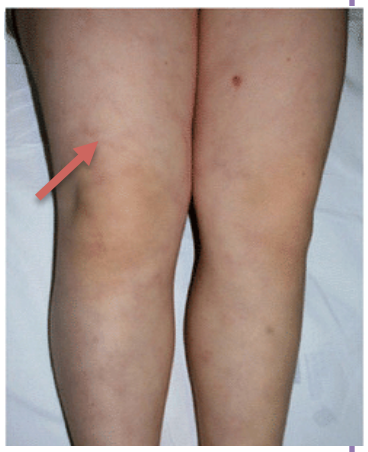
Patient cannot tolerate
azathioprine
↓
Mycophenolate mofetil

New attack or Worsening
↓
Start IVMP pulses +
stop azathioprine
+
Infliximab
or
Interferon alfa

Case 2

- 32 y/o married
- Severe headache, and seizure
- Previous miscarriage (1)
- No OCP
- Work up
  - Normal coagulation work up
  - Platelet count 110
  - Negative antibodies
    - ANA, dsDNA, LA, β2-GPI, a CL, PL





APS

Asymptomatic carrier	Unclear, no therapy or aspirin
APS and venous event	Anticoagulation with INR 2-3
APS with arterial event	Area of controversy; INR 2-3 with aspirin versus higher INR target (such as 2.5-3.5)
Arterial event with low-titre antiphospholipid antibodies	Usual treatment

Str

BS
elitis

at ≥ 10 wk
b) prematur
wks due t
c) ≥3 consec
at <10wks
d) placental
< 34 wks

coagulant

m to - high titer
t X 2 times
s apart

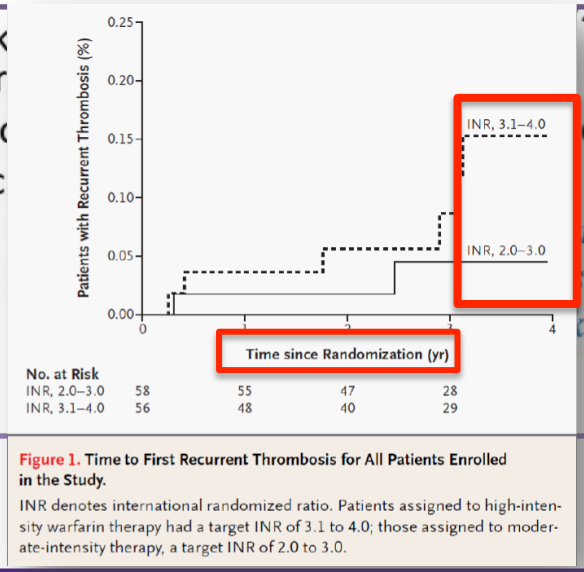


Figure 1. Time to First Recurrent Thrombosis for All Patients Enrolled in the Study.

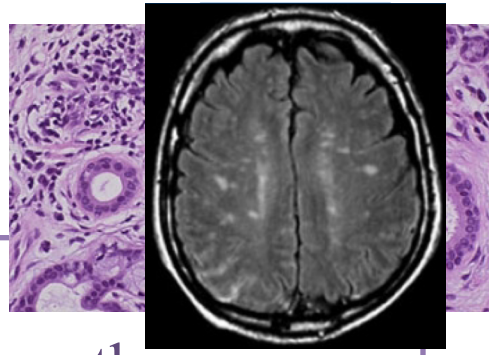
INR denotes international randomized ratio. Patients assigned to high-intensity warfarin therapy had a target INR of 3.1 to 4.0; those assigned to moderate-intensity therapy, a target INR of 2.0 to 3.0.

Epilepsy

Headache

Western

Case 3



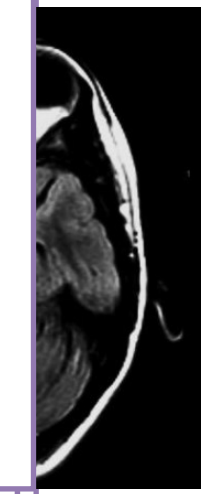
- 57 y/o M, teacher
- Disabling fatigue and Memory difficulties x 6 months
- Paraesthesia and pain in distal extremities, evolved to hands, lips and tongue x1 week
- No weakness

- Normal HbA1C, vit B12, vit B6, anti-dsDNA, ANA, ANCA, ESR, CRP, ACE, Hep B and C, MRI spine , CT chest, paraneoplastic
- Normal NCS and EMG
- Responded to steroid, maintained on azathioprine

Sjögren syndrome (SS)

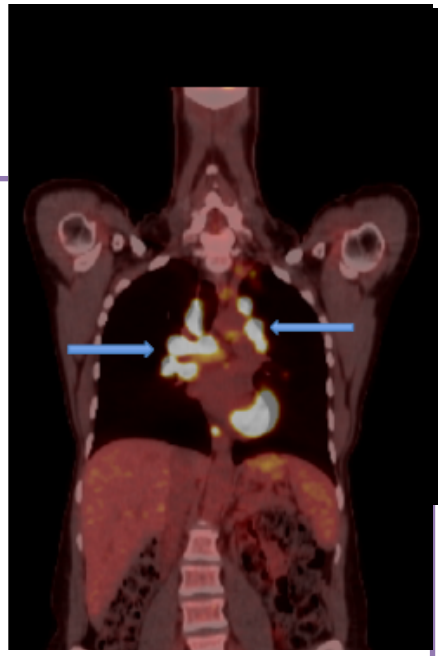
- Poo
  - A
  - A
- Sch
- Lip

- Corticosteroids: 30-40% response rate
- IVIG: 30-40% response
- Rituximab
- Infliximab
- Symptomatic treatment



Positive se

Case 4

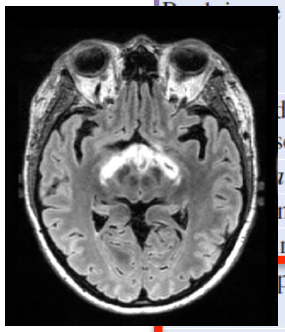


- 45 y/o M, healthy, non-smoker
- Decrease vision right eye 6 days, headache
- Unremarkable

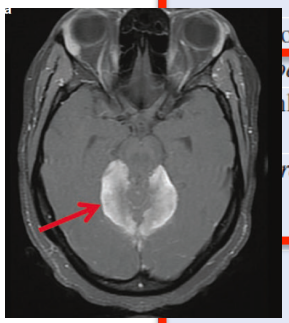
  # Respiratory ,Constitutional symptoms *#APS, Weight loss*

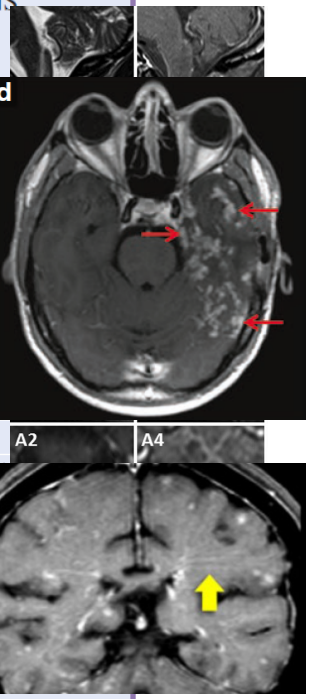
  # OGU, Skin lesions *# Dryness, joint pain*
- Improvement x 5 days of 1 gm IVMP
- Worsening on 4th day, post last dose, 60mg and tapering
- Work up
  - ESR, CRP (++++)
  - Anti-AQP4, MOG, dsDNA, ANA, ANCA, ACE, MRI spine , paraneoplastic (N)
  - CSF: 59 cells/ul (lymph), ptn 62 mg/dl, glucose 2.6 mmol/l (serum 6), OC (2 bands)
  - Trans-bronchial biopsy: Non-caseating granulomas

Sarcoidosis *"The great imitator"*

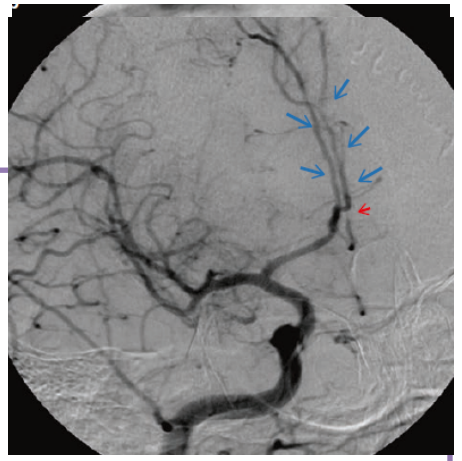


Agent	Dosage	Side effects	Comments
Glucocorticoids			
[illegible]	0.25–1 mg/kg/day PO	Numerous including: psychosis, osteoporosis, Cushing syndrome, hypertension, diabetes mellitus, gastric ulcers, glaucoma, cataracts	For mild-to-moderate NS
[illegible]dnisolone [illegible]se")	1000 mg/day [illegible] 3–5 days IV		For severe NS
[illegible]uring adjuncts			
[illegible]ne	Up to 2 mg/kg PO daily	Anemia, neutropenia, hepatitis	
[illegible]ne	2.5 mg/kg/BID PO	Hypertension, renal dysfunction	
[illegible]phamide	50–200 mg/day PO 500 mg q 2–3 weeks IV	Cytopenias, hemorrhagic cystitis, infection	
Methotrexate	10–25 mg weekly PO or SQ	Cytopenias, hepatitis, pneumonitis, mucositis	Give with at least folic[illegible] PO daily
[illegible]olate mofetil	1–1.5 g PO BID	Anemia, hepatitis, colitis	
[illegible]odulator			
[illegible]loroquine	Up to 5 mg/kg PO daily (typically 300–400 mg)	Retinopathy, myopathy, cardiomyopathy	Side effects are rare; [illegible] immunosuppressive
[illegible]rosis factor			Relatively contraindic[illegible] failure, test for TB an[illegible] testing before treatme[illegible]
	3–7 mg/kg IV at week 0, 2, 6 then 3–7 mg/kg IV q4–8 weeks	Infusion reaction, antidrug antibodies, malignancy, demyelination, hepatitis, drug-induced lupus	
Adalimumab	40 mg SQ q2wk	Injection reaction, malignancy, demyelination, hepatitis, drug-induced lupus	





Case 5



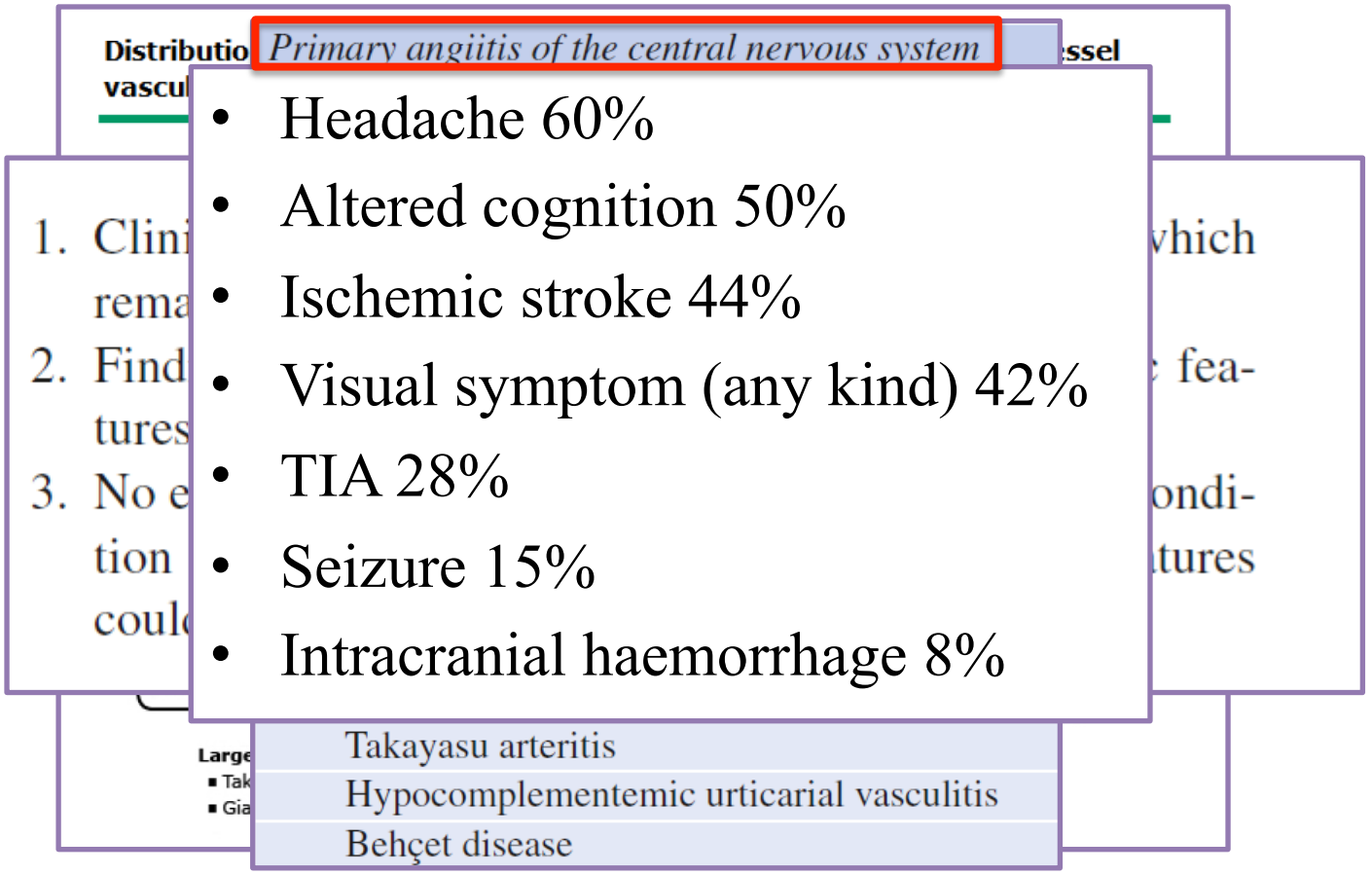
- 53 y/o healthy M
- Acute left hemiparesis
- ? TIA (right sided numbness for 2 days)
- No fever, OGU, asthma, skin lesions

- Normal HbA1c, LP, echo, holter, coagulation profile, ESR, CRP, hep B and C, HIV, treponemal, creatinine, autoimmune serology

- CSF: cells 14 ul/L (lymph), ptn 60mg/dl, glu 3.2mmol, negative virus PCR, negative bacterial and fungal c/s, no OCB, IgG index (+ +)

- Patient refused biopsy
- Improved with IVMP, started CYC & steroid for 6 months, MMF.

Vasculitis


Distributio
vascul
ssel
Primary angiitis of the central nervous system
• Headache 60%
• Altered cognition 50%
• Ischemic stroke 44%
• Visual symptom (any kind) 42%
• TIA 28%
• Seizure 15%
• Intracranial haemorrhage 8%
1. Clini
rema
2. Find
tures
3. No e
tion
coul
which
fea-
ondi-
tures
Large
Tak
Gia
Takayasu arteritis
Hypocomplementemic urticarial vasculitis
Behçet disease

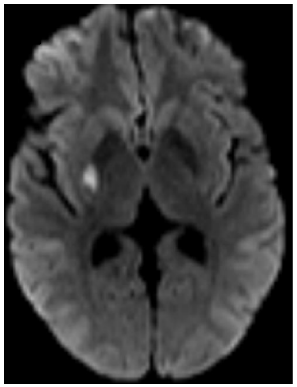
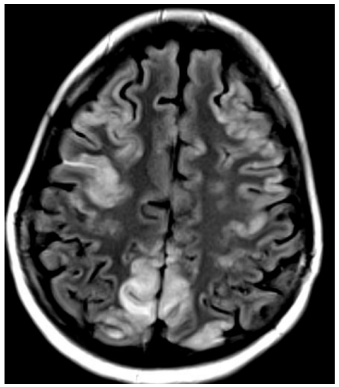
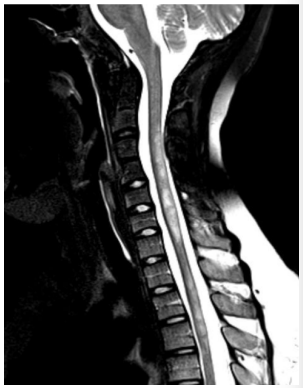
Case 6

- 23 y/o F diagnosed with SLE, 6 weeks ago
- Maintained on 50 mg prednisone
- Brought to ER
  - Insomnia for last 4 days
  - Agitation
  - Hearing of talking voices for 3 days

- CSF analysis normal, normal MRI brain, no infections,
- Antibodies dsDNA, APL, NMDA positive, ESR 13

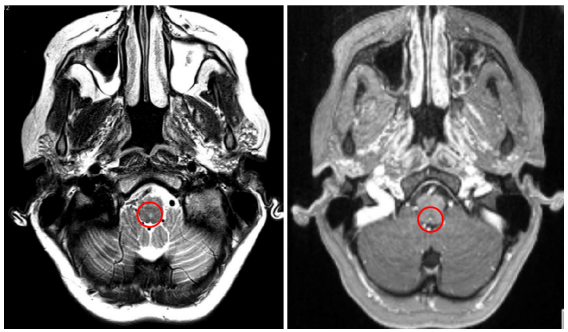
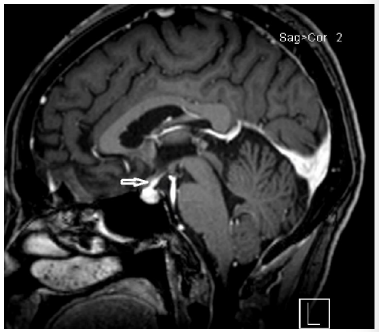
- Treated with 1gm IVMP
- patient become very agitated with inappropriate laughing

- Stopped steroid, maintained on resperidone and haloperidol PRN
- Recovered within 2 weeks

Diagnosis requires *either* of the following:

A. 4 of 17 criteria below present at any point in time, with at least 1 clinical and 1 immunologic criteria fulfilled
OR
B. Biopsy-proven lupus nephritis AND positive ANA or anti-dsDNA antibodies

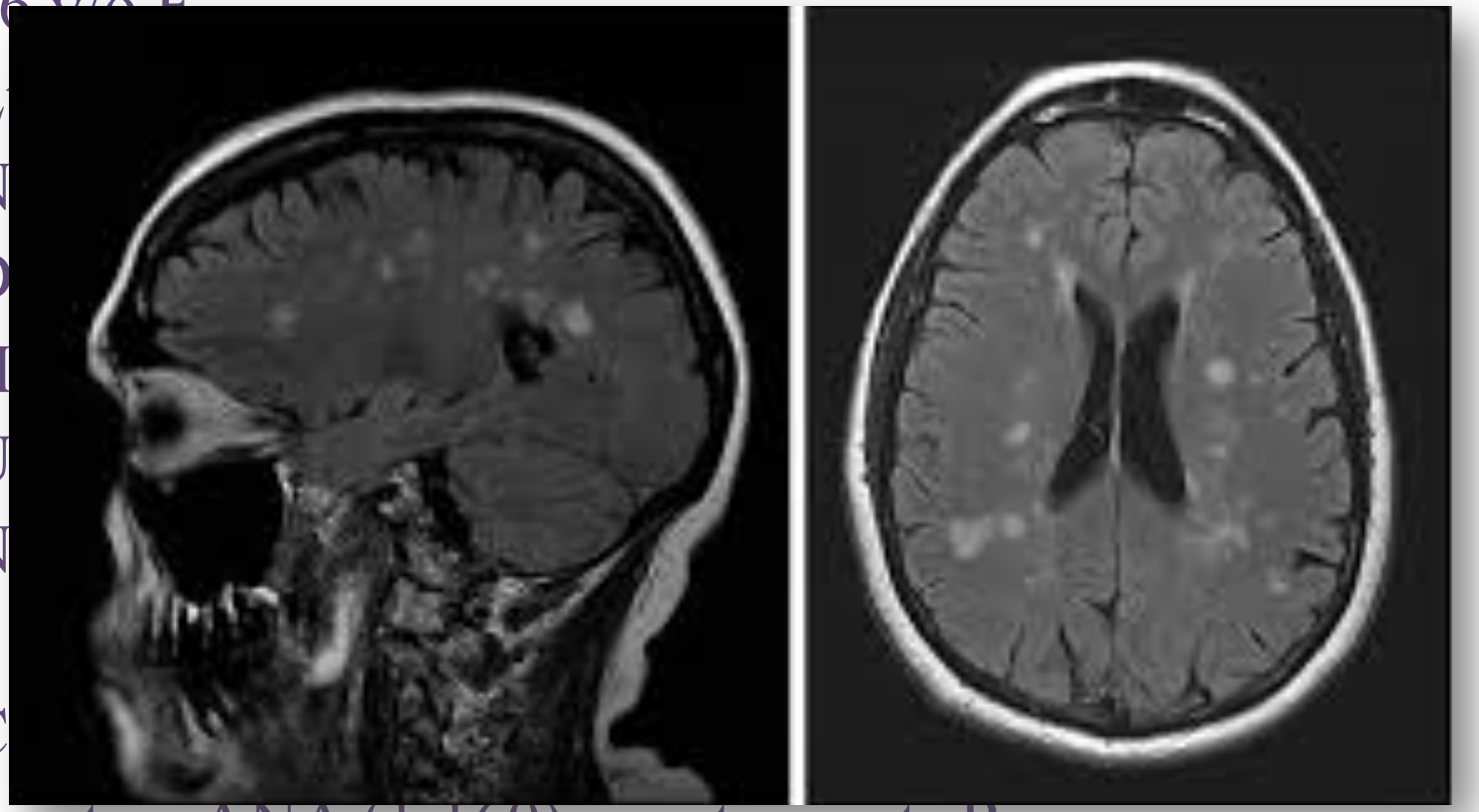
Clinical criteria	Immunologic criteria
Acute cutaneous lupus: lupus malar rash (non-discoid), bullous lupus, toxic epidermal necrolysis variant of SLE, maculopapular lupus rash, photosensitive lupus rash (in absence of dermatomyositis) or subacute cutaneous lupus	**ANA** above laboratory reference range
Chronic cutaneous lupus: classic discoid rash either localized or generalized, hypertrophic (verrucous) lupus, lupus panniculitis (profundus), mucosal lupus, lupus erythematosus tumidus, chilblain lupus, discoid lupus/lichen planus overlap	**Anti-dsDNA** above reference range, except ELISA (2× above reference range)
Oral ulcers: palate, buccal, tongue, or nasal (absence of other causes)	**Anti-Sm**
Nonscarring alopecia (absence of other causes)	**Antiphospholipid antibody** defined as lupus anticoagulant, false-positive RPR, medium or high titer anticardiolipin, anti-β (beta)2 glycoprotein I (IgA, IgG, or IgM)
Synovitis: 2+ joints with swelling or effusion OR tenderness in 2+ joints and >30 minutes morning stiffness	**Low complement** C3, C4, CH50
Serositis: >1 day of typical pleurisy or pleural effusions or pleural rub. >1 day of typical pericardial pain or pericardial effusion, or rub, or electrocardiogram evidence (absence of other causes)	**Direct Coombs** in the absence of hemolytic anemia
Renal: Proteinuria of >500 mg/24 h or equivalent urine protein/creatinine, or red blood cell casts	
Neurologic: seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy, acute confusional state (absence of other known causes)	
Hemolytic anemia: At least one occurrence of leucopenia <4000/mm³, or lymphopenia <1000/mm³ in the absence of other known causes Thrombocytopenia <100,000/mm³ at least once in the absence of other known causes	

Neuropsychiatric SLE *(NPSLE)*

- ANA: present in 95% but not specific
- Anti-dsDNA: can correlate with disease activity
- At least another >100 antibodies described
  - Anti-phospholipid antibodies
  - Anti-NMDAR NR2 subunit
  - Anti-Ribosomal
  - Anti-Aquaporin 4
  - Anti-MOG

Case 7

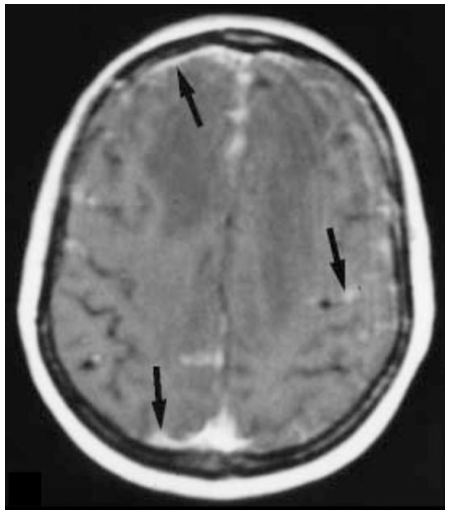
- 26 y/o F
- L
- N
- D
- H
- U
- N
- C
- Positive ANA (1:160), positive anti-Ro

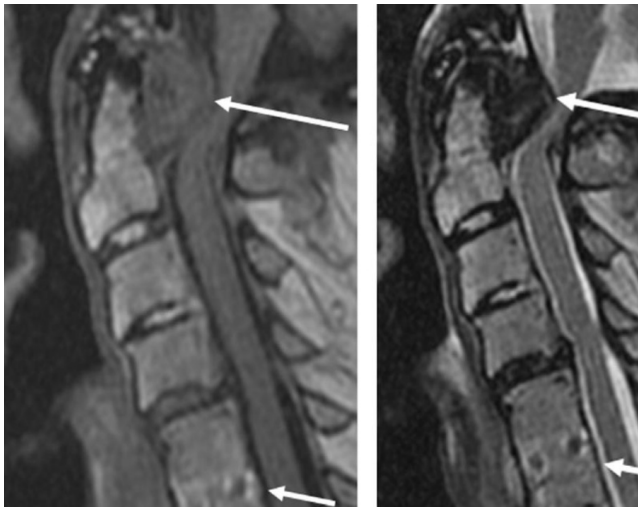


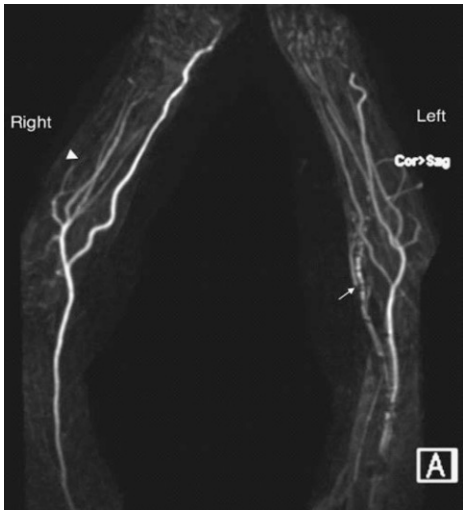
MS/NMO and Rheumatic disease

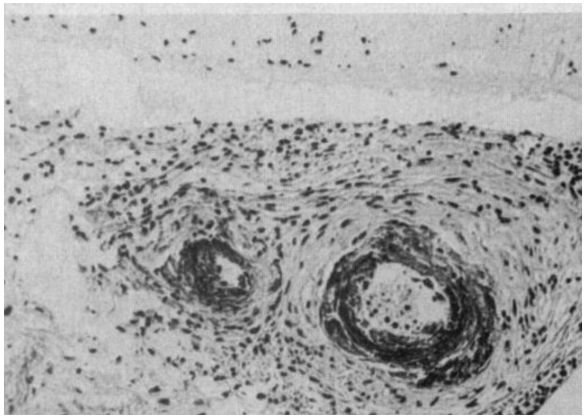
Autoantibodies	Anti-AQP4 + ($n = 12$)	Anti-AQP4 – ($n = 10$)
Anti-nucleosome*	4 (33.3)	3 (33.3)
Antinuclear antibodies	5 (41.7)	1 (10.0)
Anti-thyroperoxidase	4 (33.3)	1 (10.0)
Anti-thyroglobulin	2 (16.7)	3 (30.0)
Anti-SSA/Ro	1 (8.3)	1 (10.0)
TRAb	0 (0.0)	1 (10.0)
Anti-CCP	1 (8.3)	0 (0.0)
Anti-dsDNA	0 (0.0)	0 (0.0)
Anti-SSB/La	0 (0.0)	0 (0.0)
Anti-Sm	0 (0.0)	0 (0.0)
Anti-RNP	0 (0.0)	0 (0.0)
Anti-Scl70	0 (0.0)	0 (0.0)
Rheumatoid factor	0 (0.0)	0 (0.0)
ANCA†	0 (0.0)	0 (0.0)

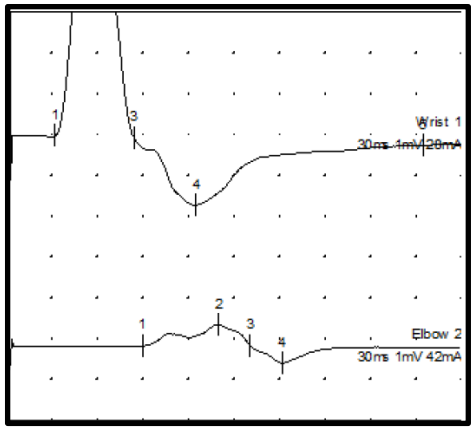
Rheumatoid arthritis











References

1. NeuroRheumatology A Comprehenisve Guide to Immune Mediated Disorders of the Nervous System. Tracey A, et al, 2019

2. Myelopathy in Behcet's Disease: The Bagel Sign, Uygunoglu U, et al, 2017, Ann of Neurology

3. Siva A, Saip S. The spectrum of nervous system involvementin Behcets syndrome and it's differential diagnosis. J Neurol

4. Chiewthanakul P, Sawanyawisuth K, Foocharoen C, Tiamkao S. Clinical features and predictive factors in neuropsychiatric lupus. Asian Pac J Allergy Immunol

5. Sibbitt WL Jr, Sibbitt RR, Brooks WM. Neuroimaging in neuropsychiatricsystemic lupus erythematosus. Arthritis Rheum

6. Rodriguez-Garcia JL, Bertolaccini ML, Cuadrado MJ, Sanna G, Ateka-Barrutia O, Khamashta MA. Clinical manifestations of antiphospholipid syndrome (APS) with and without antiphospholipid antibodies (the so-called 'seronegative APS'). Ann Rheum

7. Levine SR, Brey RL, Tilley BC, Thompson JLP, Sacco RL, Sciacca RR, et al. Antiphospholipid antibodies and subsequent thrombo-occlusive events in patients with ischemic stroke. JAMA

8. Segal BM, Pogatchnik B, Holker E, Liu H, Sloan J, Rhodus N, et al. Primary Sjogren's syndrome: cognitive symptoms, mood, and cognitive performance. Acta Neurol Scand [Research Support, NIH, Extramural Research Support, Non-US Gov't

9. Birnbaum J. Peripheral nervous system manifestations of Sjögrensyndrome: clinical patterns, diagnostic paradigms, etiopathogenesis, and therapeutic strategies. Neurologist

10. Bathon JM, Moreland LW, DiBartolomeo AG. Inflammatory central nervous system involvement in rheumatoid arthritis. Semin Arthritis Rheum

References

11. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med

12. Zajicek JP, Scolding NJ, Foster O, Rovaris M, Evanson J, Moseley IF, et al. Central nervous system sarcoidosis–diagnosis and management. QJM

13. Rybicki BA, Iannuzzi MC. Epidemiology of sarcoidosis: recent advances and future prospects. Semin Respir Crit Care Med

14. Calabrese LH, Mallek JA. Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria. Medicine (Baltimore).

15. Obusez EC, Hui F, Hajj-Ali RA, Cerejo R, Calabrese LH, Hammad T, et al. High-resolution MRI vessel wall imaging: spatial and temporal patterns of reversible cerebral vasoconstriction syndrome and central nervous system vasculitis. AJNR Am J Neuroradiol.

16. Salvarani C, Brown RD Jr, Christianson TJ, Huston J 3rd, Giannini C, Miller DV, et al. Adult primary central nervous system vasculitis treatment and course: analysis of one hundred sixty-three patients. Arthritis Rheumatol

17. Buttgereit F, Brand MD, Burmester GR. Equivalent doses and relativedrug potencies for non-genomic glucocorticoid effects: a novel glucocorticoid hierarchy. Biochem Pharmacol