CLINICAL MEET - DEPT OF NEPHROLOGY

OXALATE NEPHROPATHY WITH PROGRESSION TO END STAGE RENAL DISEASE

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- A 30 yr old gentleman, a farmer by occupation presented to the OPD with complaints of

1. diarrhoea since 2 years,
2. weight loss (upto 12 kgs in 1 year)
3. increased episodes of loose stools since 1 month
4. nausea and vomiting since 1 month
5. decreased urine output since 1 month

- No history of
- Fever
- urinary tract symptoms
- renal calculus
- long term NSAID use or parallel therapy

-Few months prior to admission,

patient had started a diet regimen containing **spinach and lemon grass in excess quantities twice a day** , which he consumed for a month.

-He is a k/c/o Diabetes Mellitus since 1 year

-no other comorbidities.

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Clinical examination

- Conscious ,co-operative, oriented to time place person
- Wt – 54 kg (loss of 12 kg in 1 year)
- BMI-17.6 kg/m^2
- signs of dehydration (tongue-dry, loss of skin turgor)
- pulse-108 beats/min, regular
- a blood pressure of 92/60 mmHg.
- Peripheral pulses- feeble
- **S/E** –
- CVS-S1S2 RS- AEBE PA-soft CNS- Pt conscious oriented

Investigations

- Hb 9.1g/dl
- WBC 6.9 × 103/µl
- Plt-1.66 lacs
- blood urea- 192 mg/dl
- serum creatinine-11.66 mg/dl
- (sr creat – 2.8 mg/dl 2 months ago)
- serum Na 146 mmol/l
- serum K 3.8
- Chloride 98mmol/l
- corrected calcium 7.8
- Phosphorus 5.7

- SGOT/SGPT- 20/19u/l
- ALP-188 u/l
- serum albumin-3.2
- serum globulin-3.1
- ph 7.28
- hco3 11.9
- pco2 31
- pO2 46

- serum Amylase -90 u/l
- sr lipase-110 u/l,

- Urinalysis –
  - ph-6.84 ,
  - proteinuria 1+ ,
  - hyaline casts , no RBCs

- Ultrasound of the abdomen pelvis –

  - right kidney of 8.5*4.3 cm (raised Echogenicity and CMD poorly maintained)

  - left kidney of 8.7*4.7 cm (raised Echogenicity and CMD poorly maintained)

  - No evidence of calcifications / renal calculi

AUTOIMMUNE PROFILE

- C3-101 mg/dl
- C4- 37mg/dl,
- c-ANCA- negative
- p-ANCA-negative
- Anti-GBM-negative,
- ANA by IF – negative
- ANA Blot-negative) and
- serum protein electrophoresis – normal
- free light chain assay - normal.

To Summarize

- **Male in his 30s**
- **Type 2 Diabetes Mellitus**
- **Progressing Renal Failure**
- **Negative autoimmune workup**
- **Features of Malabsorption syndrome**

Renal Biopsy

- **Light Microscopy** –

- Glomerulus: 12 glomeruli seen. 50% of glomeruli were sclerosed.

- The tubulo-interstitial compartment:

-foci of tubular damage ,deposition of **translucent crystals of different shapes.** predominantly intra-luminal with few intracellular and focal interstitial .

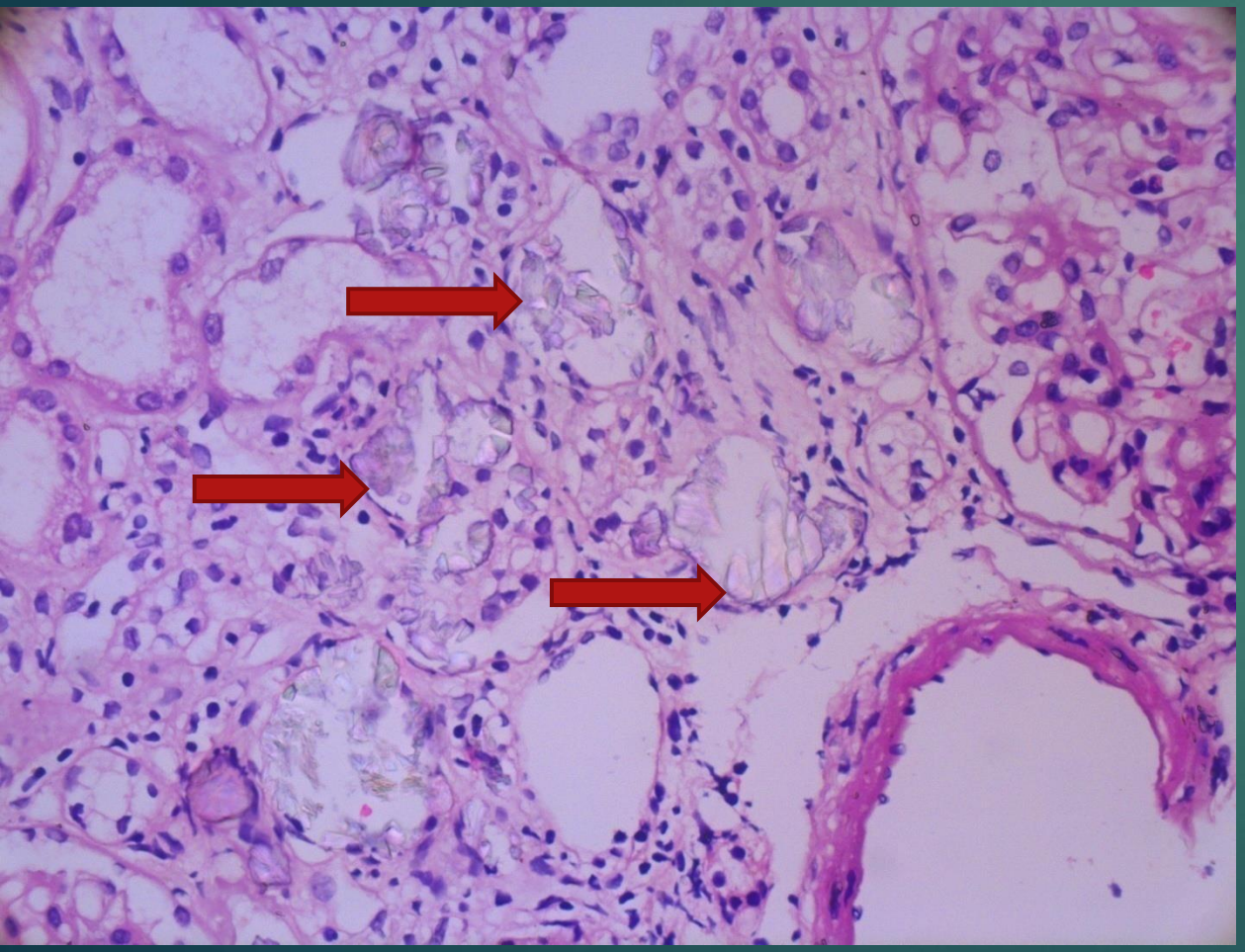
-mild interstitial inflammation with 40% of interstitial fibrosis.

Renal biopsy

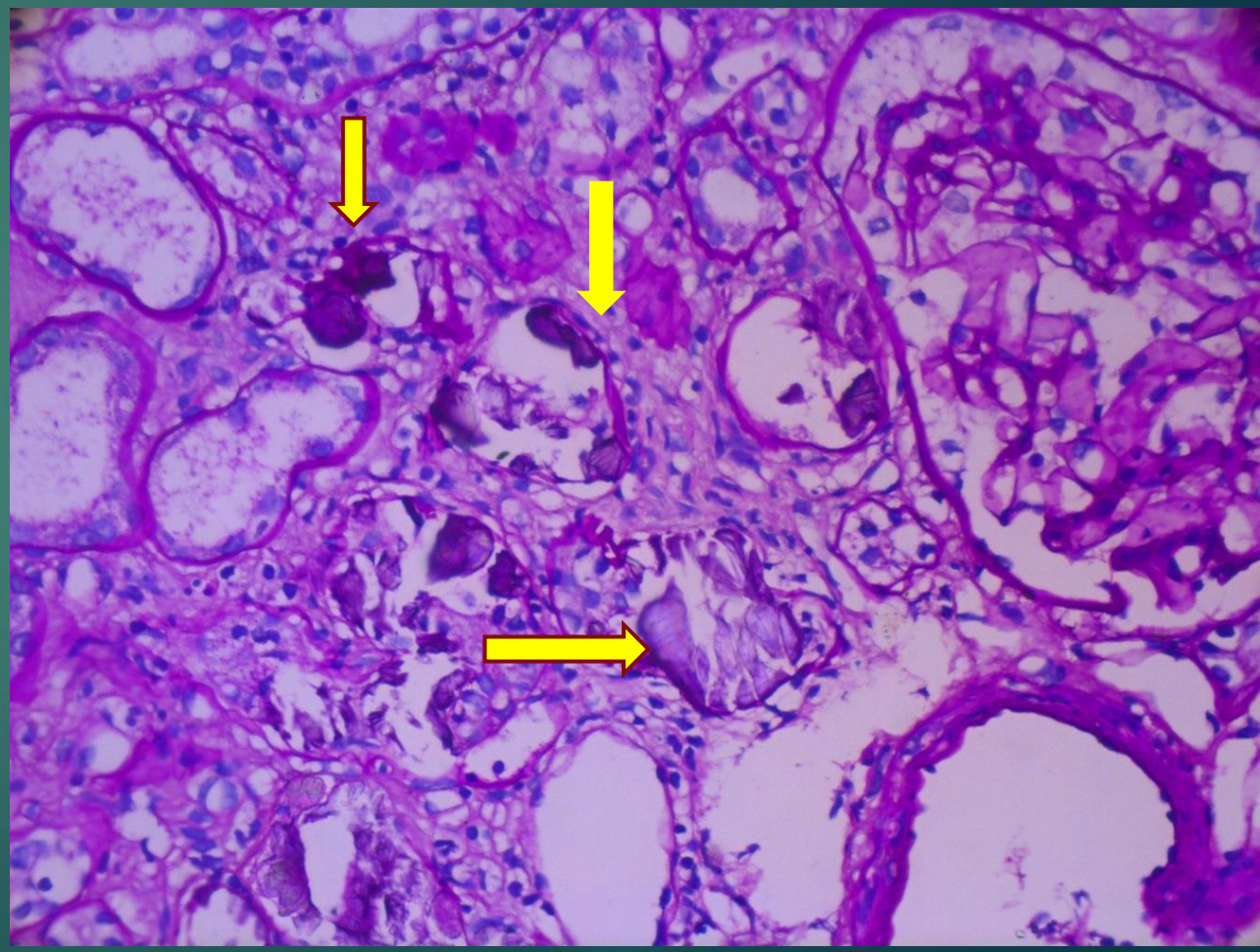
- Under polarized light, the deposits appeared strongly **birefringent** consistent with **calcium oxalate crystals**.
- Blood vessels appeared unremarkable.
- The immunofluorescence was negative

HISTOPATHOLOGY- Light Microscopy

H & E Stain

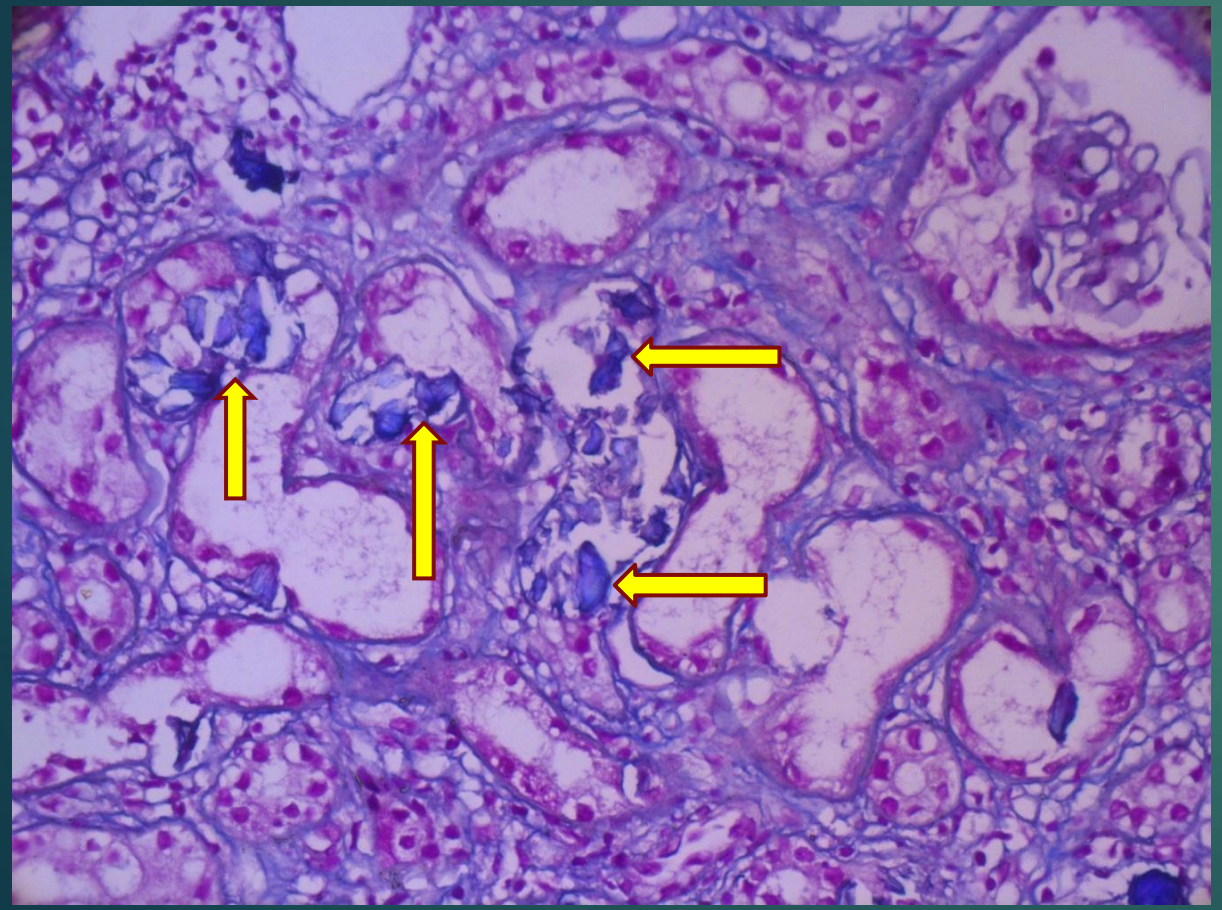


PAS Stain

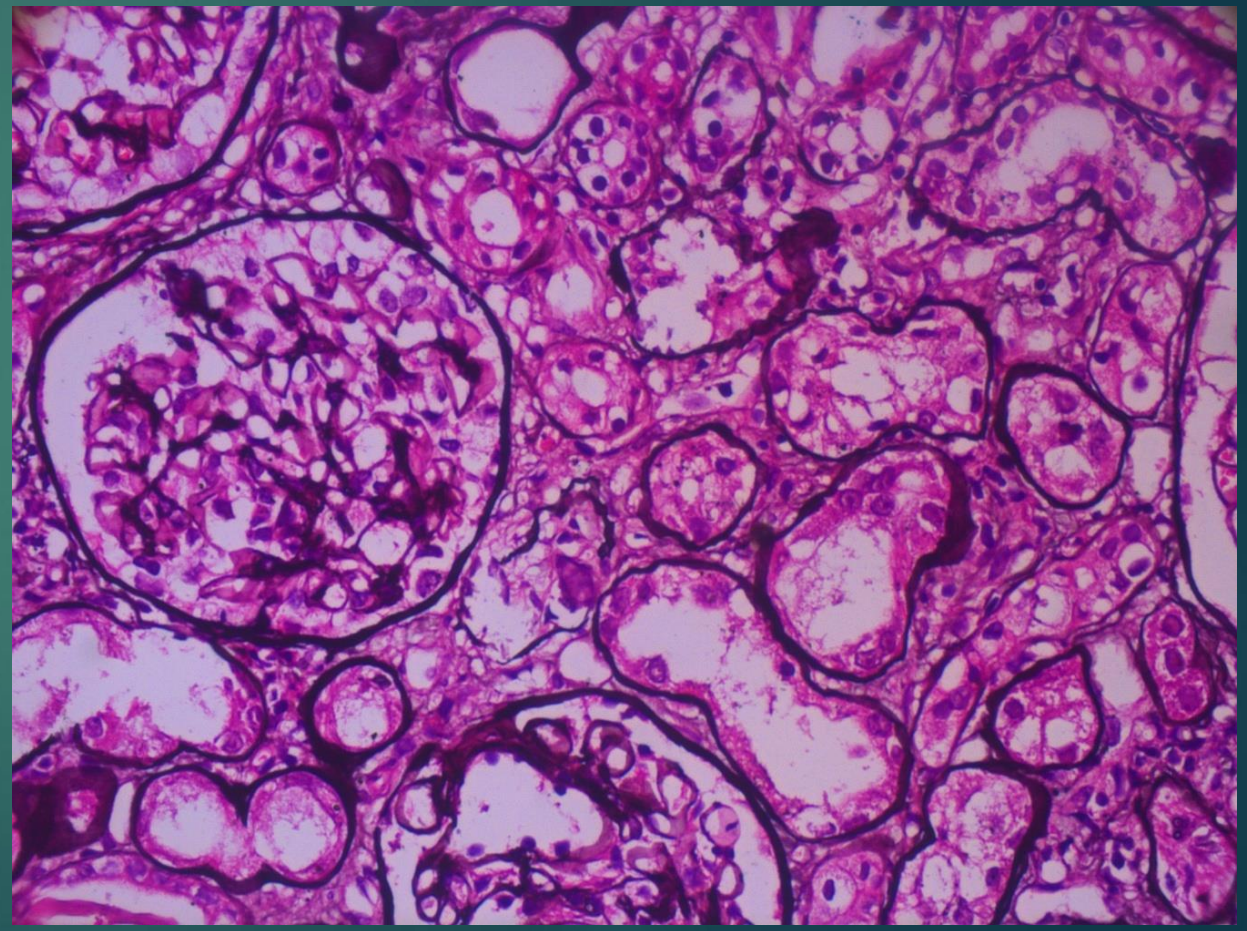


HISTOPATHOLOGY- Light Microscopy

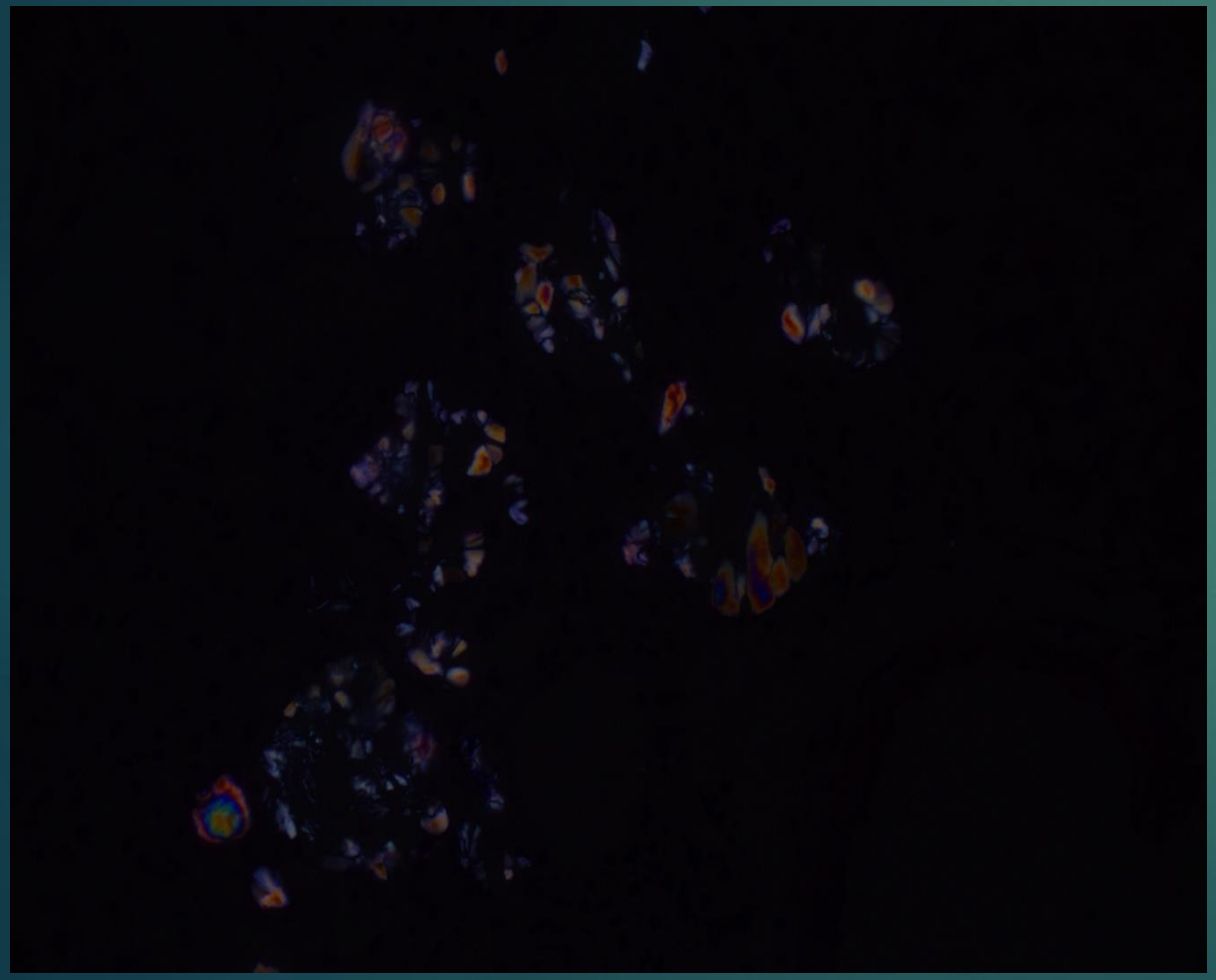
Masson's Trichrome stain

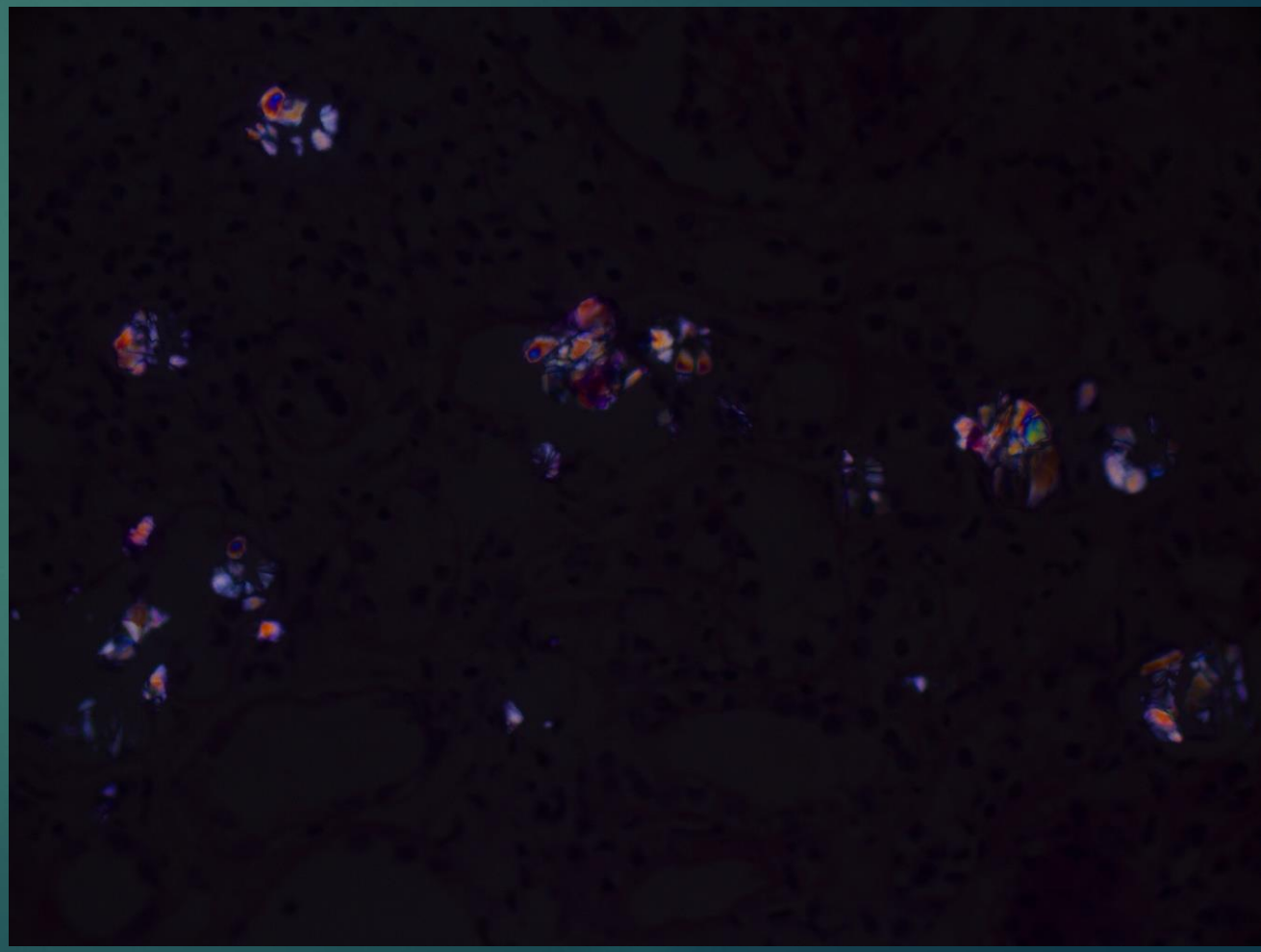


Silver Methylamine stain



Polarising Light - strongly birefringence consistent with **calcium oxalate** crystals





- 24 hr urine for volume of 400ml/24 hrs
  - Oxalate – 45 mg/24 hrs
  - citrate - 98.4 mg/24 hrs
  - Calcium - 220mg/24hrs
- stool was positive for fat globules,
  - stool culture- no growth
- Colonoscopy-

  normal colonoscopy study
- fundus examination- normal

CONCLUSION

- A case of Oxalate Nephropathy presenting as

- Acute on Chronic Kidney disease
- associated with a possibility of underlying Malabsorption Syndrome
- with a background of excessive intake of Oxalate rich foods and
- intravascular volume depletion.

TREATMENT

- Hydration status restored.
- Hemodialysis initiated
- Permanent cuffed Tunnelled catheter secured as patient required maintenance hemodialysis
- Dietary measures include a low-oxalate, low-fat, and normal calcium diet.
- Calcium supplements to reduce the bioavailability of intestinal oxalate and its absorption
- Patient counselled regarding AV fistula creation and Renal Transplant .

DISCUSSION

Definition – Oxalate Nephropathy

- Progressive kidney disease.
- Deposition of calcium oxalate crystals (birefringent on polarized light) within tubular epithelial cells, tubular lumens, and less frequently in the interstitium, associated with tubular injury and interstitial nephritis.
- Exclusion of other causes of kidney disease (apart from nonspecific microvascular lesions and/or diabetes associated glomerular lesions).
- A hyperoxaluria enabling-condition should be identified.

(American Journal of Kidney disease)

DISCUSSION

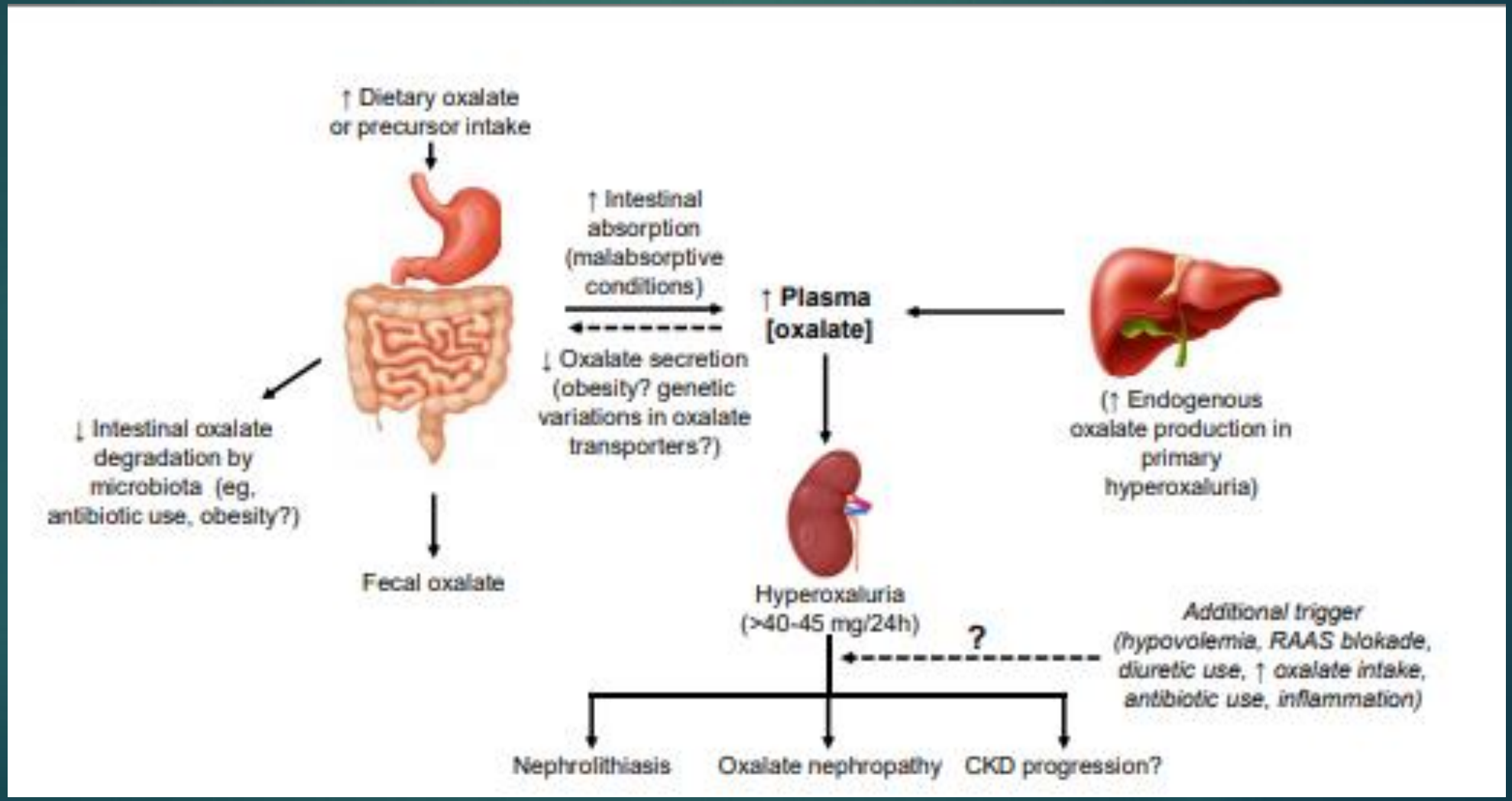
- The etiologies of oxalate nephropathy are divided into primary and secondary hyperoxaluria.

- Primary hyperoxaluria is a rare autosomal recessive inherited metabolic disorder which leads to an increase in endogenous oxalate synthesis resulting in increased urinary oxalate excretion.

- Secondary hyperoxaluria is due to –

  - increased intestinal oxalate absorption,
  - excessive dietary oxalate intake or
  - excessive intake of oxalate precursors.

Pathophysiology



- Malabsorption syndromes lead to increased oxalate absorption by

- excessive non-absorbed fatty acid chelates free calcium

- increased free oxalate that will be reabsorbed and excreted by the kidney;

- fatty acids and dihydroxyl bile acids cause an increase in the permeability of the intestinal mucosa to oxalate

- This excess of oxalate urinary excretion may lead to either acute or chronic oxalate nephropathy.

- Enteric hyperoxaluria due to malabsorption is principally caused by

  - inflammatory bowel disease,
  - jejuno-ileal bypass,
  - short bowel syndrome,
  - pancreatic insufficiency or
  - alteration of gut microbiota (oxalate degrading bacteria).

- Secondary oxalate nephropathy has also been described in-

  - ethylene glycol toxicity and
  - excessive ingestion of vitamin C.
  - excessive intake of plant-based foods high in oxalate, including the juicing of certain vegetables and fruits (Spinach, berries, dried figs, cocoa, beets, orange or lemon peel, black tea)

- precipitating factors
  - acute dehydration,
  - diuretic use,
  - antibiotic use, or
  - high dietary oxalate intake
  - RAAS blocker use

- Clinical presentation varies across the spectrum of
  - AKI,
  - AKI on CKD, and
  - CKD.

- Kidney biopsy shows
  - Crystals shown as birefringent under polarized light
    - acute tubular necrosis,
    - interstitial nephritis,
    - Glomerular changes(sclerosis)

Table 2. Current and Potential Therapies of Secondary Hyperoxaluria

Treatment	Rationale	Supporting evidence
High fluid intake (urine output >2-3 L/d)	Reduces urine calcium oxalate supersaturation.	Reduces stone formation.[67,68]
Low-oxalate diet	Reduces bioavailability of intestinal oxalate.	Reduces urinary oxalate excretion in small-sized studies; caveat: comparisons were based on a low-oxalate diet compared to a very-high-oxalate diet.[60,69,70]
Low-fat diet	Reduces intestinal oxalate absorption (by increasing bioavailability of intestinal calcium).	Reduces urinary oxalate excretion in small studies.[70,71]
Normal-calcium diet	Avoid low-calcium diets, which lead to more free intestinal oxalate.	Reduces urinary oxalate excretion in small-sized studies.[69,72]
Calcium supplements	Reduce bioavailability of intestinal oxalate and its absorption.	Reduces urinary oxalate excretion but may lead to hypercalciuria.[72-74] Calcium citrate may be more bioavailable than calcium carbonate.[75]
Cholestyramine	Binds intestinal bile acids, reduces diarrhea, and binds oxalate in vitro.	Studies show contradicting results.[70,73,76]
Oxalobacter formigenes administration	Increases intestinal oxalate degradation.	Reduces urinary oxalate excretion in rat model[61,77] and plasma oxalate levels in dialysis patients with primary hyperoxaluria (phase 2 study).[35]
Oxalate decarboxylase	Degrades intestinal oxalate.	Reduces urinary oxalate excretion in rat model[78] and in phase 3 pilot study in humans.[62]
NLRP3-specific inflammasome inhibitor	Reduces crystal-induced kidney damage.	Reduces calcium-oxalate crystal-induced kidney fibrosis in mouse model.[63]

- Identification and management of the cause of secondary hyperoxaluria is also important to minimize the risk of recurrence of oxalate nephropathy after kidney transplantation.

RESEARCH PROSPECTS

- Urinary oxalate excretion may be a potential risk factor for progression in of CKD,
- urinary oxalate may be a potential mediator of CKD development and progression in individuals with diabetes or obesity
- whether lowering urinary oxalate excretion could be beneficial in slowing CKD progression ?
- association between hyperoxaluria and faster decline in eGFR
- Therapeutic considerations concerning patients with secondary hyperoxaluria on dialysis and during the peritransplantation period

REFERENCES

- Brenner Textbook of Nephrology
- American Journal of Kidney Diseases
- World Journal of Nephrology
- Kidney International

THANK YOU

Dept of Nephrology