Managing the Stages of CKD

A case of diabetic kidney disease

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Learning Objectives

- Identify progressive CKD including etiology
- Factors that slow progression
- Dietary considerations for advanced CKD
- Preparation for options after kidney failure

 Mr. CK Davis is a 58 yo gentleman with a past medical history significant for type 2 diabetes mellitus (diagnosed about 17 years ago), hypertension, coronary artery disease, (status post coronary artery bypass grafting), and chronic kidney disease who is here for evaluation of his reduced kidney function and proteinuria.

- He has no history of blood in the urine, allergic reactions to antibiotics, lead exposure, lupus or other autoimmune disease, acute kidney injury, or need for dialysis. He does have arthritis, requiring the use of NSAIDS.
- No ETOH consumption
- Smoking 40-year pack history

- His blood pressure usually ranges in the 140s over 80s at home. He does admit a sense of increased lower leg swelling over the past few weeks.
- He does have a history of blurry vision although no known history of diabetic retinopathy, and he does see an ophthalmologist yearly.

- Insulin
- Metoprolol 25mg bid
- HCTZ 25mg daily
- Aspirin 81mg
- Simvastatin 10mg
- Ibuprofen prn
- Pertinent exam findings:
- BP 160/90
- +1 pedal edema bilateral

CASE PRESENTATION 5

Renal Function Panel		Stage: Fina	al
Test	Result	Units	Flag Reference Range
Glucose	146	mg/dL	H 74-99
Urea Nitrogen, Blood	31	mg/dL	H 7-21
Creatinine	2.14	mg/dL	H 0.80-1.30
Un/crea Ratio	14	-	12-20
Sodium Level	140	mmol/L	136-145
Potassium Level	3.9	mmol/L	3.7-4.8
Chloride	107	mmol/L	101-108
C02	23	mmol/L	22-29
Anion Gap	10	mmol/L	6-16
Total Calcium	8.8	mg/dL	L 8.9-10.2
Phosphorus	4.1	mg/dL	2.5-4.5
Albumin	2.7	g/dL	L 3.3-4.6
eGFR	32	SEE NOTE	L >60
eGFR, if Afr/am	39	SEE NOTE	L >60
(NOTE)			

eGFR = estimated GFR; eGFR units = mL/min/1.73 sq meters Chronic Kidney Disease is considered if eGFR <60 mL/min/1.73 sq meters Kidney failure is considered if eGFR is <15 mL/min/1.73 sq meters. eGFR assumes steady state plasma creatinine concentration; not applicable if renal function is rapidly changing or patient is on dialysis.



UA with Reflex Microscopic		Stage:	Final	
<u>Test</u> Urine Color	<u>Result</u> COLORLESS	<u>Units</u>	Ela	g Reference Range
Urine Clarity Urine Spec Grav	CLEAR 1.008			1.001-1.030
Urine Ph	6.0			5.0-6.5
Urine Protein		mg/dL	Н	<15
Urine Glucose Urine Ketone	NEGATIVE	mg/dL mg/dL		NEG
Drine Blood	NEGATIVE	ng an		NEG
Urine Bilirubin	NEGATIVE			NEG
Urine Urobilinogen	<2.0	mg/dL		<2.0
Urine Nifrite	NEGATIVE			NEG
Urine Leuk Esterase	NEGATIVE			NEG

CASE PRESENTATION 7

- URINE PROTEIN / CREATININE
 - 10.7

- URINE ALBUMIN / CREATININE
 - 9409

IMPORTANCE OF ALBUMINURIA

- REFLECTS KIDNEY DISEASE SPECTRUM (MILD TO SEVERE)
- INCREASED RISK OF CV DISEASE

- INCREASED RISK OF MORTALITY
- INCREASED RISK OF PROGRESSION OF CKD

AT THIS TIME, THERE ARE A FEW OPTIONS, <u>PICK</u> <u>A CHOICE</u>, THEN LET'S DISCUSS EACH

- A. NO CHANGE IN MEDICATIONS
- B. TRIAL OF PREDNISONE FOR SUSPECTED MINIMAL CHANGE DISEASE
- C. HOLD OFF FURTHER WORKUP UNTIL DIABETES IS BETTER CONTROLLED
- D. SEND SEROLOGIC WORKUP FOR SUSPECTED GLOMERULONEPHRITIS, INCLUDING ANCA TITERS AND ANTI-GBM
- E. PERFORM A RENAL BIOPSY

A. PERFORM A RENAL BIOPSY:

A REASONABLE CHOICE TO MAKE SURE OF THE DIAGNOSIS, PARTICULARLY IF NO PAST LAB VALUES AND LACK OF RETINOPATHY IS CONFIRMED

Diabetic Nephropathy Nodular Glomerulosclerosis "Kimmelstiel-Wilson Nodules"



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H&E stain

PAS stain

Interventions that delay progression

- Proper diagnosis of the etiology
- Blood sugar control
- BP control
 - Angiotensin inhibition
- Weight and Lipid control

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United Kingdom Prospective Diabetes Study

- Intensive glucose policy A1c 7.0% vs 7.9% reduces risk
 - Any diabetes related endpoint 12% p 0.030
 - Microvascular endpoint 25% p 0.010
 - Myocardial infarction 16% p 0.052
- Tight blood pressure 144/82 vs. 154/87
 - Any diabetes related endpoint 24% p 0.005
 - Microvascular endpoint 37% p 0.009
 - Stroke 44% p 0.013

Approach to pharmacologic therapy for hyperglycemia in DM2 and CKD

- Metformin common first line
 - Avoid in eGFR <30 due to risk of lactic acidosis (not nephrotoxic)
- SGLT2 inhibitors weak glucose lowering impact
 - Safe to initiate in eGFR as low as 20
- CKD4
 - GLP-1
 - Glipizide / Repaglinide / Linagliptin dose adjusted are alternatives
- Insulin / CGM

Sodium glucose co-transporter 2 inhibitors

- Blocks proximal tubule reabsorption of glucose, significant glycosuria but minimal effects on blood glucose
- Blocks sodium reabsorption and subsequent natriuresis increases sodium delivery to macula densa and reduces tubuloglomerular feedback > Afferent constriction > Reduced intraglomerular pressure
- CREDENCE canagliflozin
 - Reduced ESKD and heart failure
- DAPA-CKD dapagliflozin
 - Reduced ESKD and mortality
 - Similar effects in non-diabetic patients with proteinuria

Sodium glucose co-transporter 2 inhibitors

- Target patients with eGFR >20
- Recommendation is strongest for patients with severely increased albuminuria
- Risks:
 - Known eGFR dip (5ml/min expected, >30% associated with potassium)
 - Genital infections; candida, Fournier's gangrene
 - Euglycemic diabetic ketoacidosis

GLP-1 receptor agonists

- Weight loss, improved glucose, dyslipidemia, and blood pressure
- FLOW trial
 - Kidney and Cardiovascular protection in CKD/DM2
- SELECT trial
 - Kidney protection in CKD without DM
- Patient education for dehydration signs (nausea / satiety)

Nonsteroidal mineralocorticoid receptor antagonists (Finerenone)

- Reduces progression of CKD and cardiovascular events in patients with DM2
 - No substantial blood pressure impact
 - Slight increase in potassium (caution with K > 5)
- Target patients with albuminuria >30 after ACE/ARB and SGLT2i

Interventions the delay progression

- Proper diagnosis of the etiology
- Blood sugar control
- BP control
 - Angiotensin inhibition
- Weight and Lipid control

Blood Pressure control

- Goal below 130/80
 - Reduced mortality and CV morbidity
 - Reduces progression in urinary albumin ratio >300
- ACE or ARB titrated to maximally tolerated dose
 - Combination therapy often needed (avoid ACE + ARB)

Interventions that delay progression

- Proper diagnosis of the etiology
- Blood sugar control
- BP control
 - Angiotensin inhibition
- Weight and Lipid control

Weight reduction and Lipids

- N=30 (14 with DM2)
- BMI ~27 kg/m2
- 5 months, 4% weight loss in diet group
- 31% decrease IN PROTEINURIA
- Lipid management
 - Consensus mixed, all patients eGFR <60 versus calculated risk assessment criteria
 - Atorvastatin / Fluvastatin / Pravastatin

- Insulin
- Metoprolol 25mg bid
- HCTZ 25mg daily
- Aspirin 81mg
- Simvastatin 10mg
- Lisinopril 40mg bid

Pertinent exam findings:

- BP 130/90
- +2 edema bilateral
- Crackles on lung exam

Comprehensive Metabolic Panel

			-	
Test	Result	Units	Fla	ng Reference Range
Glacose	119	me/dl	н	74-99
Urea Nitrogen, Blood	42	mg/dL	н	8.23
Creatinine	2.86	me/dL	н	0.80-1.30
Un/crea Ratio	15	ng ac		12.20
Sodium Level	140	mmol/L		136-145
Potossium Level	60	mmol/L	н	37.48
Result not affected by current level of	hemolysis	nanos is		3.)-1.0
Read Back completed	Territoryala			
Chloride	110	mmol/I	н	101-108
CO2	19	mmol/L	ï	22.29
Anion Gan	11	mmol/L	L	5.11
Total Calcium	80	ma/dl		8 9.10 2
Aspartate Aminotransferace	14	11/1	1.1	10.48
Alanina Aminotransferare	14	0/12	1	13-40
Altahine Ahnhouransterase	0	U/L	L	40.115
Aikaline Phosphaiase	114			40-115
Total Billruoin	0.1	mg/aL	L	6.2-1.1
1 otal Protein	7.1 di bishasia ambulatan astisa	g/dL		0.3-7.9
Reference range is as much as 0.5 g/	dL nigher in ambulatory patien	IS.		
Albumin	3.3	g/dL		3.3-4.6
eGFR	23	SEE NOTE	L	>60
eGFR, if Afr/am	27	SEE NOTE	L	>60
(NOTE)				

Final

Stage:

• EKG revealed normal sinus rhythm, no peaked T waves or widening of QRS

At this time, there are a few options, **pick a choice**, then let's discuss each

- Continue Lisinopril to maintain good BP control and slow disease progression
- Admit for emergent dialysis
- Establish peripheral IV and give 2 liters of normal saline
- No changes, recheck in one month
- Reduce Lisinopril, provide low potassium diet education, and recheck K in 2 days

- Reduce Lisinopril, provide low potassium diet education, and recheck K in 2 days:
- Correct! This is very reasonable choice.

High potassium foods

- Fruit
 - Bananas, oranges, melons
- Vegetables
 - Potatoes, tomatoes, beans
- Others
 - Milk, chocolate, salt substitutes

- Insulin
- Metoprolol 25mg bid
- Furosemide 40mg daily
- Lisinopril 20mg bid
- Amlodipine 10mg
- Pertinent exam findings:
- 145/95
- +3 edema bilateral

Subjective:

- Low Energy

- Sleeps in recliner now, easier to rest/breath

- Activity limited due to feeling short of air

Renal Function Panel		Stage: Fi	nal	
Test	Result	Units	Fla	g Reference Range
Glucose	168	mg/dL	н	74-99
Urea Nitrogen, Blood	85	mg/dL	н	7-21
Creatinine	4.41	mg/dL	н·	0.80-1.30
Un/crea Ratio	19			8-20
Sodium Level	140	mmol/L		136-145
Potassium Level	3.8	mmol/L		3.7-4.8
Chloride	103	mmol/L		101-108
C02	23	mmol/L		22-29
Anion Gap	14	mmol/L		6-16
Total Calcium	8.5	mg/dL	L	8.9-10.2
Phosphorus	4.2	mg/dL		2.5-4.5
Albumin	2.7	g/dL	L	3.3-4.6
¢GFR	14	SEE NOTE	L	>60
eGFR, if Afr/am (NOTE)	17	SEE NOTE	L	>60

eGFR = estimated GFR; eGFR units = mL/min/1.73 sq meters Chronic Kidney Disease is considered if eGFR <60 mL/min/1.73 sq meters Kidney failure is considered if eGFR is <15 mL/min/1.73 sq meters. eGFR assumes steady state plasma creatinine concentration; not applicable if renal function is rapidly changing or patient is on dialysis.

Hemogram		Stage:	Final
			1
Test	Result	Units	Flag Reference Range
WBC Count	8.4	k/uL	3.7-10.3
RBC	3.20	M/uL	L 4.6-6.1
Hemoglobin	9.2	g/dL	L 13.7-17.5
Hematocrit	28.4	%	L 40-51
Platelet Count	155	k/uL	155-369
MCV	89	fL	79-98
MCH	28.8	pg	26-32
MCHC	32,4	g/dL	30.7-35.5
RDW	13.0	%	11.5-14,5
MPV	10.6	fL	8,8-12.5
NRBC Count	0	%	0

At this time, there are a few options, **pick a choice**, then let's discuss each

- Admit for urgent red blood cell transfusion
- Add angiotensin receptor blocker to ACE inhibitor
- Stop diuretics given decline in kidney function
- Refer for education regarding dialysis modalities

- Refer for education regarding dialysis modalities:
- It is very appropriate now that his clearance is <20 ml/min and he is predictably progressing.

Anemia in ckd management

- Erythropoietin stimulating agents
 - First, Rule out causes of anemia common in general population
 - Target hemoglobin > 10
 - Ensure stable iron stores
 - Caution in patients with history of malignancy/stroke

- Insulin
- Metoprolol 25mg bid
- Furosemide 80mg daily
- Lisinopril 20mg bid
- Amlodipine 10mg
- Epogen injections
- Aspirin 81mg
- Simvastatin 10mg

• Pertinent exam findings:

- BP 140/80
- +1 edema bilateral

Subjective:

- Appetite poor
- Sour taste
- ++Fatigue
- Gaining fluid weight
- Dyspnea with minimal activity

Comprehensive Metabolic Panel		Stage: Fin:	al	
Test	Result	Unite	Fla	o Deference Dance
Gheore	202	<u>toinia</u>	110	24.00
Chuckse Blood	303	mg/dL	H	/4-99
Creatining	0.53	ing/dL	- 11	8-23
Creatinine Defense Basia	9.33	mg/dL	н	0.80-1.50
Concernance Read	8			8-20
Sodium Level	134	mmol/L	L	136-145
Potassium Level	6.1	mmoi/L	н	3.7-4.8
Chloride	92	mmol/L	L	101-108
CO2	21	mmol/L	L	22-29
Anion Gap	21	mmol/L	н	6-16
Total Calcium	8.5	mg/dL	L	8.9-10.2
Aspartate Aminotransferase	11	UĽ	L	19-48
Alanine Aminotransferase	7	U/L	L	11-41
Alkaline Phosphatase	106	U/L		40-115
Total Bilirubin	0.7	me/dl.		0.2-1.1
Total Protein	8.0	e/dL	н	63.79
Albumin	3.6	aidi		33.46
eGFR	6	SEE MOTE	5	5.5.4.0
eGER if a diam		SEE NOTE	L.	200
active and an		SEE NOTE	L	>60

(NOTE)

CKD Education

- Patient options with progression of CKD:
- In-center Hemodialysis
- Home dialysis Peritoneal and Hemodialysis
- Transplant
- Conservative care

HD vs PD Overall Mortality

- Five-year survival
 - HD 33.5% and PD 33.9%
- PD is associated with better survival during the first 1-2 years of dialysis
- HD is associated with better survival thereafter
- Choosing the right patient for the right modality has been shown to have a great impact not only on health-related outcomes but on quality of life

When to consider conservative kidney management?

- In patients unlikely to gain survival
 - End-stage heart failure
 - End-stage liver failure
 - Frail with significant functional or cognitive impairment
 - Long-term care facilities
- Factors associated with a poorer prognosis
 - Advanced age, male gender, decreased serum albumin, malnutrition, impaired functional status, diabetes mellitus, and coronary heart disease.

Conservative kidney management

- Survival with CKD5 can be significant with a slow rate of GFR loss
- Hemodialysis can hasten loss of residual kidney function
 - Even small residual function improves quality / survival
- <u>Time-limited trial</u> of dialysis can be used
 - It will give the patient and family a better understanding of what life on dialysis entails
 - It allows time for further discussion between all parties
 - Palliative dialysis



•Thank you!