QUESTION 54

A 45-year-old woman presents with a three-year history of recurrent rash, characterised as palpable purpura over both legs. Some of these lesions have ulcerated.

Laboratory results include:

- serum:
  - creatinine: 0.10 mmol/L [0.06-0.11]
  - alanine transaminase (ALT): 51 U/L [15-50]
  - aspartate transaminase (AST): 64 U/L [15-45]
  - hepatitis C antibody: positive
  - cryoglobulins: positive with 8% cryoprecipitate
- urinalysis normal

Which of the following is the most appropriate management?

A. Plasmapheresis and corticosteroids.
B. Corticosteroids and interferon α.
C. Interferon α and ribavirin.
D. Cyclophosphamide and corticosteroids.
E. Cyclophosphamide and ribavirin.

HAEMATOLOGICAL MANIFESTATIONS OF HEPATITIS C

- Essential mixed cryoglobulinaemia
- Monoclonal gammopathies (can be associated with myeloma)
- Lymphomas

ESSENTIAL MIXED CRYoglobulinaemia (TYPE II CRYoglobulinaemia)

- Lymphoproliferative disorder
- Cryoglobulins are immunoglobulins that precipitate in the cold and dissolve on rewarming
- Leads to deposition of circulating immune complexes in small to medium-sized blood vessels
- Cryoglobulins associated with myeloma/Waldenstrom’s macroglobulinaemia (type I), Hep C (type II), chronic inflammatory conditions and autoimmune disease (type III)
- 95% of pts with essential mixed cryoglobulinaemia have hepatitis C or IgG to hep C
- May be due to hep C virus binding to B lymphocytes via CD81 and lowering their threshold for activation
- Patients with hep C and cryoglobulinaemia also have high levels of rheumatoid factor – secreted by HCV-infected lymphocytes

Clinical Manifestations

- Classic triad of:
  - Palpable purpura
  - Arthralgias
  - Weakness
- Other features include lymphadenopathy, hepatosplenomegaly, peripheral neuropathy, renal disease
- Renal disease occurs in 35-60% of pts with type II cryoglobulinaemia
- Generally chronic, smoldering course

Diagnosis

- Low complement (especially C4)
- Raised RF
- Hepatitis C serology
- Circulating cryoglobulins
- Can biopsy the purpuric skin lesions
- Consider renal biopsy if diagnosis still in doubt
- Can get spurious leukocytosis and thrombocytosis

Treatment
- Main indication for treatment is progressive systemic disease
- First confirm hepatitis C infection
- Interferon alpha plus ribavirin is treatment of choice
- In patients with normal or near normal renal function, use pegylated interferon but if Cr clearance <50 use non-pegylated interferon
- In patients with severe/fulminant disease, plasmapheresis and immunosuppressive therapy is appropriate (methylprednisolone or cyclophosphamide)
- Risk of worsening hep C infection if immunosuppression used

Prognosis
- Untreated patients tend to die of hepatic or cardiovascular disease, not due to complications of cryoglobulinaemia
- No long term studies in treated patients
- Variable prognosis in renal disease – some patients undergo complete remission, some develop ESRF

Answer: C