Rheumatological emergencies

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Emergencies in rheumatology

Overview

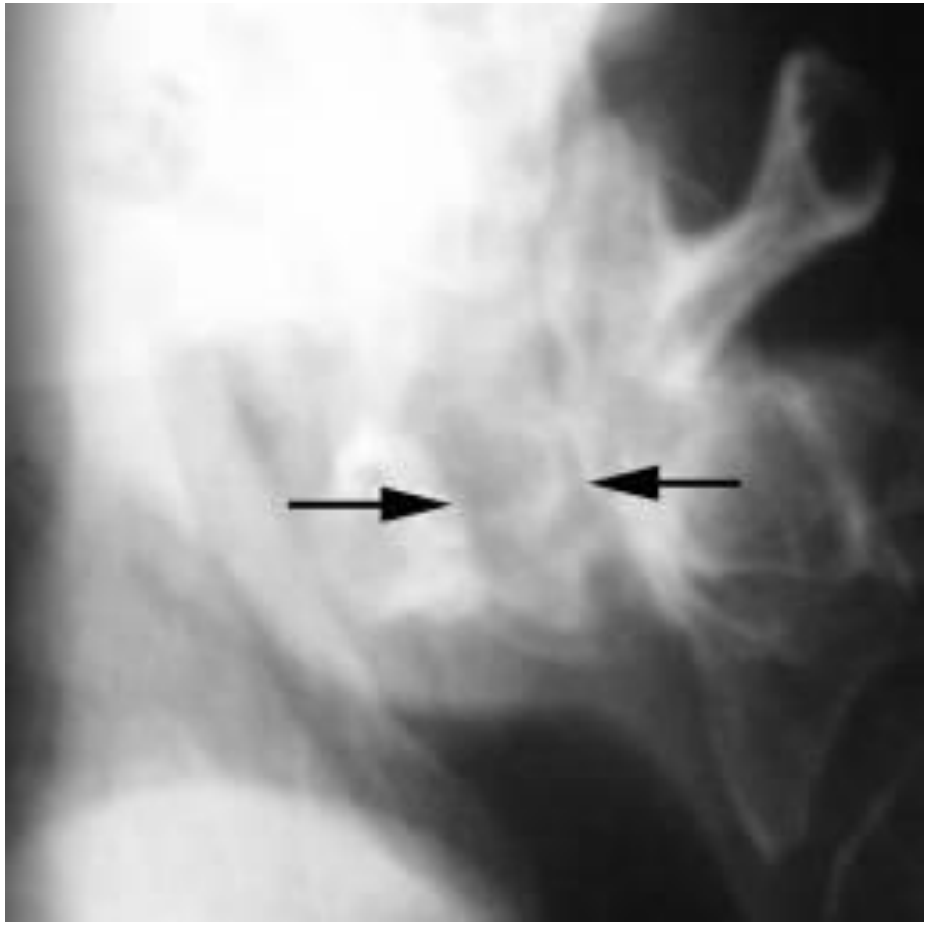
- Inflammatory rheumatic diseases (IRDs), typically is a broad spectrum of disorders
- Typically exhibit a chronic nature and necessitate prolonged therapeutic interventions
- Sometimes manifest as acute emergencies necessitating immediate and intensive medical intervention.
- These need to be efficiently handled, as they have the potential to be life-threatening and can result in severe morbidity and death if not promptly addressed.

Emergencies in RMDs

Overall;

- Emergencies in IRDs differ in frequency and presentation.
- Mainly involve severe infections, pulmonary emboli, renal crises, and cardiovascular issues.
- The pathophysiological processes that cause rheumatic emergencies are intricate and have multiple aspects
- Attributed to inflammatory nature of rheumatic diseases and multiple systemic factors.
  - Active inflammation can cause hypercoagulable states – thromboembolic events
  - Immunosuppressive effects of drugs used etc.

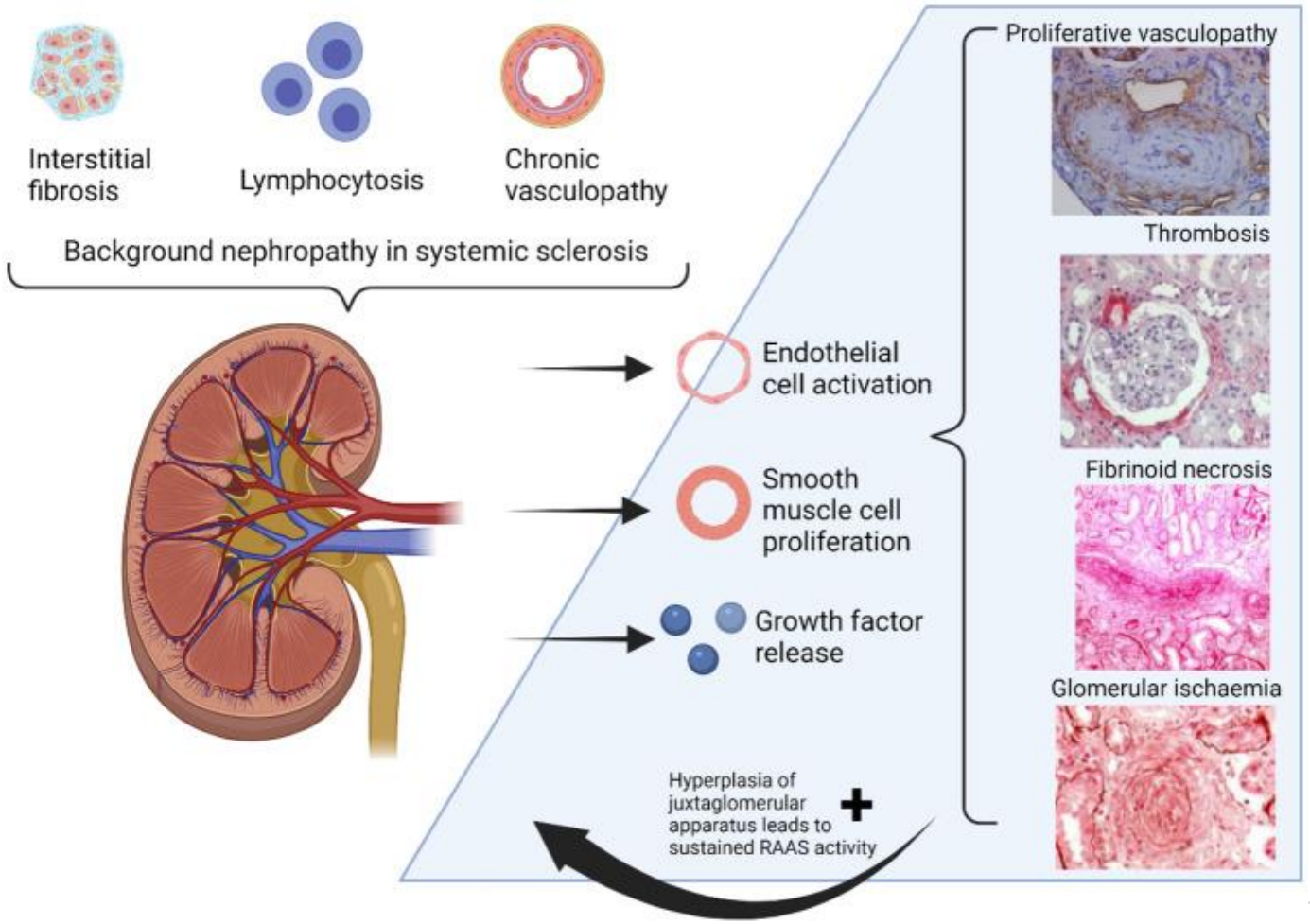
Cervical atlantoaxial subluxation in RA



Scleroderma renal crisis

- Is a life-threatening complication of systemic sclerosis (SSc) with a mortality of 20% at 6 months.
- Classically presents with accelerated hypertension and acute kidney injury (AKI) defined as an increase in serum creatinine > 1.5 × baseline.
- Differentials include,
  - anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis,
  - membranous nephritis,
  - other primary causes of thrombotic microangiopathies (TMA) such as thrombotic thrombocytopenic purpura (TTP) or disseminated intravascular coagulopathy (DIC

Pathophysiology



Denton C, Hudson M, Varga J (2021) Scleroderma.Chapter: Renal crisis and other renal manifestations of scleroderma.

Outcomes in SRC and follow up

- Outcomes in SRC remain poor compared to other organ complications of SSc
- Overall improved by 50% since the introduction of ACEi treatment in 1981.
- Reported 36% mortality and 25% remain on dialysis at 1 year.
- Permanent dialysis is required in 19–40% of SRC cases

Kim H, et al. Mortality and morbidity in scleroderma renal crisis: a systematic literature review. Journal of Scleroderma and Related Disorders. 2020;6(1):21–36.
Hudson M, et al. Exposure to ACE inhibitors prior to the onset of scleroderma renal crisis-results from the International Scleroderma Renal Crisis Survey. Semin Arthritis Rheum. 2014;43(5):666–672.

Long term

- ACEi should be continued life-long, even if the patient is dialysis-dependant.
- Angiotensin receptor blockers (ARB) can be used if ACEi is contraindicated or not tolerated;
  - Note: ARBs are not clinically equivalent in treatment of SRC. ARBs do not inhibit degradation of bradykinin, an agent which is needed in SRC due to its vasodilatory effects.
  - Beta blockers should not be used in SRC due to their negative chronotropic effects on a circulatory system experiencing increased peripheral resistance and may lead to reduction in cardiac output

Acute lupus pneumonitis

- Rare manifestation of SLE
  - affecting 1%–4% of cases, with poor prognosis
- Clinical presentation is similar to pneumonia
  - characterized by fever, cough and dyspnea with physical examination revealing tachypnoea, tachycardia, hypoxia and lung crackles
- Xray will show multiple and bilateral lung opacities, with predominance in the lower lung zones
- Being a diagnosis of exclusion

Management

- Bronchoscopy with bronchoalveolar lavage (BAL) and lung biopsy have no value in establishing diagnosis of acute lupus pneumonitis.
  - BAL allows to exclude infection and diffuse alveolar hemorrhage.
- Systemic steroids associated with immunosuppressive therapy (cyclophosphamide, rituximab, hydroxychloroquine and intravenous immunoglobulin).

Pulmonary hemorrhage

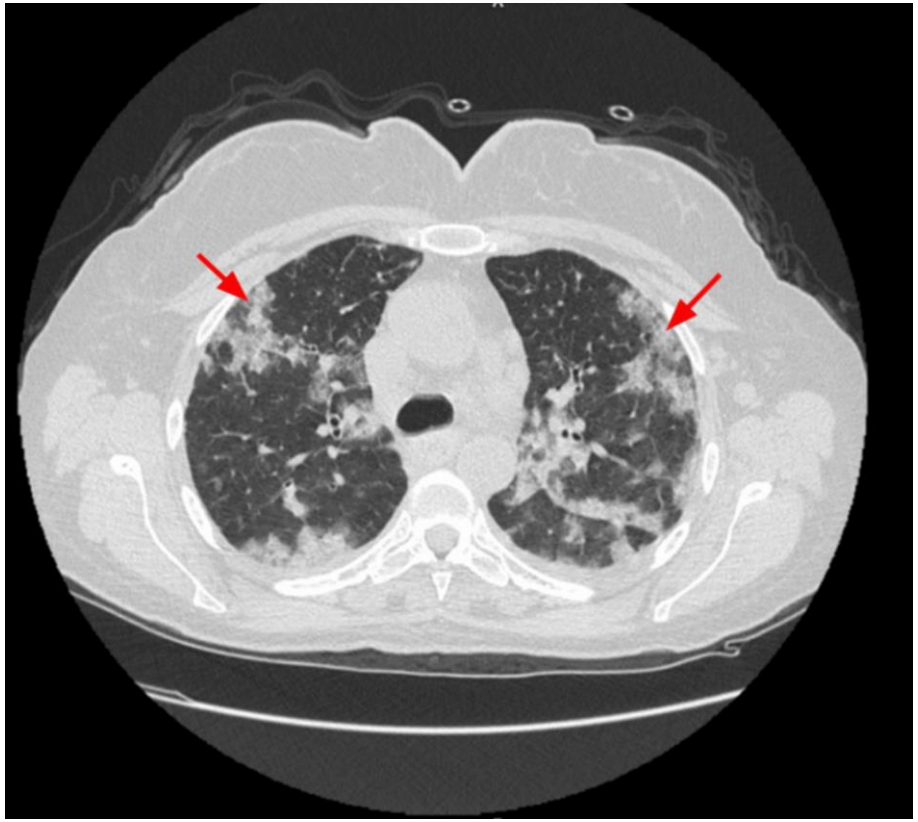
- A potentially catastrophic complication of SLE with mortality rate exceeding 50%
- Association with autoimmune diseases
  - SLE
  - Goodpasture's syndrome
  - Microscopic polyangiitis ……
- Shares similar clinical, radiological and histopathological features with acute lupus pneumonitis
- Results from acute injury to the alveolar-capillary unit

Pulmonary hemorrhage

- The incidence of DAH in patients with SLE ranges from 0.6% to 5.4% with an average estimated mortality rate of 50%
- Lupus nephritis linked to DAH, with active renal disease reported in as many as 64-100% of patients with lupus DAH

- Hemoptysis in < 50% of cases
- Marked drop in Hb over 12-36 h
- Unexplained rise or elevated single-breath diffusing capacity for carbon monoxide,
- Bronchoscopy
  - Blood-filled airways
  - Hemosiderin-laden macrophages in BAL fluid or within alveolar spaces of lung bx specimens

HRCT with patchy infiltrates and hemorrhage



Diffuse alveolar hemorrhage

- Present with dyspnea, cough and fever, blood-stained sputum and sometimes hemoptysis, with symptoms developing rapidly in hours or over a few days.
- The exact cause of DAH pathology is unknown but the general view is that IC-induced pulmonary capillaritis or bland hemorrhage leads to damage to basement membranes and leakage of erythrocytes into the alveolar space
- AH incidence in SLE patients can range from 0.6% to 5.4%,

DAH management

- There is a paucity of RCTs to better treat patients with SLE-associated DAH and management remains individualized across different medical centers.
- Therapies used are methylprednisolone, cyclophosphamide, and plasmapheresis.
- Other agents used
  - azathioprine (7%), intravenous immunoglobulin (IVIG, 5%), mycophenolate (3%), the B cell-targeting therapy rituximab (RTX, 6%), and stem cell transplantation (2%)

Long term and follow up

- Depends on etiology and severity of the disease.
- Can be induction or maintenance generally, dictates the intensity of the initial treatment and the risk of complication.
- Need of mechanical ventilation, severe dyspnea associated with severe lung failure, and a higher risk of ventilator-associated pneumonia.
- Watch for kidney failure which also contributes to poor outcomes.
- Other factors such as thrombocytopenia, infections, age, and multi-organ failure scores also cause higher mortality

Antiphospholipid syndrome (APS)

- Thromboembolic phenomena
- Obstetric morbidity
- Antiphospholipid antibodies
  - Anticardiolipin Ab
  - Lupus anticoagulant
  - Anti-β2 glycoprotein I Ab

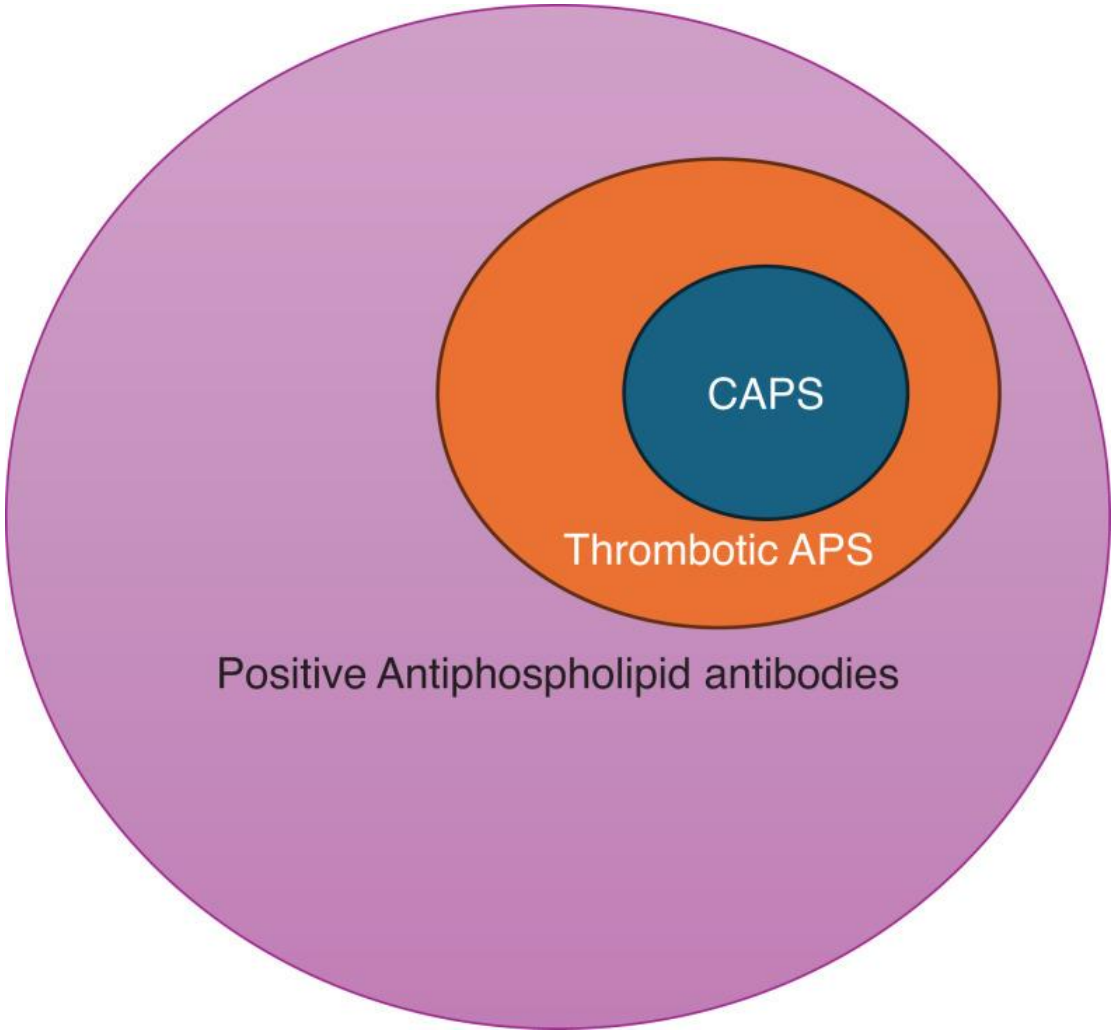
Catastrophic APS (CAPS)

Classification criteria:

- multiorgan thrombosis developed simultaneously or in less than a week
- affecting at least 3 organs, systems and/or tissues
- histopathologic confirmation of small vessels occlusion in at least one organ or tissue Presence of anti-PL

Asherson RA, et al. Lupus 2003;12:530-4

Overlap of CAPS and thrombotic antiphospholipid



Approach to Catastrophic Antiphospholipid Syndrome

Clinical Features

Hematologic:
- Hemolysis
- Low Platelets
- Thrombosis

Central Nervous System (56%):
- Focal Neurologic Deficits
- Confusion
- Seizures

Liver (34%) & Gastrointestinal (12%):
- Infarcts
- Ulcerations

Cardiac (50%):
- Infarction
- Valvular Disease

Kidneys (73%):
- Acute kidney injury
- Hypertension
- Proteinuria
- Hematuria

Lungs (60%):
- Acute Respiratory Distress Syndrome
- Pulmonary Hemorrhage
- Pulmonary Embolism

Skin (45%):
- Livedo Reticularis
- Purpura
- Skin necrosis

Investigations

- CBC
- Hemolytic Markers
- Blood Smear
- Basic Metabolic Panel
- Coagulation Tests
- Inflammatory Markers

Special Testing: aPL Antibodies

Beware of false negative & positive tests

Tissue Biopsy

Classification Criteria

1. Rapid onset (< 1 week)
2. Involving 3 or more tissues, organs, or organ systems
3. Antiphospholipid antibodies, meeting Antiphospholipid Syndrome criteria
4. Histopathological confirmation of microvascular ischemia

Management

Triple Therapy

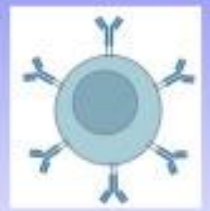
Heparin

Plasma Exchange

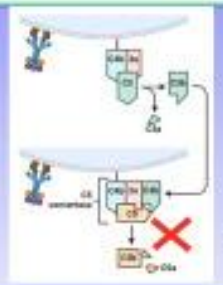
Glucocorticoids

IVIG

Refractory



Rituximab



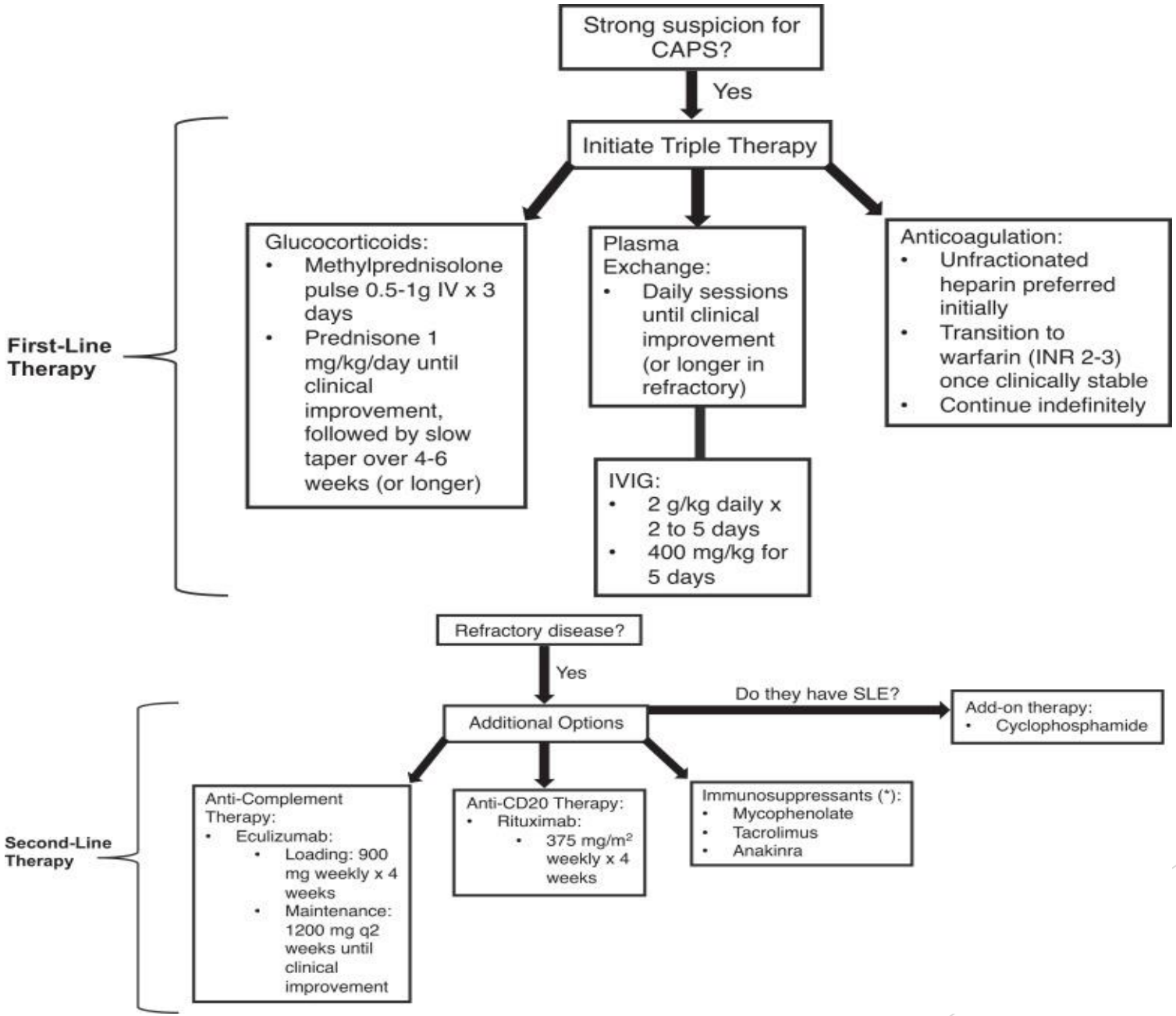
Eculizumab

Conclusion:

1) **CAPS is an acute & life-threatening form of APS with macrovascular & microvascular thrombosis**
2) **Rapid identification (with or without aPL or biopsy confirmation) & management can improve outcomes**

Salter BM, Crowther MA. Catastrophic antiphospholipid syndrome: a CAPS-tivating hematologic disease. Hematology Am Soc Hematol Educ Program. 2024 Dec 6;2024(1):214-221

Management


Strong suspicion for CAPS?
Yes
Initiate Triple Therapy
First-Line Therapy
Glucocorticoids:
• Methylprednisolone pulse 0.5-1g IV x 3 days
• Prednisone 1 mg/kg/day until clinical improvement, followed by slow taper over 4-6 weeks (or longer)
Plasma Exchange:
• Daily sessions until clinical improvement (or longer in refractory)
Anticoagulation:
• Unfractionated heparin preferred initially
• Transition to warfarin (INR 2-3) once clinically stable
• Continue indefinitely
IVIG:
• 2 g/kg daily x 2 to 5 days
• 400 mg/kg for 5 days
Refractory disease?
Yes
Additional Options
Do they have SLE?
Add-on therapy:
• Cyclophosphamide
Second-Line Therapy
Anti-Complement Therapy:
• Eculizumab:
• Loading: 900 mg weekly x 4 weeks
• Maintenance: 1200 mg q2 weeks until clinical improvement
Anti-CD20 Therapy:
• Rituximab:
• 375 mg/m² weekly x 4 weeks
Immunosuppressants (*):
• Mycophenolate
• Tacrolimus
• Anakinra

Outcomes

- The outcomes for CAPS are poor, with an overall mortality of 36%.
- Triple therapy has best chance of survival
  - Significantly reduces mortality compared to no treatment (28.6% vs 75% mortality)
- In patients who do survive a first episode of CAPS, recurrence is relatively rare,
- For women with APS or a history of CAPS, the implications for subsequent pregnancies are significant.
  - Careful pre-pregnancy planning and multidisciplinary management during pregnancy are crucial.
  - Careful attention should be given to the well-being of the fetus, and delivery should be preplanned

Others

- Pulmonary embolism
- Vasculitis
- Neuro-psychiatric complications
- Cardiac complications – heart failure, myocardial ischemia, arrythmias etc.
- Vascular ischemia, thrombosis and aneurysmal ruptures etc.