PROTEINURIA IN PREGNANCY

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CLINICAL CASE FOR DISCUSSION

- 30 year old female, 15 weeks pregnant
- RFR: proteinuria
- PMHx:
  - DM1 diagnosed at age 15
    - Poor diabetic control in early years of diagnosis
    - Single admission with DKA, did not require ICU
    - Since age of 24-25 has had much better control of DM with insulin pump.
    - Current control: very good with HgA1c 0.065
    - Followed by endocrinologist who is the referring physician.
  - asthma
    - Not active
    - Ventolin PRN only if URTI, no previous admission or ICU care

CLINICAL CASE FOR DISCUSSION

- Allergies: none
- Medications:
  - pregvit, ventolin PRN, insulin pump (humolog)
- Habits:
  - Smoker: during pregnancy 1-4 cigs/day
  - No EtOH
  - No recreational drugs
  - Denies over counter medication use

CLINICAL CASE FOR DISCUSSION

- PG&OHx:
- $G_1P_0A_0$
- 15 weeks pregnant, EDC: Dec 12, 2010
- Irregular menstruation requiring BCP treatment.
- Came off the BCP for a planned pregnancy
- Unable to have regular periods, required gyne consultation and hormonal treatment to induce menses.

CLINICAL CASE FOR DISCUSSION

- HPI:
- Given planned pregnancy and DM1, patient aware that she was pregnant at 6 weeks gestation.
- Presented to her endocrinologist for more strict control of her DM during pregnancy.
- Urinalysis done by endocrinologist showed "proteinuria" which had not been there before.

CLINICAL CASE FOR DISCUSSION

- Within a few days patient started to develop lower limb edema
- Progressively worsening edema, extending to sacrum, hands, face
- Increasing weight of 19 lbs from 6 to 15 weeks of gestation
- No longer able to wear regular shows, ambulates with pain in lower limbs, unable to wear rings
- Returns to her endocrinologist who repeats urinalysis and reports worsening proteinuria

CLINICAL CASE FOR DISCUSSION

- Referral to our clinic, to nephrologist
- 24 hour urine done → total protein in 24 hours= 2.64 gram
- No other blood work available.

CLINICAL CASE FOR DISCUSSION

- Physical exam:
  - BP
  - Uncomfortable, wearing flip-flops to accommodate the 3+ lower limb edema.
  - Facial, periorbital, bilateral hand edema. Lower limb edema extending to the T12 level.
  - Normal cardiopulmonary exam
  - Over weight abdomen but no sign of ascites. No hepatosplenomegaly.

CLINICAL CASE FOR DISCUSSION

- Questions are:
  - What are the possible causes of such rapid onset, clinically symptomatic proteinuria in a DM1 patient with no previous documented history of proteinuria?
  - Is this her DM or are we dealing with another process all together?
  - What is the prognosis of this patient with regards to:
    1. Her renal function
    2. her pregnancy
    3. are there any associated fetal outcomes reported in such patients?

TYPES OF PROTEINURIA

- There are three types of abnormal proteinuria:
- 1) glomerular
  - Glomerular disease results in increase filtration of macromolecules, especially Albumin across the golmerular capillary wall.
- 2) tubular
  - Usually due to tubulointerstitial disease which leads to interference with tubular reabsorption of smaller molecular weight proteins. This type of proteinuria is not detected by dipstick.
- 3)overflow
  - Marked overproduction of particular proteins may lead to increased excretion of these proteins (multiple myeloma).

AMOUNT OF PRTEINURIA

- The exact amount of albumin filtered each day by kidneys is controversial.
- Normal rate of albumin excretion is less than 20 mg/day.
- The net normal daily protein excretion is considered to be less than 150mg (usually between 40-80mg).
- Total protein excretion, however, increases to 150-250 mg daily in normal pregnancy.

ABNORMAL PROTEINURIA (NON-PREGNANT)

- Defined as excretion of more than 150 mg of protein per day.
- Early renal disease, however, can be detected by lesser degree of proteinuria (microalbuminuria).
- Microalbuminuria: persistent albumin excretion between 30 -300 mg per day.

PROTEINURIA IN PREGNANCY

- Protein excretion is considered abnormal in pregnant women when it exceeds 300 mg/24 hours.
- Proteinuria is one of the cardinal features of preeclampsia in pregnancy.
- Proteinuria secondary to DM, essential HTN and or primary renal disease may also present during pregnancy.

SCREENING FOR PROTEINURIA IN PREGNANCY

- Screening for proteinuria is essential in detection of preeclampsia in antepartum care of pregnant women.
- Usual approach:
  - Urinay dipstick
    - Negative
    - Trace – between 15 and 30 mg/dL
    - 1+ – between 30 and 100 mg/dL
    - 2+ – between 100 and 300 mg/dL
    - 3+ – between 300 and 1000 mg/dL
    - 4+ – >1000 mg/dL
  -

SCREENING FOR PRTEINURIA IN PREGNANCY

- Presence of 30mg of protein in 100 ml of urine results in a positive reaction (1+) on a urinary dipstick.
- This is not very accurate since the severity of proteinuria is a function of quantity of protein as well as urine volume.

QUANITFYING PROTEINURIA

- Can be in form of either total protein or albumin measurement.
- Methods:
  - 24 hour urine
    - Can be measured for both protein and albumin
    - It has the advantage of estimating GFR
    - Requires good understanding of collection method
    - Can be cumbersome and or incomplete
  - Urine protein/creatinine ratio
    - Random sample which calculates protein or albumin to creatinine ratio

USE OF PRTEIN/CR RATIO FOR IDENTIFICATION OF PROTEINURIA IN PREGNANCY

- When compared to 24 hour urine collection in pregnant women:
  - Spot urine has sensitivity of 83% and specificity of 76% for identifying proteinuria
  - In presence of stable renal function:
    - Protein to creatinine ration of > 0.19 gram of protein/one gram of creatinine predicts protein excretion of more than 300 mg per day (sensitivity of 90% ; specificity of 70%)
    - Protein/creatinine ratio of >0.14 gram of protein to one gram of creatinine has sensitivity of 100% and specificity of 51%.
    - Normal urinary protein/cr ratio in non-pregnant woman is 0.025 gram protein to one gram of creatinine.

- In Canada on a spot urine:
  - Albumin is measured in mg/L
  - Creatinine is measured in mmol/L
  - The ratio is, therefore, in form of mg/mmol
- Normal albumin / creatinine ratio is
  - Males: <2.0 mg/mmol
  - Females: <2.8 mg/mmol

ASSESSMENT OF PROTEINURIA IN PREGNANCY

- Differential diagnosis:
  - Primary renal disease
  - Systemic disease
  - Preeclampsia
- Considerations:
  - Timing:
    - was renal disease known prior to conception
    - If no preexisting conditions, then did proteinuria began before or after 20th week of pregnancy.

Examples of some renal diseases encountered in pregnancy

Glomerular
Primary renal
Minimal change disease
Glomerulonephritis
Membranous nephropathy
Chronic glomerulosclerosis
IgA nephropathy
Interstitial
Interstitial nephritis
Polycystic kidney disease
Systemic
Glomerular
Diabetes mellitus
Systemic lupus erythematosis
Systemic vasculitis
Hypertensive nephrosclerosis
Reflux nephritis
Obstruction
Congenital anomalies
Multiple myeloma
Infection (eg, HIV, hepatitis B/C)

UpToDate

WORKUP OF PRTEINURIA

- CBC, smear, coagulation profile, Fibrinogen,ferritin, iron panel, SPEP,
- SMA-10,albumin, LDH, LFTs
- 24 hr urine, urinalysis, urine microscopy, UPEP
- TSH, fasting lipids, fasting glucose, HgA1c
- ESR, CRP, ANA, ENA, C3, C4, IgA,G,M, RF, anti-PR3, anti-MPO
- Imaging: Ultrasound of the kidneys

MORE CONTROVERSIAL WORKUP

- Despite extensive workup, often a clear picture or a definite diagnosis can not be achieved in absence of a renal biopsy.
- Is there evidence that maternal renal disease is associated with poor outcome and if so, could renal biopsy play a role in improving such an outcome?
- What is the evidence for renal biopsy in patients who present with renal disease in early pregnancy?

KIDNEY DISEASE IS AN INDEPENDENT RISK FACTOR FOR ADVERSE FETAL AND MATERNAL OUTCOMES IN PREGNANCY

FISCHER ET AL., AM J KIDNEY DIS 2004; 43: 415

- Goal: better describe the population of women with kidney disease and provide an assessment of their risk for adverse events caused by kidney disease after adjustment for other contributing factors.
- *Methods:* Colorado birth and death certificate data for 1989 to 2001. Of 747,368 births during this period, 911 births from women with kidney disease were identified, and 4,606 births from women without kidney disease were randomly selected for comparison.
- Adverse fetal outcomes: fetal prematurity, low birth weight, or neonatal death
- Adverse maternal outcomes: preeclampsia, eclampsia, or abruptio placenta.

TABLE 2. ADVERSE FETAL AND MATERNAL OUTCOMES IN WOMEN WITH AND WITHOUT KIDNEY DISEASE, COLORADO, 1989 TO 2001

Outcome	Kidney Disease (n = 911)	No Kidney Disease (n = 4,606)	*P*
Adverse fetal outcomes	166 (18.22)	438 (9.51)	< 0.001
Adverse maternal outcomes	125 (13.72)	197 (4.28)	< 0.001

TABLE 3. FACTORS ASSOCIATED WITH ADVERSE FETAL OUTCOMES, COLORADO, 1989 TO 2001

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Kidney disease	2.12 (1.74–2.58)	1.76 (1.40–2.21)
Preeclampsia	4.07 (3.09–5.37)	3.68 (2.71–5.00)
Eclampsia	6.33 (3.28–12.22)	4.44 (2.12–9.29)
Abruptio placenta	13.23 (6.73–25.99)	11.92 (5.53–25.70)
Chronic hypertension	5.34 (3.33–8.56)	3.83 (2.18–6.73)
Attending clinician		
Physician	1.00∗	1.00∗
Midwife	0.56 (0.39–0.81)	0.56 (0.37–0.84)
Prenatal care		
Intensive	0.89 (0.67–1.19)	0.66 (0.48–0.91)
Adequate	1.00∗	1.00∗
Inadequate	1.14 (0.93–1.38)	0.98 (0.79–1.22)
Marital status		
Married	1.00∗	1.00∗
Unmarried	1.54 (1.28–1.84)	1.28 (1.03–1.58)
Cigarette use	1.71 (1.38–2.12)	1.64 (1.29–2.10)
Race		
White	1.00∗	1.00∗
Black	1.75 (1.27–2.42)	1.58 (1.09–2.28)
Asian	0.71 (0.39–1.30)	0.79 (0.42–1.52)

TABLE 4. FACTORS ASSOCIATED WITH ADVERSE MATERNAL OUTCOMES, COLORADO, 1989 TO 2001

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Kidney disease	3.55 (2.81–4.51)	∗
Diabetes	3.68 (2.37–5.72)	2.48 (1.53–4.02)
Attending clinician		
Physician	1.00†	1.00†
Midwife	0.57 (0.34–0.93)	0.46 (0.28–0.78)
Prenatal care		
Intensive	1.89 (1.40–2.54)	1.51 (1.10–2.06)
Adequate	1.00†	1.00†
Inadequate	0.85 (0.64–1.14)	0.90 (0.67–1.20)
Parity		
Nulliparous	1.93 (1.54–2.42)	∗
Multiparous	1.00†	∗
Hispanic ethnicity		
Yes	0.74 (0.54–1.01)	0.66 (0.47–0.92)
No	1.00†	1.00†
Birth year		
1988–1991	0.82 (0.62–1.01)	∗
1992–1998	0.79 (0.61–1.04)	∗
1999–2001	1.00†	∗

THE ROLE OF RENAL BIOPSY IN WOMEN WITH KIDNEY DISEASE IDENTIFIED IN PREGNANCY

DAY ET AL., NEPHROL DIAL TRANSPLANT (2008) 23: 201-206

- In some situations, it may be important to know the exact aetiology of the renal disorder in order that immediate disease-modifying treatment can be commenced to enable the pregnancy to reach viability.
- However, in other circumstances, such as the detection of non-nephrotic range proteinuria in the absence of features of a systemic disease process, definitive diagnosis of renal disease can be delayed until post-partum.

- Renal biopsy has been performed during pregnancy since its introduction in the 1960s.
- Initial series showed a high incidence of complications but subsequent reports indicate a complication rate similar to non-pregnant women.
- Although it has been established that there is no greater risk of complications of renal biopsy in pregnancy, the consequences to the mother and fetus of post-biopsy haemorrhage could be severe.
- There is no standard of practice.

- 20 women presenting with renal disease of a severity to warrant renal biopsy during pregnancy were compared to 75 women who had an initial presentation of renal disease in pregnancy and underwent post-partum renal biopsy.

- Twenty women underwent renal biopsy during pregnancy during 1983–2004.
- Median age at biopsy was 28 years (range 17–39)
- median gestation at biopsy was 20.5 weeks.

INDICATION FOR BIOPSY

- Four patients had a previous diagnosis of lupus nephritis with a deterioration of renal parameters during pregnancy,
- four presented for the first time with proteinuria and positive autoimmune serology during pregnancy,
- four presented with first onset of nephrotic syndrome,
- three were biopsied in the first trimester with proteinuria and impaired renal function to assess degree of renal damage
- five were biopsied in the second trimester with worsening proteinuria and hypertension.

OBSTETRIC OUTCOME

- Pre-eclampsia in this cohort was common and occurred in 7/20.
- Median gestation at delivery was 34 weeks (range 25–40 weeks)
- nine of the women were delivered by Caesarian section.
- There were two intra-uterine deaths
- one still-birth
- one neonatal death (born at 25 weeks gestation)

COMPLICATIONS OF BIOPSY

- One patient had minor post-biopsy haematuria which settled spontaneously.
- Nine of the 20 patients had an immediate change in therapy (mainly the initiation or increase in dose of immunosuppressive medication) as a consequence of knowledge of renal histology.

FOLLOW-UP OF WOMEN WHO UNDERWENT RENAL BIOPSY IN PREGNANCY

- Median time of follow-up was 103.3 months (2.5–256).
- At last follow-up, nine (45%) had a GFR of <60 ml/min/1.73 m^2 and of these six (30%) had reached end-stage renal failure (ESRF)
- Three (15%) of the women had died
- Of the 14 patients not reaching ESRF, 11 are on hypertensive medication with the remaining 3 having blood pressure measurements of less than 130/80

POST-PREGNANCY BIOPSIES

- Seventy-five women underwent renal biopsy following pregnancy with abnormal renal parameters diagnosed either during pregnancy or immediately post-partum.
- Median age at biopsy was 31 years (15–55).
- Only those with acute renal failure were biopsied immediately post-partum.
- In those with persistent proteinuria renal biopsy was generally delayed at least 6 months.

INDICATIONS FOR BIOPSY

- Median creatinine at biopsy was 86 µmol/l (57–896) with a median estimated GFR (MDRD) of 70.5 ml/min/1.73 m^2 (5–122).
- Ten women (13%) had an eGFR of >90
- 37 (49%) an eGFR 60–89
- 11 (15%) an eGFR of 30–59
- 5 (7%) an eGFR of 15–29
- 4 women had an eGFR of <15
- Data was missing on 8 (10% of women).
- Fifteen women (20%) had albumin excretion of <0.3 g/24 h,
- 27 (36%) 0.3–2 g/24 h
- 13 (17%) more than 2 g/24 h
- Data was unavailable on 20 (26%).

CLINICAL PRESENTATION

- Fifty (83%) of the women presented with proteinuria in pregnancy
- In 23 cases this was associated with superimposed pre-eclampsia with proteinuria persisting for several months post-partum
- Twenty-seven women presented with newly diagnosed proteinuria in the absence of pre-eclampsia
- Six women presented with nephrotic syndrome
- six with newly diagnosed renal impairment
- four with isolated haematuria
- three with acute renal failure.

FOLLOW-UP

- Follow-up data is available on 47 patients with a median duration of 51.5 months (range 1–212).
- These are generally the patients with more severe disease at presentation, as those with minor abnormalities had been discharged to primary care follow-up.
- In total seven women had reached ESRF requiring renal replacement therapy.

OUTCOME BY CATEGORY

- thin glomerular basement membrane disease and normal renal biopsies: good renal outcome at follow-up.
- The diagnosis of pre-eclampsia made no difference to the CKD category at follow-up in those with proteinuria persisting following pregnancy with 40% of both reaching CKD 3-5.

OUTCOME BY CATEGORY

- The worst outcome occurs in those with:
  - interstitial non-glomerular disease with four of five being classified as CKD 3-5.
  - Those reaching ESRF had diagnoses of
    - acute cortical necrosis following ante-partum haemorrhage and
    - intra-uterine death,
    - late tubulo-interstitial damage,
    - late FSGS,
    - renal tuberculosis,
    - sickle cell nephropathy,
    - glomerular dense deposit disease
    - lupus nephritis.

DISCUSSION

- Previous recommendations suggest performing renal biopsy only when there is a sudden deterioration of renal function before 32 weeks with no obvious cause or in the case of symptomatic nephrotic syndrome before 32 weeks, there remains a substantial variation in clinical practice.

DISCUSSION

- The occurrence of ESRF in 6 of the 20 biopsied during pregnancy but only 6 of the 75 biopsied post-partum reflects the severity of the renal disease biopsied during pregnancy.
- with the severity of the renal disease there was a high incidence of obstetric complications in the women requiring a renal biopsy whilst pregnant.

DISCUSSION

- renal biopsy is not indicated in all pregnant women presenting with renal disease.
- recommend performing biopsies only in highly selected women before 28 weeks gestation in the presence of sterile urine and kidneys >10 cm in size where pre-biopsy coagulopathy or thrombocytopaenia has been excluded or reversed and blood pressure well controlled.
- The primary renal presentation should be such that knowledge of renal histology may be likely to lead to an immediate therapeutic intervention that would enable the pregnancy to progress to fetal viability.

DISCUSSION IN THE FIRST TRIMESTER

- consider performing a renal biopsy in those with:
  - structurally normal kidneys
  - an active urinary sediment
  - nephrotic syndrome
  - unexplained CKD (with proteinuria and no evidence of scarring)
  - those with evidence of renal impairment and proteinuria in the context of systemic disease or positive autoimmune serology
- diagnosis at this stage of pregnancy is of benefit to guide treatment and allow an informed discussion of the risks:benefit ratio of continuation of pregnancy.

DISCUSSION IN THE SECOND TRIMESTER

- pre-eclampsia and any physiological rise in proteinuria should be first excluded
- Renal biopsy should be reserved for those with:
  - unexplained nephrotic range proteinuria,
  - progressive CKD and renal disease in the presence of active systemic disease.
- If these criteria are not met then suggest performing a renal biopsy post-partum if indications remain.
- suggest that after 28 weeks of pregnancy, when fetal viability is good, delivery should be induced if felt to be clinically necessary and biopsy performed post-partum.

RENAL BIOPSY IN PREGNANCIES COMPLICATED BY UNDETERMINED RENAL DISEASE.

CHEN ET AL.,ACTA OBSTETRICIA ET GYNECOLOGICA SCANDINAVICA (2001) 80:888

- 15 pregnant women from Taiwan biopsied over 10 years between 1990 and 1999 with a median follow-up only of 2 years.

CLINICAL PRESENTATION

- Twelve had nephrotic syndrome
- three significant renal impairment
- All underwent ultrasound guided biopsy between 20 and 25 weeks of gestation

BIOPSY OUTCOMES

- Eight were diagnosed with lupus nephritis
- three with chronic glomerulonephritis
- two had mesangial proliferative GN
- one endocapillary GN
- one diabetic nephropathy

MATERNAL AND FETAL OUTCOMES

- one stillbirth
- five children were small for gestational age
- After 2 years' follow-up three of the women had died and another two reached ESRF.

A CASE OF "PURE" PREECLAMPSIA WITH NEPHROTIC SYNDROME BEFORE 15 WEEKS OF GESTATION IN A PATIENT WHOSE RENAL BIOPSY SHOWED GLOMERULAR CAPILLARY ENDOTHELIOSIS

IMASAWA ET AL., AMERICAN JOURNAL OF KIDNEY DISEASES VOLUME 48, ISSUE 3, SEPTEMBER 2006, PAGES 495-501

- A 35-year-old Japanese woman primigravida, previously healthy.
- Health checkup at 11 weeks of gestation showed normal blood pressure and urinalysis results without serological abnormalities.
- Echography showed a twin placenta
- Her first subjective symptom was edema of the legs and hands at 14 weeks of gestation
- The health checkup at 15 weeks of gestation showed the patient had severe hypertension (blood pressure, 174/116 mm Hg) and proteinuria (4^{+}) on dipstick urinalysis

LABORATORY DATA

- nephrotic syndrome with proteinuria of 16 g/d
- decreased total serum albumin 24 g/L
- increased total cholesterol level 8.59 mmol/L

- Biopsy was performed
- Results indicated that the patient's glomerular damage was caused by the mechanisms of preeclampsia without complication with glomerulonephritis.

- clinical manifestation and result of the renal biopsy __ preeclampsia
- patient underwent an elective abortion at 18 weeks of gestation
- The delivered fetuses were both females without gross congenital abnormalities.
- In addition, pathological findings of the delivered placentas showed increased syncytial knots around infarcted lesions and deposition of fibrin right under the chorionic plate, which suggested the presence of ischemia.

OUTCOME

- Three weeks after the medical termination, the patient's blood pressure
- proteinuria decreased to 1.3 g/d of protein
- Subsequently, proteinuria on dipstick urinalysis was 2^+ after 2 months and became negative by 3 months after the abortion.
- Clinical abnormalities had completely vanished within 3 months after the elective abortion.

OTHER LITERATURES FINDINGS:

- **Diabetic glomerulosclerosis with nephrotic syndrome in early pregnancy.**
  Furukawa et al., Nippon Jinzo Gakkai Shi. 1987 May;29(5):541-5.
- **Steroid-responsive nephrotic syndrome with renal insufficiency in the first trimester of pregnancy.**
  Uribe et al., Am J Obstet Gynecol. 1991 Feb;164(2):568-9.
- **Rapid development of nephrotic syndrome, hypertension, and hemolytic anemia early in pregnancy in patients with IDDM.**
  Weinstock et al., Diabetes Care. 1988 May;11(5):416-21.

BACK TO THE CASE
POSITIVE FINDINGS ON INVESTIGATION:

- 24 hr urine
  - **albumin1703 mg**
  - **Kappa 0.217 gram**
  - **Total protein 2.64 gram**
  - Crcl 2.2 ml per sec.
- Urine microscopy:
  - RBC 20-50
  - Leukocytes 20-50
  - Bacterial 3+
  - Hyaline cast more than 10
  - Epithelial squamous cells: loaded
- Cr 71
- Triglyceride 2.3
- Albumin 28, normal Calcium

BACK TO THE CASE
POSITIVE FINDINGS ON INVESTIGATION:

- Hgb 88
- MCV 90
- Plt 208
- IgA, G, M → N
- CRP 16
- ESR 120
- Autoimmune workup negative
- SPEP, UPEP, B2 microglobulin pending

BACK TO THE CASE

- 30 year old type I diabetic female, G1P0A0 at 15 weeks gestation, presenting with progressive and symptomatic edema, proteinuria of 2.64, associated with Kappa light chains, normocytic anemia, hypoalbuminemia, ↑ TG, elevated ESR, CRP but normal C3, C4 and autoimmune workup. No previously documented history of significant proteinuria or DM nephropathy.

BACK TO THE CASE

- Prior to discovery of kappa light chains:
- DDx
  - DM nephropathy
  - Primary renal disease
    - Minimal change
    - Nephrotic glomerulonephritis
  - Systemic disease
    - Rule out autoimmune such as lupus
  - Preeclampsia
    - Unlikely given presentation at 6-8 weeks gestation

BACK TO THE CASE

- In presence of proteinuria with light chains:
- Need SPEP and UPEP results
- DDx:
  - Primary amyloidosis
  - Light chain deposition disease
  - Multiple myeloma
  - Lymphoma
  - Waldenstrom's macroglobulinemia

BACK TO THE CASE

- Awaiting SPEP and UPEP results.
- Nephrology and hematology consultation
- Repeat 24 hour urine at 17 weeks to reassess proteinuria and progression of disease.
- Amniocenthesis as per patient Normal, therefore no indication of chromosomal abnormality.
- Currently patient on diuretic for symptom control with good effect
- Discussed case with nephrologist. Given current history unlikely that she will get a kidney biopsy at this point in time.

Thank you

MINIMAL CHANGE DISEASE

- Major cause of nephrotic syndrome in both children and adults
- Sudden onset of the signs and symptoms of the nephrotic syndrome, often following an upper respiratory or systemic infection.
- Nephrotic syndrome is characterized by the constellation of edema, proteinuria (usually greater than 3 g/day), hypoalbuminemia, and hyperlipidemia.
- With MCD, the explosive onset of proteinuria is in sharp contrast to some other glomerular disease, in which proteinuria increases gradually.
- Microscopic hematuria is common in adults with MCD.
- The plasma creatinine concentration is usually normal, but in adults is often slightly elevated at presentation.

GLOMERULONEPHRITIS

- There are many causes of glomerular disease.
- The patient's age and the characteristics of the urine sediment usually allow the differential diagnosis to be narrowed prior to renal biopsy.
- In general, three different urinary patterns may be seen:
  - focal nephritic
  - diffuse nephritic
  - nephrotic

GLOMERULONEPHRITIS

- Focal glomerulonephritis
  - Associated with inflammatory lesions in less than one-half of glomeruli on light microscopy.
  - The urinalysis reveals dysmorphicred cells, occasionally red cell casts, and mild proteinuria (usually less than 1.5 g/day).
  - The findings of more severe disease are usually absent, including nephrotic range proteinuria, edema, hypertension, and renal insufficiency.
  - These patients often present with asymptomatic hematuria and proteinuria discovered on routine examination or, in IgA nephropathy for example, with episodes of gross hematuria.

GLOMERULONEPHRITIS

- Diffuse glomerulonephritis
  - affects most or all of the glomeruli
  - urinalysis is similar to focal disease, but heavy proteinuria (which may be in the nephrotic range), edema, hypertension, and/or renal insufficiency may be seen.

GLOMERULONEPHRITIS

- Nephrotic glomerulonephritis
  - urinary sediment is associated with heavy proteinuria and lipiduria, but few cells or casts
  - Patients who also have edema and hyperlipidemia
  - The relatively bland sediment in the nephrotic disorders results from the lack of inflammatory cell infiltration in the glomeruli.
  - This finding is in large part due to the absence of immune complex deposition in most of these disorders, such as minimal change disease, diabetic nephropathy, and amyloidosis.