Evidence for HCV in Essential-Mixed Cryoglobulinemia (EMC)

- Anti-HCV Ab’s in 91%
- HCV RNA detected in 86%
- HCV RNA and anti-HCV Ab to C22-3 are concentrated in cryoglobulin

(Feari, Clin Exp Rheum 9(621), 1991)

Case I

- An 8 yo boy develops pedal edema and is found to have 4+ proteinuria on dipstick of urine by pediatrician. His Ccr is normal; 24 hour urine proteinuria is 9 g/day; Palbumin is 2.3 g/dl; P cholesterol 346 mg/dl; all serologic tests including ANA, complement, VDRL, Hep B Sag-Ab, etc are normal.

Case I

- A) The boy’s mother, your friend asks should a renal biopsy be performed? You answer (Yes, No, Maybe, Patient is too young for you to be concerned with – never happens in adults).
- B) The mother wants to know if there is specific Rx for this disease. You answer (Yes, No, Maybe, Don’t know never happens in adults).
- C) If a renal biopsy were performed it would most likely show on light microscopy (1, 2, 3, 4).
Case I

- D) If the biopsy is done it will most likely show by IF (1,2,3,4).
Case I

- Electron microscopy would most likely show (1,2,3,4).
Minimal Change Disease

- 5-10% Adults with NS, >85% children
- Usually sudden onset, hvy proteinuria, and edema
- In adults HBP 30%, Microhem 30 %, +/- Low GFR (volume depletion)
- Course: Respond to Strds, Relapse, No RF

Case 2

- A 19 yo AA college student is referred for 2nd opinion re her nephrotic syndrome. At 15 yo she was dxed w idiopathic NS w 16 g/d proteinuria, Palbumin 2.8 g/dl, Pcholesterol 300 mg/dl, Pcreatinine 1.0 mg/dl and neg. ANA, HBsAg-Ab, HCV, normal serum complement and BS. Bx then showed 22 glomeruli all WNL by LM, Neg by IF, and only fused foot processes by EM. She was Rxed w Prednisone 60 mg/d for several mo. w/o any change in proteinuria. Edema has been controled w diuretics over 4 yrs and proteinuria is 5-10 g/day. Proteinuria is non-selective and

Case 2

- A) The pts GFR now is probably closest to 1) 10 cc/min, 2) 85 cc/min 3) 35 cc/min, 4) 70 cc/min.
- B) Since the patient’s proteinuria is non-selective it is composed mostly of middle size globulins rather than albumin (T, F).
- C) If a biopsy is done now it would most likely show by LM (1,2,3,4).
Case 2

D) Electron microscopy of the biopsy would most likely show (1, 2, 3, 4).
Creatinine Clearance as a Measure of Glomerular Filtration Rate

- \( C_{cr} \) = volume of serum totally cleared of creatinine in a given interval (usually expressed as ml/min or L/Day)

- Problems:
  - Collection problems
  - Must be steady state
  - Over-estimates true GFR by 10-15% due to secretion of creatinine by tubule. Significant over-estimation at low GFR's

Case 2

E) The patient asks if she will need dialysis some day. You answer (Yes, No, Maybe, Everyone eventually will need dialysis if they live long enough).

F) The patient asks if there is any proven therapy for her disease. You answer (Yes, No, Maybe, If there is I don't know it).

G) If the patient develops renal failure and gets a kidney TXP what are the chances the disease will recur in the TXP? (0%, 30%, 70%, 100%)

Focal Segmental Glomerulosclerosis

- Increased frequency > 20% NS – Blacks!
- In adults onset 2/3 NS, 1/3 proteinuria
- HBP > 30%, Microhematuria >30%, renal dysfunction 50%
- Predictors of ESRD: heavy prot., Blacks, high creatinine, on BX – int fibrosis & Collapse
- Strds >50% respond, cytoxan, cyA, MMF
- Recurs 1/3 Txps-
Case 2

- Morphologic features similar to those seen in this case can also be seen frequently in which disease (Use of Gold salts in rheumatoid arthritis, SLE, HIV disease, diabetes)?

Focal Glomerulosclerosis (FSGS)

- Clinical.
  - Associated with heroin nephropathy, Obesity, SS disease, chronic reflux nephropathy, HIV.
- Path:
  - LM – Focal segmental hyaline – no inflammation
  - IF – IgM & C3 “trapped” in sclerotic lesions
  - EM – No deposits, fused foot processes
- Rx+Course
  - Some respond to steroids or cytotoxic
  - Usual relapse and/or become unresponsive
  - Progresses to ESRD
  - Can recur in Txp (up to 30%)
Case 4

A 45 yo W M lawyer develops swelling of his feet. He states his eyes are swollen in the AM and he cannot put on his ring on his finger in the morning. At the end of the day his ankles and legs are swollen.

His 
Pcreatinine 1.0 mg/dl, 
Palbumin 2.0 g/dl, 
Pcholesterol 642 mg/dl, 
U/A 4+ protein 1+ heme, microscopic 3-5 rbc’s. All serologic tests including ANA, complement, HepB and HCV, etc are WNL or negative.

Case 4

A) The medical student you says he has cared for 2 pts already w edema: one with CHF and one w cirrhosis and ascites. He asks why neither pt c/o periorbital edema like this pt. You answer.... (alternative – tell medical student to do rectal exam on patient and quickly leave room to call nbephrologist for answer )

Case 4

B) You ask the patient if he has noted anything unusual about his urine. He answers:

1) It is dark
2) It is foamy
3) It is cloudy
4) It is coca cola colored

Case 4

C) Looking at this patient’s urinalysis would most likely show: (1,2,3,4)
Case 4

- D) Statistically this Caucasian adult with idiopathic nephrotic syndrome will most likely have which of the follow patterns on Bx by LM? (1,2,3,4).
Case 4

• E) Silver stain can be very helpful in some cases. In this biopsy silver stain would most likely show?
• (1,2,3,4)
Case 4

- F) IF staining for immunoglobulins and complement would be likely to show?
- (1,2,3,4)
Case 4

• G) Electron microscopy might show? (1, 2, 3, 4)
**Case 4**

- H) The patient has the most likely pattern predicted on his biopsy. Your friend asks you the pathogenesis of this glomerular lesion. You answer... (alternative, another rectal exam and call nephrologist again)
- I) The patient asks if there is a cure for his disease. You answer (Yes, No, Maybe).
- J) The patient asks what the odds of his being on dialysis 10 yrs from now are. You answer (5%, 20%, 50%, 80%).
- K) What secondary form of NS has NOT been associated with this pattern? (w lung cancer, w gold salt Rx, w HBV)

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**Nephrotic Syndrome**

- Proteinuria: > 3.5 grams/24 hours
- Edema
- Hypoalbuminemia
- Hyperlipidemia

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**Membranous Nephropathy**

Most common pattern idiopathic NS Caucasians

Presents - proteinuria and NS HBP, microhematuria not rare

Thromboses - RVT

Pathology: thick cap walls + spikes IF + granular deposits, EM subepi deposits

Course: ¼ spont remit, slow progressive RF

Rx: Steroids alt cytoxan, CyA, other
Membranous Glomerulonephropathy

Clinical: 30–40% W Adults with Idiopathic N.S. (most common pattern)
- Associated with infections (Hep. B, Lues, malaria, schisto), SLE, Carcinomas, Medications (gold, penicillamine)
- Hypercoagulable state - Renal vein thrombosis

Rx: Steroids + cytotoxic, Cyclosporine, MMF

Course: Over 10 years
- 25% dead or ESRD
- 50% persistent prot / N.S.
- 25% Remit.

1. Sudden Deterioration
   • Think RV T

2. Elderly - ? Underlying Tumor

Case 5

- A 26 yo stock analyst while on vacation in Antigua develops a facial rash, low grade fever, lymphadenopathy, and arthritis of her hands, wrists, and ankles. Her ANA is + at 1:160, serum complement low, anti-DNA antibody very elevated (1250 by ELISA), P creatinine 1.6 mg/dl, and she has 3.4 g proteinuria/day.

Case 5

- A) Urinalysis would most likely show which of the following (1,2,3,4)?
Case 5

- B) Renal biopsy might show all of the following EXCEPT which pattern by LM?
  (1,2,3,4)?
Case 5

- B) How often do patients with SLE have an entirely normal kidney biopsy? (almost never, 10-20%, 30-40%, over 90% if no clinical renal disease).
- C) What pattern or Class of LN is most likely to be seen on the biopsy? (Class II, III, IV, V)?
- D) The mechanism(s) of immune damage in DPLN include which of the following 1) chronic immune complex deposition 2) acute one-shot immune complex deposition c) in situ immune complex formation d) anti-GBM antibodies.

Table I
Morphologic Patterns of Renal Involvement in SLE

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mesangial deposits, no proliferation</td>
</tr>
<tr>
<td>II</td>
<td>Mesangial Proliferative GN</td>
</tr>
<tr>
<td>III</td>
<td>Focal Proliferative GN</td>
</tr>
<tr>
<td>IV</td>
<td>Diffuse Proliferative GN</td>
</tr>
<tr>
<td>V</td>
<td>Membranous GN</td>
</tr>
</tbody>
</table>

Case 6

- A 43 yo jeweler has had insulin dependent diabetes mellitus for 21 yrs. His is poorly compliant with all his medications. Recently his MD noted proteinuria on the urine dipstick. On referral you find a BP of 145/85, a BS of 165 mg/dl, Pcreatinine 1.2 mg/dl, Cholesterol 320 mg/dl, LDL cholesterol 222 mg/dl, 24 hr urinary protein 4 g/d, and negative serologic evaluation.

- A) The pt asks if a biopsy is necessary.
Case 6

- B) If the biopsy is done it would be LEAST likely to show (1,2,3,4).

Diabetes Mellitus: A Worldwide Public Health Problem

- 124 million patients with diabetes
- 2.1% of the world population
- 97% are patients with type 2 diabetes
- 221 million estimated by 2010
- Complications of diabetes include
  - Coronary artery disease
  - Blindness
  - Peripheral vascular disease
  - Renal failure

Diabetes: The Most Common Cause of ESRD

Primary Diagnosis for Patients Who Start Dialysis

- Diabetes 50.1%
- Hypertension 27%
- Glomerulonephritis 13%
- Other 10%
- No. of Patients: 243,524
- Projection: 520,242
- 95% CI: 849.9%


Case 6

- C) What would be the most likely finding on EM of the biopsy?
- D) Without a change in therapy the odds that this patient will progress to ESRD in 5 yrs are (low, moderate, high, very high).
- E) What might be done to slow the course to progressive ESRD here?

Treatment of Diabetic Nephropathy

I. Control Glomerular Capillary Hypertension (ACEinhib/ARBs)
II. Role of Glycemic Control
III. Role of Blood Pressure Control
IV. Role of Lipid Control
The Glomerulus

Angiotensin II Vascular Hypertrophy

Angiotensin II affects factors that modulate growth in cultured vascular smooth muscle cells

- Fibroblast Growth Factor
- Transforming Growth Factor Beta-1
- Platelet Derived Growth Factor
- Insulin-like Growth Factor


Study Titration Schedule

- N = 1520
- Goal BP < 140/90 mmHg
- Maintain prior Antihypertensive Therapy (excluding ACEI, ARB)
- NIDDM Patients with proteinuria

- Los 100 mg + Other Antihypertensive Therapy (including ACEI, ARB)
- Los 50 mg + prior therapy
- Placebo + prior therapy
- Placebo + Other Antihypertensive Therapy (excluding ACEI, ARB)

RENAAAL Primary Components

- Doubling of Serum Creatinine
  - Risk Reduction: 25%
  - p=0.006
  - Months
- ESRD
  - Risk Reduction: 28%
  - p=0.002
  - Months

Case 7

- A 52 yo F has had rheumatoid arthritis for 20 yrs and has been taking aspirin daily but no other medications for her disease. She develops edema and is found to have the following labs: U/A 4+ protein, and maltese crosses, Pcreatinine 2.4 mg/dl, 24 hr prtoein 5.4 g/d, and negative or normal tests for complement, anti-DNA antibody, HBV, BS, HCV, etc.

Case 7

- A) Renal biopsy is most likely to show?
  - 1,2,3,4.
Case 7

- B) What special stains might be useful here?
- C) What other diseases are commonly associated with this pathology?
- D) What is a differential diagnosis of proteinuria in a patient with Rheumatoid Arthritis?
Renal Disease in Rheumatoid Arthritis

1) Majority of patients no lesions or non-specific changes (in spite of high levels of CIC)
2) Occasional proliferative glomerular lesions (r/o SLE, MCTD, etc.)
3) Amyloid 5 – 10%
4) Arteritis (r/o PAN)
5) Complications of therapy
   a) Analgesics
   b) Gold
   c) Penicillamine
   d) Non-steroidal anti-inflammatory agents
      i. AIN
      ii. Minimal Change in GN

Analgesic Nephropathy

An international disease (Australia, Switzerland, Scandinavia, USA)
Abusers and Users – Headaches and Arthritis
Female:Male 6:1
Large amounts over prolonged time periods
Renal abnormalities
   - sterile pyuria
   - only mild proteinuria and hyperperfusion
   - Decreased concentration ability
   - Decreased net acid excretion
   - Salt wasting
   - Papillary necrosis
Patients can recover function if they stop analgesic use
Causes of Papillary Necrosis

- Pyelonephritis
- Obstruction
- Sickle Cell Disease
- Tuberculosis
- Cirrhosis
- Analgesic Abuse
- Radiation
- Diabetes

(POSTCARD 1)