A CASE OF NEPHROCALCINOSIS

Department of Nephrology

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A 30 years / female , Mrs.Devi , from Poondi, Dindigul admitted with complaints of

Nausea and vomiting

Abdominal pain

for past 4 days

H/O Presenting illness:

Patient apparently normal before 8 years developed fever, abdominal pain, vomiting for which she was admitted in a private hospital

↓

Diagnosed with Right renal calculus with pyelonephritis

↓

Right Nephrectomy done

Before 6 months she developed similar complaints for which she was admitted in a private hospital, diagnosed as left upper ureteric calculi with hydronephrosis

DJ Stenting done → stones retrived → stent removal done by 9/2017

Pt 12/2017 developed nausea and vomiting which is insidious onset , slowly progressive, non-projectile, non-bilious, not associated with food intake, more during the past four days.

Associated with diffuse, non-colicky abdominal pain

h/o loss of weight / loss of appetite +

h/o easy fatiguability +

No h/o fever

No h/o dysuria, oliguria, pyuria, hematuria

No h/o increased frequency of micturition

No h/o swelling of legs, abdominal distension, facial puffiness

No h/o hiccough, constipation, diarrhoea

No h/o pruritus , paraesthesia, restless legs

No h/o breathlessness, cough/expectoration

No h/o chest pain , palpitation, giddiness

No h/o visual disturbances, head ache

No h/o weakness of limbs, sensory disturbances

No h/o involuntary movements, seizures, loss of conciousness

No h/o skin rashes, bleeding tendency, joint pain

Past history:

No h/o Hypertension, Diabetes, Tuberculosis, Heart Disease, Epilepsy, Bronchial Asthma, Thyroid Disorder

No h/o other surgery, blood transfusion, drug allergy

Proper records not available for the procedures previously done

Personal history:

Mixed diet

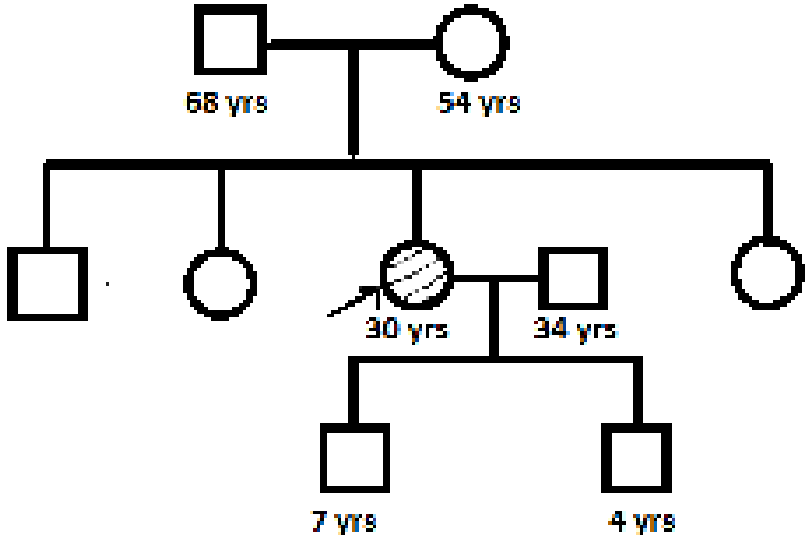
No specific addiction, sleep disturbance

Bladder and bowel habits normal

Family history:

Born as third child to

non- consanginious marriage



Menstrual history:

Menarche -13 yrs,

4/30 regular menstrual cycles, normal flow

General examination:

Pt conscious

Comfortable at rest

Thinbuilt, moderately nourished

Afebrile

Hydration fair

Pallor +

Anicteric

No cyanosis, clubbing

No pedal edema , significant lymphadenopathy

BP:120/70 mm of Hg	PR: 110/ min
SpO2: 96% in room air	JVP: →

Systemic examination:

Cvs: SIS2 +

No murmur, no pericardial rub

RS: B/L NVBS +

No added sounds

P/A: Not distended,

Rt subcostal transverse scar +

Epigastric tenderness +

Lt renal angle tenderness +

No organomegaly, bowel sounds +

No abnormal bruit/ venous hum

External genitalia normal, hernia orifices free

Provisional Diagnosis :

Right post-nephrectomy single kidney status

?Left renal calculi- recurrence

Chronic kidney disease / uremic gastritis

Investigations done

- CBC: Hb- 5.7 gm

  TC- 6700 cells/ cu mm

  DC- 67/26/7

  platelet- 1.64 lakhs cells / cu mm

  PCU- 17% , ESR- 140 mm
- RBS: 117 mg%
- Sr urea-128 mg % / Sr creatinine- 11.8 mg %
- LFT: WNL, ALP: 54 U/L
- Urine routine: albumin- ++, sugar- ++, deposits- 2-6 pus cells

- Urine spot PCR : 17/ 148
- Viral markers : HIV/ HCV/HBsAg- non-reactive
- Blood grouping/ typing: B positive
- Urine culture: scanty growth of staphylococcus aureus
- Blood culture: (tip culture of rt IJV catheter) no growth
- Sr uric acid: 9.8 mg/dl (2.6-6),
- Sr calcium: 8.0 mg/dl (8.5-10.1), Sr Phosphate: 4.5 mg/dl
- Sr electrolytes: Na+: 130 meq/l

  K+: 4.0 meq/l

  Mg++: 2.1meq/l
- Sr.total proteins:6 gm/dl

Complete urine analysis:

Colour	yellow
pH	5.0
Protein	+
Acetone	-
Sugar	++
Specific gravity	1.025
Bile pigments	-
Urobilinogen	normal

RBC	4-5
PUS cells	2-4
EPITHELIAL cells	6-8
Cast	nil
Bacteria	nil
Nitrite	-
Crystals	NIL

Other investigations

- ECG: WNL
- USG Abdomen & pelvis:

Acute on chronic Lt pyelonephritis with multiple intra renal calculi

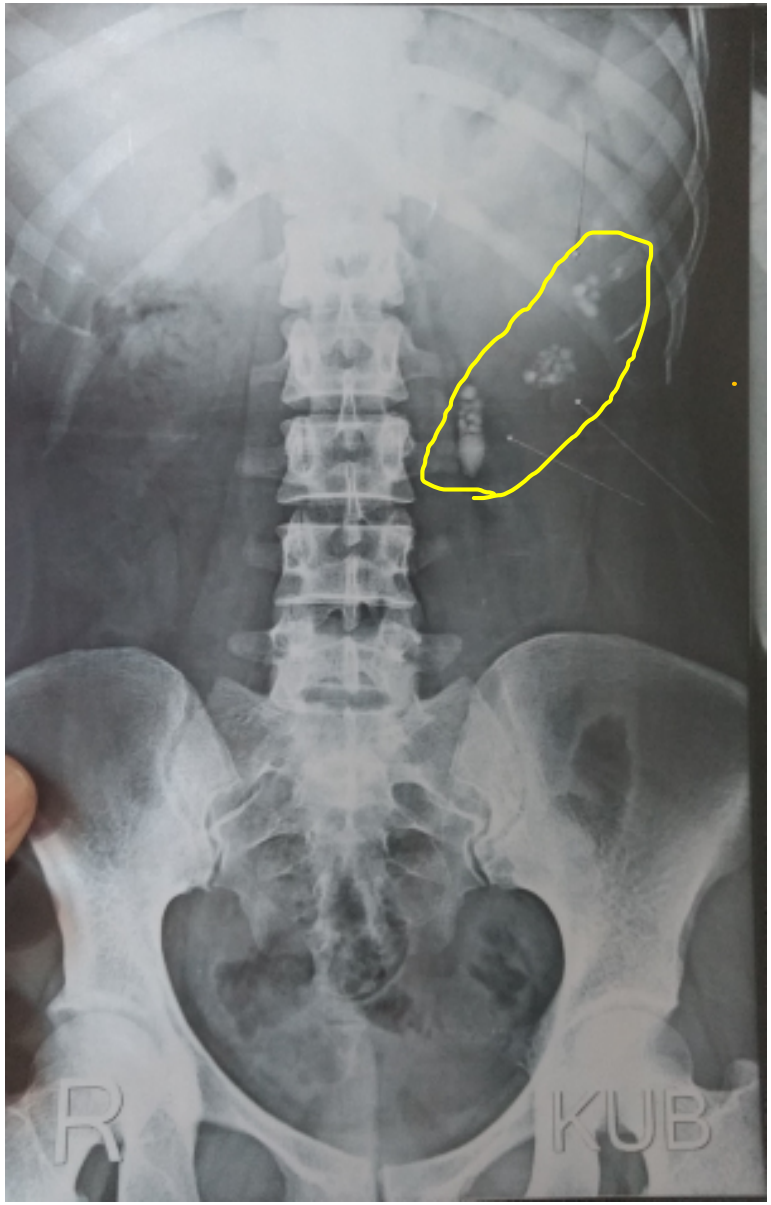
Adenomyosis

- CT Abdomen & pelvis:

Rt kidney- surgically absent

Lt kidney- e/o diffuse hyperdensity noted along the cortical surface, e/o multiple intra-renal calculi upper , mid and lower pole, pelvic calculi

Impression : P/O Lt Nephrocalcinosis, Lt renal calculi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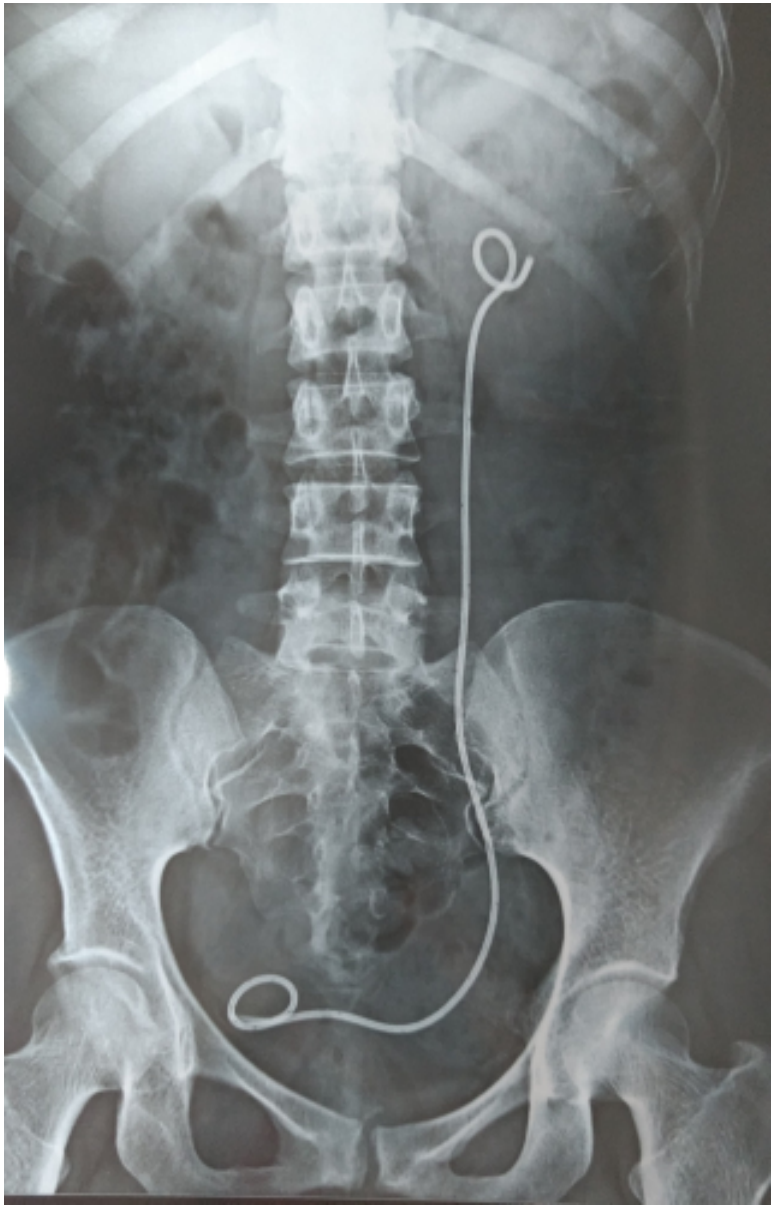

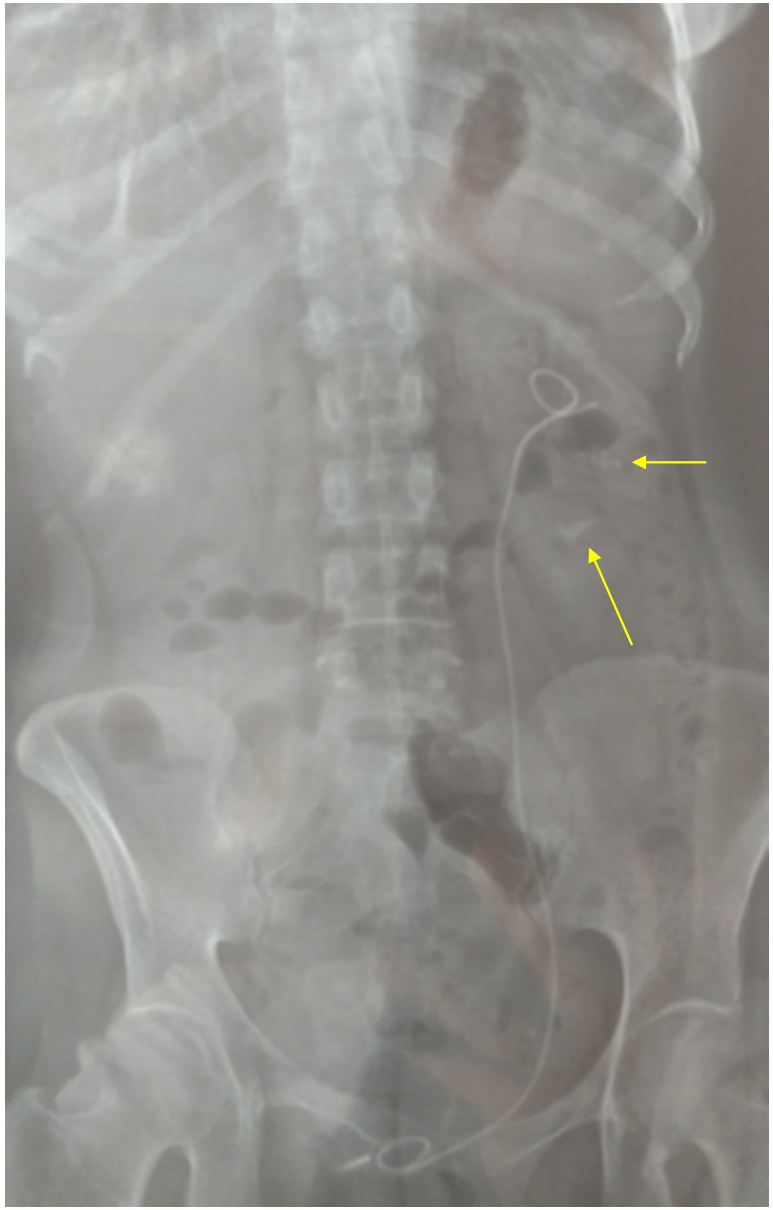

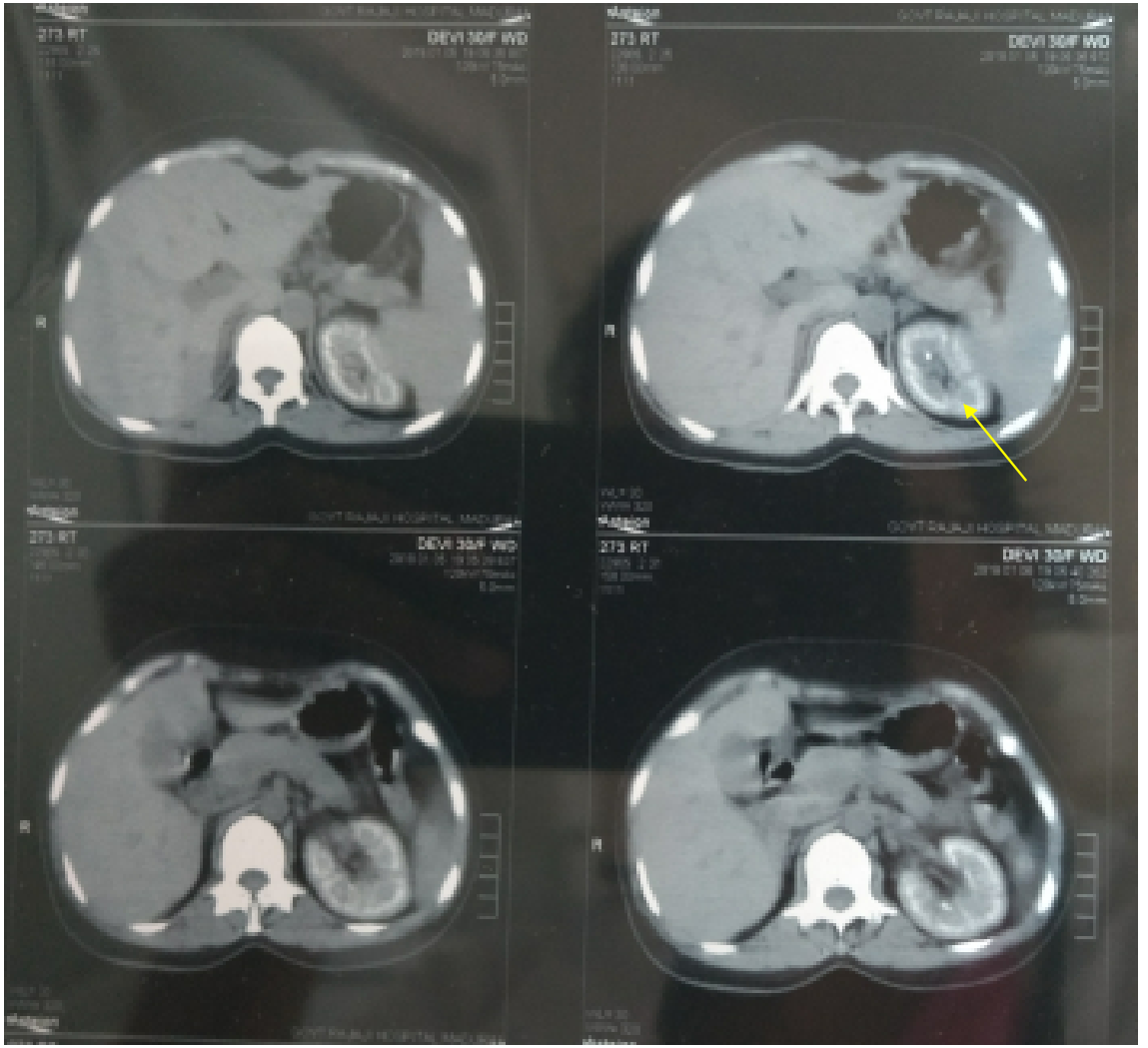
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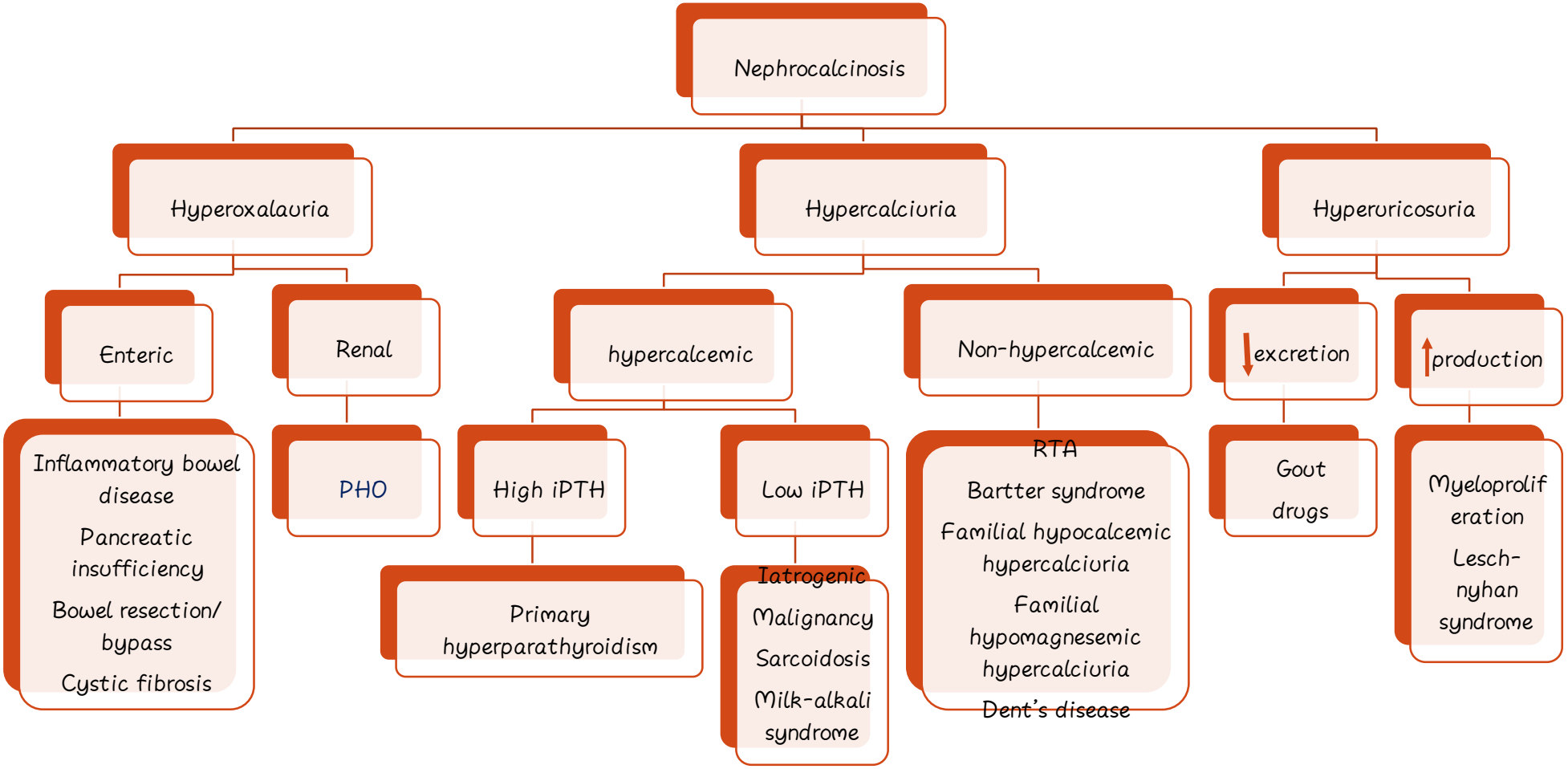

Nephrocalcinosis
Hyperoxaluria
Hypercalciuria
Hyperuricosuria
Enteric
Renal
hypercalcemic
Non-hypercalcemic
↓excretion
↑production
Inflammatory bowel disease
Pancreatic insufficiency
Bowel resection/ bypass
Cystic fibrosis
PHO
High iPTH
Low iPTH
RTA
Bartter syndrome
Familial hypocalcemic hypercalciuria
Familial hypomagnesemic hypercalciuria
Dent's disease
Gout
drugs
Myeloproliferation
Lesch-nyhan syndrome
Primary hyperparathyroidism
Iatrogenic
Malignancy
Sarcoidosis
Milk-alkali syndrome

In view of

Recurrent renal calculi,

Nephrocalcinosis,

Absence of hypokalemia,

Absence of hypercalcemia,

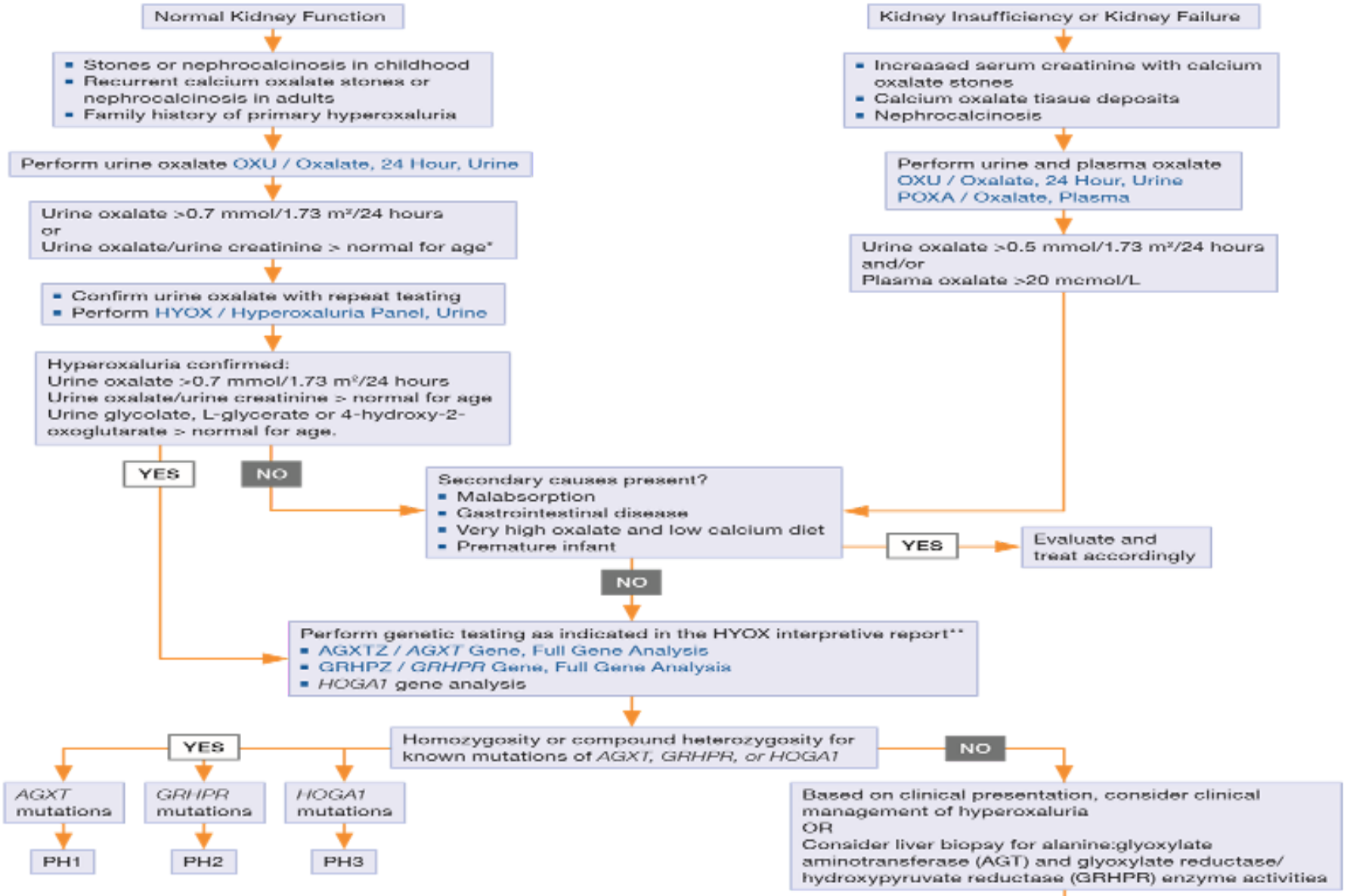
Absence of hypomagnesemia,

Urine pH 5.0

PRIMARY HYPEROXALURIA

was suspected and diagnostic work up done

Hyperoxaluria Diagnostic Algorithm



Opinion obtained

Urology opinion:

Lt URS & DJS

Stones couldn't be retrived for analysis

Ophthalmology opinion:

BE KF ring +

BE Fundus normal

Vascular surgeon opinion:

Lt BC Fistula done

Vein biopsy: no e/o calcification or oxalate crystal deposition

24 hrs Urine Oxalate / Creatinine Ratio : 24.9/0.096 mg/g

259.3 mg/g (< 32 mg/g)

RESULTS

Gene (Transcript)[1]	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
AGXT (+) (ENST00000307503)	Exon 6	c.614C>T **(p.Ser205Leu)**	Homozygous	Type I primary hyperoxaluria	Autosomal recessive	Likely Pathogenic

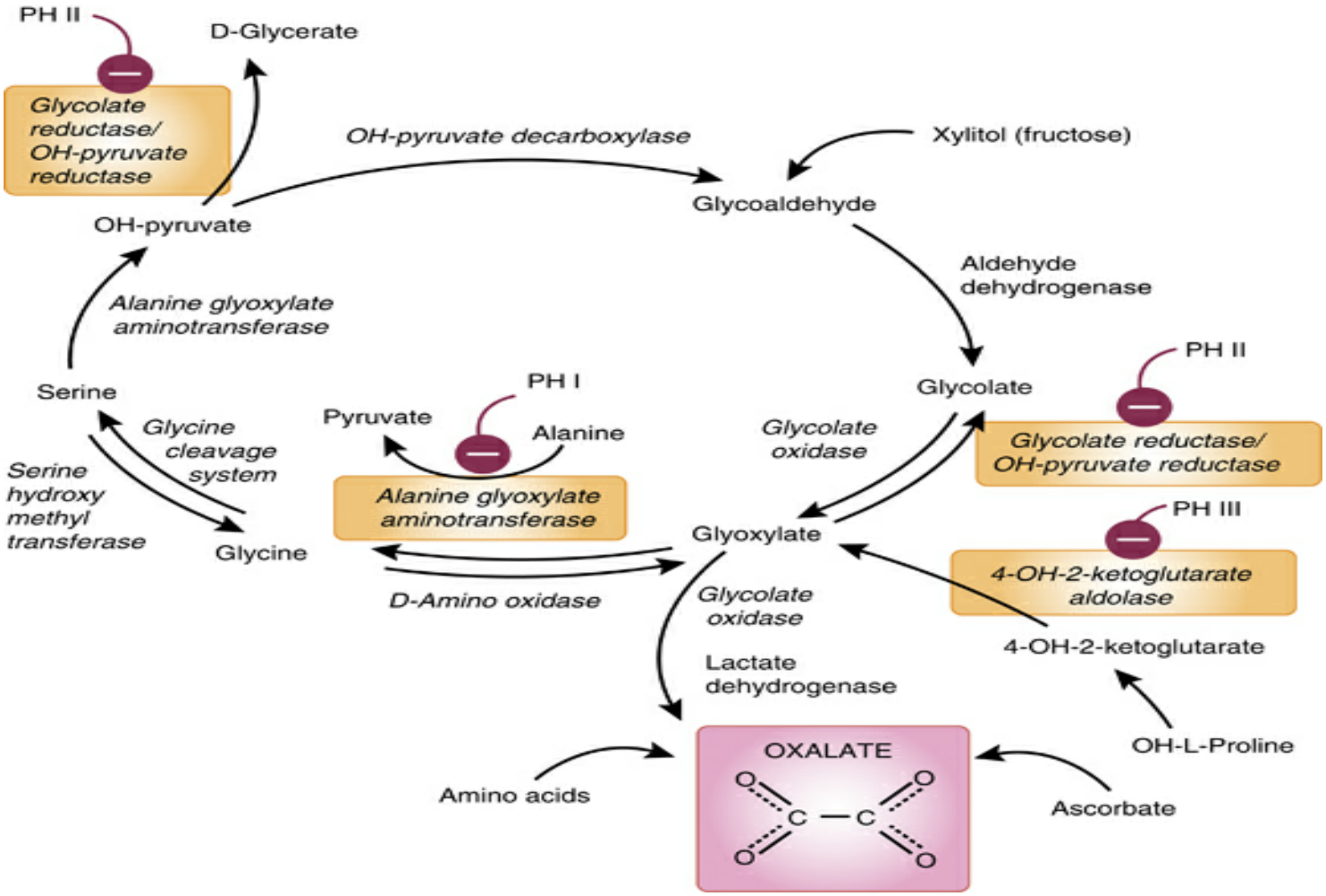
ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

No other variant that warrants to be reported was detected. Variations with high minor allele frequencies which are likely to be benign will be given upon request.

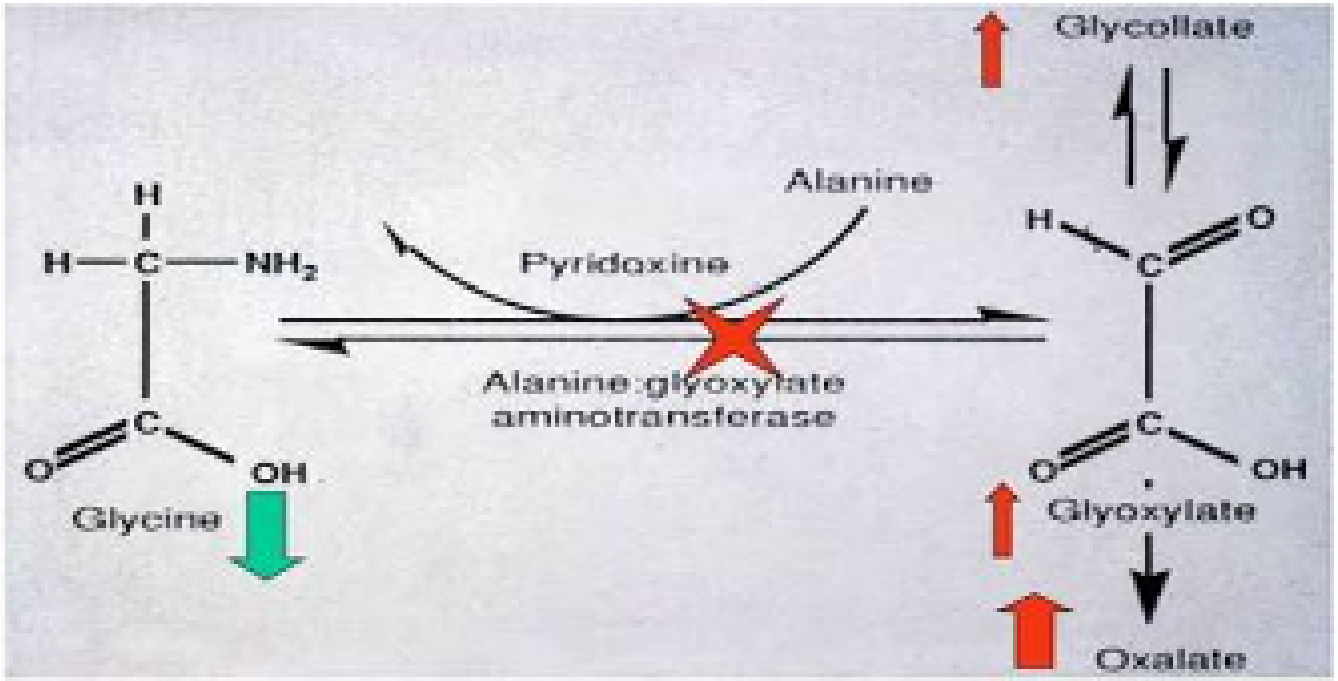
VARIANT INTERPRETATION AND CLINICAL CORRELATION

Variant description: A homozygous missense variation in exon 6 of the *AGXT* gene **(chr2:241813413C>T; Depth: 28x)** that results in the amino acid substitution of Leucine for Serine at codon 205 **(p.Ser205Leu; ENST00000307503)** was detected (Table). The observed variation lies in the aminotransferase class-V domain of the AGXT protein (23) and has previously been reported in a patient affected with type I primary hyperoxaluria (24). The Ser205Leu variant has not been reported in the 1000 genomes and our internal databases and has a minor allele frequency of 0.0008% in the ExAC database. The *in silico* predictions[#] of the variant are probably damaging by PolyPhen-2 (HumDiv and HumVar) and damaging by SIFT and MutationTaster2. The reference codon is conserved across species.

Primary hyper oxaluria



Primary Hyperoxaluria I (PHI):
peroxisomal enzyme (AGT) deficiency in the liver



PRESENTED FOR ITS RARITY

INCIDENCE: 1/120,000 LIVE BIRTH

PREVALENCE: 1-3 / 1,000,000 PEOPLE

PLAN:

COMBINED LIVER-KIDNEY TRANSPLANTATION

HD till definitive procedure

thank you!