CLINICAL CASE FOR RESIDENTS (VI)

24-year-old woman with recent-onset SLE presenting with subacute meningeal syndrome

1. Case Presentation

A 24-year-old woman ***was diagnosed with systemic lupus erythematosus (SLE) two months earlier***, based on the presence of:

- Cutaneous involvement
- Polyarthritis
- Pleuropericarditis
- ANA positivity
- Anti–double-stranded DNA antibodies
- Leukolymphopenia
- Class IV diffuse proliferative lupus nephritis confirmed by kidney biopsy

She is currently receiving:

- Prednisone 40 mg/day
- Mycophenolate mofetil 1 g twice daily (2 g/day)
- Belimumab 10 mg/kg intravenously every 4 weeks

Renal function has progressively improved since treatment initiation.

She now presents to the emergency department with a 4–5 day history of:

- Headache
- Low-grade fever (maximum 37.8°C)
- Nausea
- Progressive malaise
- Increasing somnolence

No seizures or focal neurological symptoms are reported.

Physical examination:

- Temperature: 37.6°C
- BP: 108/68 mmHg
- HR: 96 bpm
- Mild neck stiffness
- No focal neurological dèficit. No active cutaneous lupus lesions

Initial laboratory tests:

- Leukocytes: 3,200/mm³
- Lymphocytes: 680/mm³
- CRP: 18 mg/L
- Creatinine: 0.9 mg/dL
- Complement: C3: 62 mg/dL; C4: 9 mg/dL
- Anti-dsDNA: 135 IU/mL
- Urinalysis: proteinuria: 0.7 g/24h; 5–10 erythrocytes/HPF; 3–5 leukocytes/HPF

Brain CT scan is unremarkable. Lumbar puncture shows:

- Opening pressure: 24 cmH_2O (↔ / ↑)
- Pleocytosis: 210 cells/µL (↑)
- Differential count: 62% lymphocytes (↑), 28% neutrophils
- Protein: 132 mg/dL (↑)
- Glucose: 58 mg/dL (serum glucose 96 mg/dL) (↔)
- Macroscopic appearance: clear
- CSF Gram stain: negative

2. Main Clinical Problem

Subacute meningeal syndrome in a patient with recently diagnosed SLE and active lupus nephritis under intensive immunosuppressive therapy.

3. Differential Diagnosis

A. Neuropsychiatric SLE (NPSLE)

Possible given:

- Recent diagnosis
- Persistently active immunological profile
- Low complement levels

However:

- Fever
- Meningeal signs
- CSF pleocytosis

Require exclusion of infection prior to treatment escalation.

B. Aseptic meningitis

May be:

- Viral
- Immune-mediated
- Drug-related

Supporting features:

- Subacute onset
- Lymphocytic pleocytosis
- Normal CSF glucose

C. Bacterial meningitis (*S. pneumoniae*, *N. meningitidis*)

Possible in immunocompromised hosts.

However, CSF findings are not typical, as bacterial meningitis usually presents with:

- Marked neutrophilic pleocytosis
- Significantly reduced CSF glucose
- Elevated opening pressure
- Turbid CSF appearance

D. Opportunistic central nervous system infection

Risk factors:

- High-dose glucocorticoids
- Mycophenolate mofetil
- Belimumab

CSF findings compatible with:

- *Listeria monocytogenes*
- *Mycobacterium tuberculosis*
- *Cryptococcus neoformans*

However, some clinical and laboratory features may help to orient the differential diagnosis:

Listeria monocytogenes:

More likely in this context due to:

- Recent and intensive immunosuppression
- Subacute onset (4–5 days)
- Low-grade fever
- Mixed or lymphocyte-predominant pleocytosis
- Normal CSF glucose
- Clear macroscopic appearance
- Negative initial Gram stain

Cryptococcal meningitis

Typically presents with:

- More indolent clinical course
- Higher opening pressure (>25–30 cmH_2O)
- Lower CSF cellularity
- Predominantly lymphocytic pleocytosis

Specific diagnostic tests should include:

- CSF cryptococcal antigen
- India ink staining

Tuberculous meningitis

Usually associated with:

- More prolonged clinical evolution
- Markedly elevated CSF protein
- Reduced CSF glucose
- Lymphocytic pleocytosis

Microbiological workup should include:

- Ziehl–Neelsen staining
- Mycobacterial culture
- PCR for Mycobacterium tuberculosis

4. Empirical Treatment Decision Point

Pending microbiological confirmation, the presence of a subacute meningeal syndrome in an immunocompromised host requires prompt empirical antimicrobial therapy.

Standard empirical treatment for acute bacterial meningitis in immunocompetent adults (third-generation cephalosporin ± vancomycin) does not provide coverage against Listeria monocytogenes.

In immunocompromised patients, empirical antimicrobial therapy should therefore include: ampicillin, third-generation cephalosporin, vancomycin

5. Most Likely Diagnosis

Central nervous system infection due to *Listeria monocytogenes* presenting as subacute meningitis in an immunosuppressed patient with recent-onset SLE.

6. Description of the Diagnosis

Meningitis due to *Listeria monocytogenes* may differ from classical bacterial meningitis, particularly in immunocompromised patients.

CSF findings may resemble those observed in aseptic meningitis, including:

- Moderate lymphocytic pleocytosis
- Normal glucose concentration
- Clear macroscopic appearance

This atypical presentation may delay recognition and appropriate antimicrobial therapy.

7. Key Diagnostic Elements

- Recent exposure to intensive immunosuppression
- Subacute onset of neurological symptoms
- Low-grade fever
- Meningeal signs
- CSF lymphocytic pleocytosis with elevated protein
- Normal neuroimaging
- Negative Gram stain
- Absence of focal neurological deficit
- Microbiological confirmation through CSF culture or PCR is required.

8. Activity Plan for Residents

Group work (30 min):

- Identify main clinical syndromes

- Establish differential diagnosis (infection vs NPSLE)
- Select appropriate empirical treatment
- Discuss management of immunosuppressive therapy

Presentation (15 min)

Tutor-led discussion (15 min):

- CNS infections in SLE
- Empirical treatment of meningitis in immunocompromised hosts
- Role of glucocorticoids and biologics in infectious risk