A cold case…

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The Case

- Mr T, 52 yr old male
- Inpt. Haematology- for Inv of progressive B symptoms over 4-5 yrs
- 2 admissions in 3 months

Rheum Consult on 2nd adm:

- Long standing intermittent disabling polyarthralgias

Background

- Leucocytoclastic Vasculitis 2008- initial event
- 7yrs h/o drug abuse: Opiates and Methamphetamines- On Meth program
- Previous IVDU
- Current Smoker

Active medical issues:

- Diffuse Lymphadenopathy with splenomegaly -on CT CAP
- New AKI- Cr 120s, eGFR 57
  ACR 10.8, PCR 24
- Cytopenias: IDA, Leucopenia

- Progressive symmetrical LL sensory neuropathy
- Cold peripheries with poor peripheral circulation

Thoughts?

Laboratory Tests:

- Hb 84, hypochr, microcytic, Plts 255
- WCC 3.46, Ly 0.85-1.0
- Blood film- Cryoglobulins
- Flow cytometry negative

- **Rh Factor 370**
- ANA, ANCA, ENA, ds-DNA -neg
- **C3 0.46, C4 <0.02**
- Anti cardiolipin Ab neg

Laboratory tests:

- B2 microglobulin 12.1
- Pr 51, Glob 19
- IgG 2.2
- Kappa LC 197, Lambda LC 29, Ratio 6.86
- SPEP: IgM paraprotein
- Hepatitis B, C negative
- **Cryoglobulins: 7 days: small amount**
  Cryocrit 1

Tissues:

- Renal biopsy:
  MPGN of Immune complex type resembling Lupus Nephritis

  Immunoflorescence:
  -IgG, IgM, IgA ++++
  -C3 ++++
  -C1q ++
  - Kappa ++++, Lambda +++
- EM: More likely SLE, no evidence of Cryo, but difficult to differentiate

Tissues:

- BM & trephine 1st:
  No morphological evidence of Lymphoma, Type 1 Cryoglobulin
  -LN excision biopsy- Reactive changes

BM & trephine 2nd (6 weeks): B cell clonal population highly suggestive of LPD ? Splenic marginal zone lymphoma

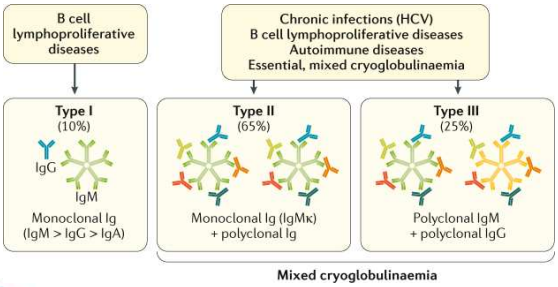
Imp: Possible Low Grade Lymphoma

Classification of cryoglobulinemia

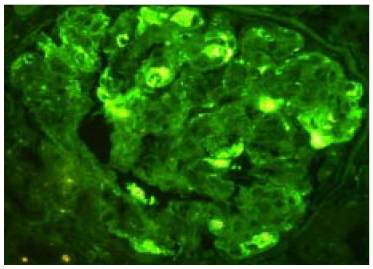
Types	%	Monoclonal	Polyclonal	Associated diseases
Type I	10-15	Monoclonal IgM or IgG	–	Lymphoproliferative disorders
Type II 'also called MC'	50-60	Monoclonal IgM	Polyclonal IgG	Infections (mainly HCV) Autoimmune disorders Lymphoproliferative disorders
Type III 'also called MC'	30-40	–	Polyclonal IgM & IgG	Often autoimmune disorders Infections (mainly HCV)

Ferri C. Mixed cryoglobulinaemia. Orphanet J Rare Dis 2008; 3: 25.

Brouet Classification of Cryoglobulinemia



Cryoglobulins in a Glomerulus- EM



Learning points:

- Cryoglobulins are difficult to detect

- High Rh factor in absence of Anti-CCP antibodies-
  - -CTDs
  - -Cryoglobulinemias
  - -Liver Cirrhosis, PBC
  - -Malignancy
  - -Multiple Immunisations
  - -Parasitic Infections:
    Chagas', Malaria, Toxoplasmosis
  - -Age

Thank you