CLINICAL CASE PRESENTATIONS

BY DEPARTMENT OF GENERAL MEDICINE

AN UNUSUAL CASE OF QUADRIPARESIS

DR. SAI PRIYA ANDE
UNIT - 1
DEPARTMENT OF MEDICINE

CLINICAL HISTORY

- 50 year old female patient , home maker presented with c/o

Weakness in both lower limbs since 8-10 days

Weakness in both upper limbs since 3-4 days

Pain in both lower limbs since 8-10 days

- Patient had developed loose stools 6-8 episodes one week prior to the onset of weakness.
- No sensory loss, or incontinence of bowel or bladder.
- No shortness of breath, skin rash, joint pain, or trauma.

PAST HISTORY

- Patient is a known case of **Hypertension** since 3 years.

- Eight months ago, patient was admitted in a private hospital with **unstable angina.** Patient was started on *aspirin-atorvastatin* (75/20).

- Six months prior, **Coronary angiography** was performed and patient was diagnosed to have **single vessel disease in LAD** and stenting was performed. Patient was started on

  Tab Ticagrelor (90mg) PO 2-0-1

  Tab Rosuvastatin(40mg) PO 0-0-1 post PTCA.

ON EXAMINATION

General examination:-

No pallor, icterus, cyanosis, clubbing, koilonychia, lymphadenopathy, edema.

Vitals:

- Pulse rate-90 bpm
- BP-130/90 mm hg in right arm measured in supine position. No postural hypotension.
- RR- 15/min.
- SpO2-98% on room air.

Systemic examination:

- **CNS:**
  - Higher mental functions, Cranial nerves-normal.
  - Motor-
  - Nutrition- no wasting
  - Tone - normal

- **Power**
  - **B/L upper limb:-**

❑ Shoulder; elbow; wrist **-1/5**.

- **B/L lower limb:-**

❑Hip; knee; ankle-**0/5.**

❑**Reflexes- absent in both upper and lower limbs.**

❑ Co-ordination- could not be tested. No involuntary movements.

- Sensory- normal.
- Cerebellar signs- negative.

❖ **OTHER SYSTEMS NORMAL ON EXAMINATION**

DIFFERENTIAL DIAGNOSIS BASED ON HISTORY

- HYPOKALEMIC PARALYSIS .
- GUILLAIN-BARRE’ SYNDROME(GBS) / AIDP
- COMPRESSIVE MYELOPATHY(IN SPINAL SHOCK).
- ACUTE TRANSVERSE MYELITIS.
- INFLAMMATORY MYOPATHY.

LAB INVESTIGATIONS

HAEMOGRAM	
HB	12.5 gm/dl
TLC	12,700/mic lt
PLATELETS	3,34,000 /mic lt
ELECTROLYTES	
SODIUM/POTASSIUM	131/5.80 mmol/lt
PHOSPHORUS	> 9 mg/dl
CALCIUM	7.90 mg/dl
MAGNESIUM	3.20 mg/dl

LFT	
BILIRUBIN	TOTAL-0.59 mg/dl CONJUGATED-0.27 mg/dl
SGOT[AST]	325 U/L
SGPT[ALT]	362 U/L
ALP	83 U/L
RFT	
UREA	273mg/dl
CREATININE	11.25 mg/dl

S. URIC ACID	14.20 mg/dl
S.PROTEINS	TOTAL- 6.50 MG/DL; ALBUMIN- 3.10 mg/dl
CPK-TOTAL	15,034 U/L [NORMAL VALUE IN FEMALES-26-192 U/L]
PT-INR	13.30 SEC; INR-1.14
HIV/HBSAG/HCV	NON REACTIVE
ANA[IF] AND ANA BLOT	NEGATIVE
TFT	T3- 0.38 mic/dl; T4- 2.37 mic/dl; TSH –6.23mIU/L
ESR;CRP	87 mm/hr; CRP-27.70 mg/L
CSF EXAMINATION-R/M	WNL
CULTURES-BLOOD,URINE AND CSF	NO GROWTH
URINE	R/M:- PROTEIN-TRACE; UPCR:- 2.63 [MODERATE PROTEINURIA 1.10-3.00] URINE FOR MYOGLOBIN-NEGATIVE


LATEX
LATEX FREE
GLOVES
UROMETER®
Romsons®
APPROXIMATE ML
250 ml
200
150
100

- **USG ABDOMEN AND PELVIS-**WNL

- **MRI WHOLE SPINE SCREENING WITH DEDICATED CERVICAL SPINE-** WNL.

- **MRI BRAIN-** WNL.

- **NERVE CONDUCTION STUDY (NCV)-**WNL.

ELECTROMYOGRAPHY(EMG)

- EMG done in the following muscles-left tibialis anterior, right vastus lateralis, and right biceps brachii.

- Spontaneous activity in the form of positive sharp waves and fibrillations noted in the tested muscles.

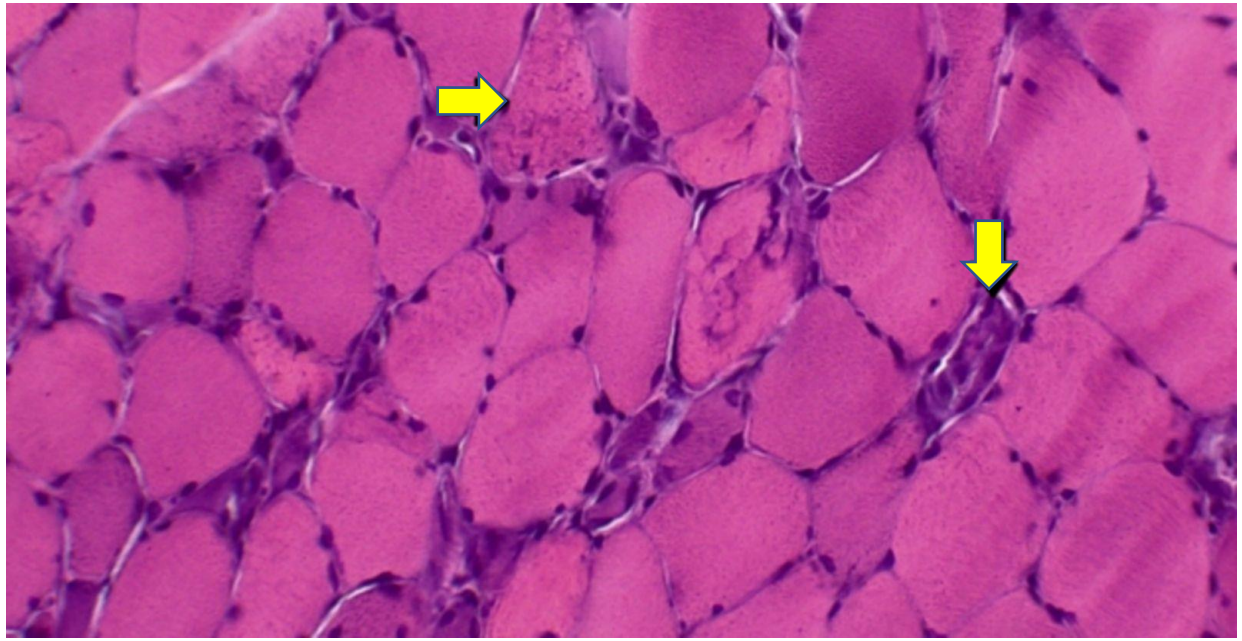
- Small and polyphasic Motor Unit Action Potentials (MUAP were)noted in all of the tested muscles.

- Early and complete recruitment noted in all tested muscles suggestive of a myogenic pattern.

Impression-s/o PRIMARY INFLAMMATORY MUSCLE DISEASE.

MUSCLE BIOPSY FINDINGS

- **Necrosis** of individual muscle fibres as well as a small groups of muscle fibres.
- These fibres show loss of striations.
- Necrotic muscle fibres are surrounded by macrophages.
- Occassional interstitial focus of lymphocytes seen.
- Regeneration of muscle fibres seen.
- Fibrinoid necrosis, perivascular atrophy, significant fibrosis and inclusion bodies are not seen



- MUSCLE BIOPSY-INFLAMMATORY MYOPATHY;
- INCLUSION BODIES OR VASCULITIS NOT SEEN.
- **PROMINENT MYONECROSIS IS PRESENT WITH A MILD INTERSTITIAL INFLAMMATORY INFILTRATE.**

In view of

- Muscle weakness following use of statins
- Elevated CPK-TOTAL
- ANA(IF) and ANA blot negative
- Nerve Conduction Study(NCV) –WNL
- ELECTROMYOGRAPHY(EMG)-s/o inflammatory muscle disease
- Muscle biopsy-s/o necrotising myopathy

- **Final diagnosis - Statin Induced Necrotizing Myopathy(SINAM).**

TREATMENT GIVEN

- Statin was stopped.
- Patient was started on haemodialysis.
- Tablet wysolone 1mg/kg was started and was tapered off over 4 weeks.

CLINICAL COURSE IN THE HOSPITAL

- On presentation, patient was bed ridden with prominent muscle weakness.
- Treatment was initiated along with physiotherapy.
- A marked improvement in muscle weakness was noted over the course of next 4 weeks.

AFTER FOUR WEEKS OF TREATMENT

DISCUSSION

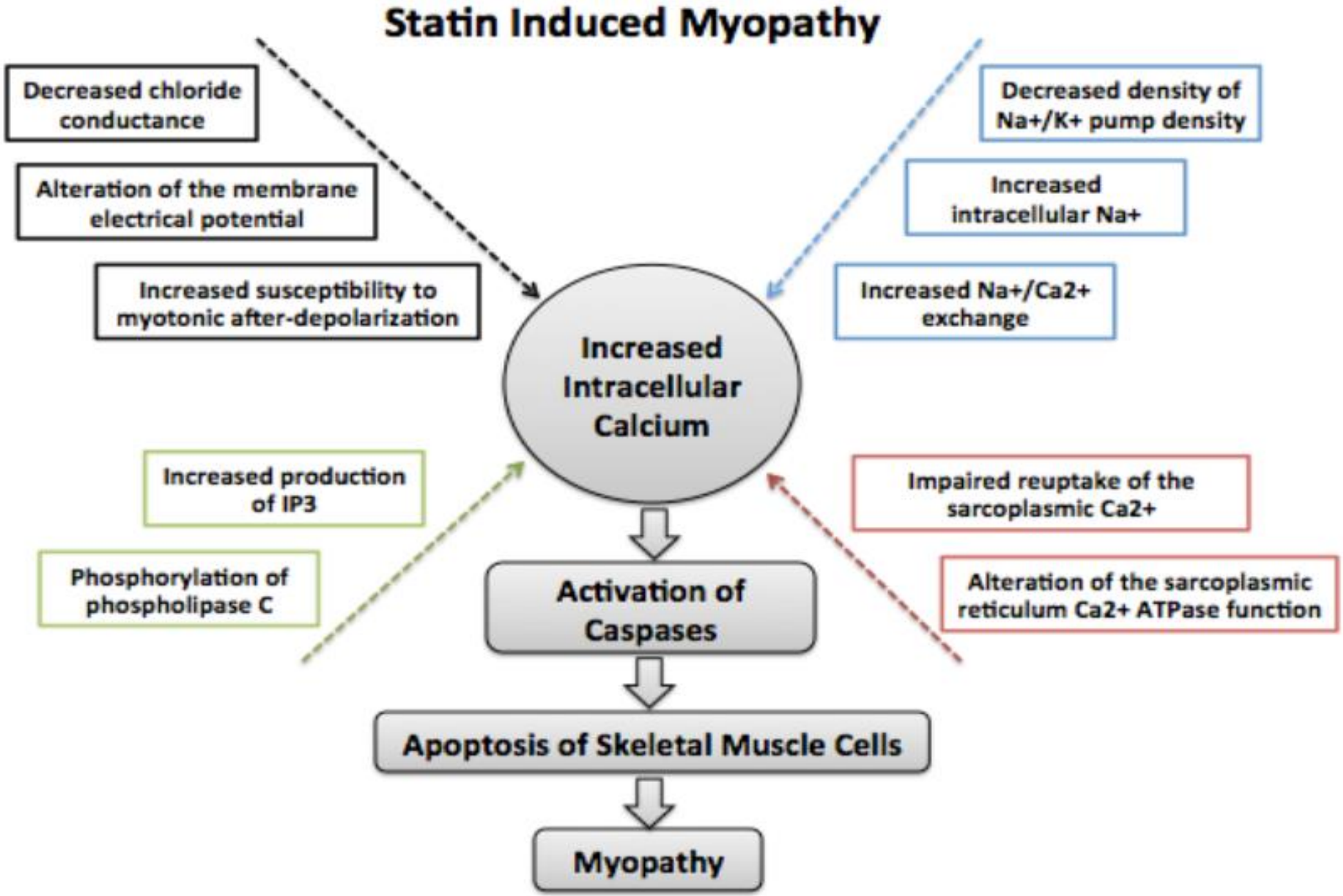
- Since their introduction over 20 years ago,statins has effectively reduced the cardiovascular morbidity and mortality.
- Evidence presented by the American College of Cardiology/American Heart Association Blood Cholesterol Treatment Task Force solidified **statins as the only cholesterol-lowering agent that showed mortality benefit.**
- The clinical spectrum of statin induced myopathy includes myalgia, myositis, rhabdomyolysis, and asymptomatic increase in the concentration of creatine kinase.
- Risk factors include Advanced age Female sex, prior history of myopathy with use other statins ,high dose statin therapy, multisystem diseases (for example, diabetes mellitus),Hypothyroidism, Excess alcohol ,intercurrent infections, major surgery or trauma .
- In randomized controlled trials, **incidence** is thought to be **1.5% to 5%** of patients, although this is believed to be an underestimation in real world patients.

➢Highest incidence - Rosuvastatin followed by atorvastatin

➢Least incidence - Fluvastatin .

CLINICAL ENTITY	ACC/AHA/NHLBI	NLA(4)	FDA(3)
MYOPATHY	General term referring to any disease of muscles	Symptoms of myalgia(muscle pain or soreness),weakness or cramps plus creatinine kinase > 10*ULN	Creatinine kinase >= 10*ULN
MYALGIA	Muscle ache or weakness without creatinine kinase elevation	NA	NA
MYOSITIS	Muscle symptoms with creatinine kinase elevation	NA	NA
RHABDOMYOLYSIS	Muscle symptoms with significant creatinine kinase elevation (typically > 10*ULN) and creatinine elevation (usually with brown urine and urinary myoglobin)	Creatinine kinase >10,000 IU/L or creatinine kinase > 10* ULN plus an elevation in serum creatinine or medical intervention with intravenous hydration	Creatinine kinase > 50 * ULN and evidence of organ damage such as renal compromise

ACC/AHA/NHLBI=American College of Cardiology/American Heart Association/National Heart, Lung and Blood Institute ; FDA= U.S. Food and Drug Administration ;NA-=not available; NLA=National Lipid Association ; ULN=Upper Limit of Normal.


Statin Induced Myopathy
Decreased chloride conductance
Alteration of the membrane electrical potential
Increased susceptibility to myotonic after-depolarization
Decreased density of Na+/K+ pump density
Increased intracellular Na+
Increased Na+/Ca2+ exchange
Increased Intracellular Calcium
Increased production of IP3
Phosphorylation of phospholipase C
Impaired reuptake of the sarcoplasmic Ca2+
Alteration of the sarcoplasmic reticulum Ca2+ ATPase function
Activation of Caspases
Apoptosis of Skeletal Muscle Cells
Myopathy

TAKE HOME MESSAGE

- This case highlights the need for awareness of common side effects associated with statins.
- It also emphasizes the need for early recognition and treatment of rhabdomyolysis to prevent the development of complications.
- The use of statins should be closely monitored.

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THANK YOU

TWO YOUNG PATIENTS SUCCESSFULLY TREATED FOR CONSUMPTION OF RAT-KILL POISON

Dr Sindhuri Goud Nimmala

UNIT 2

Dept of medicine

Case 1

- 23 year old female, IT employee alleged history of ingestion of rat kill (Zinc phosphide) came within 4 hours of ingestion of poison
- 40 gm mixed with milk
- c/o palpitations and vomiting 7-8 episodes non projectile, non bilious
- Menses started on day 2 of admission with Excessive bleeding

Case 2

- 20 year old female , student alleged history of consumption of rat kill (zinc phosphide) referred from another hospital after gastric lavage
- 20 gms
- c/o vomiting ; 7-8 episodes
- c/o pain in abdomen
- Menses started on day 4 of admission which was normal

Case 1

O/E: PR 122 bpm

BP 96/60 mm Hg

RR 18 cpm

SPO2 96% on Room air

P/A: Tender hepatomegaly present

Case 2

- O/E: PR 110bpm

  BP 130/80 mmHg

  SPO2 97% on Room air

  RR 17cpm

- S/E: WNL

case 1	INVESTIGATIONS	case 2
• Hb fell from 11.6 to 9 gm%		• Hb fell from 12.9 to 11.7 gm%
• TLC rose to 14700 and later ..Normal		• TLC rose to 14900...later... Normal
• Platelets remained normal		• platelets remained normal
• **LFT : deranged on day 5**		• **LFT :**
• Bilirubin T:5.4 D/I:3.1/2.3		• Bilirubin T:1.7,D:0.5,I:1.12
• SGOT/SGPT/ALP:544/338/223		• SGOT/SGPT/ALP: 24/63/51
• PT/INR :22.6/2.05		• INR : 1.77

CASE 1

On DAY 4, had hemodynamic collapse and was Intubated

TROP I 4400,CPKMB 56

NT Pro BNP 5256

2DECHO: LVEF 30%, Global LV hypokinesia, A 10mm OS ASD incidentally detected

Imp: Toxic cardiomyopathy with OS ASD with L to R shunt

Patient improved on treatment Extubated on day 12 and discharged on day 25

CASE 2

- vitally stable
- **On Day 6 patient had tetany "chovsteck sign positive"**
- Serum Calcium 7.7
- Ionised calcium 1.12
- Inj Calcium Gluconate was given

Case 1

Inj PANTOPRAZOLE infusion 200mg in 50 ml NS @4ml/hr

Inj N ACETYL CYSTEINE infusion 6000mg in 1000ml D5 over 16 hours @60ml/hour extended over 5-6 days

Inj GLUTATHIONE 600mg IV 1-0-1

Inj CEFTRIAXONE 1 gm IV 1-0-1

Inj ONDANSETRON IV 4mg 1-1-1

Inj VITAMIN K 30 mg IV stat f/b 10mg IV OD

Inj Furosemide 40mg 1-0-1 and later tapered

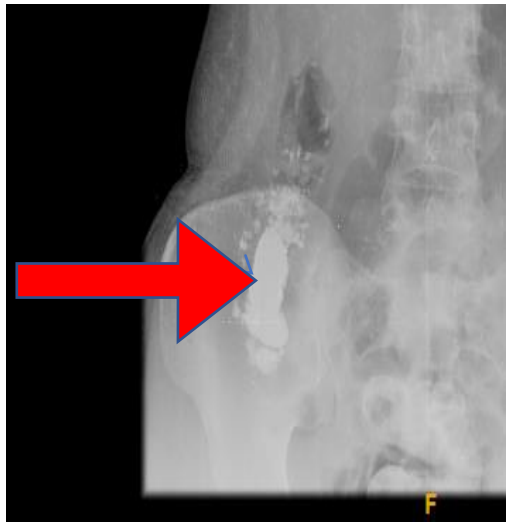
FFP was given till INR was normalised

PCV transfused on day 7

Case 2

- **Inj PANTOPRAZOLE infusion 200mg in 50 ml NS @4ml/hr**
- **Inj NACETYLCYSTEINE infusion 6000mg in 1000ml D5 over 16 hours @60ml/hour extended over 5-6 days**
- **Inj GLUTATHIONE 600mg IV 1-0-1**
- Inj CEFTRIAXONE 1gm IV 1-0-1
- Inj ONDANSETRON 4 mg IV 1-1-1
- Inj VITAMIN K 30mg IV stat □ 10mg IV 1-0-0 for 3 days
- Tab SHELCAL 500mg PO 1-0-1

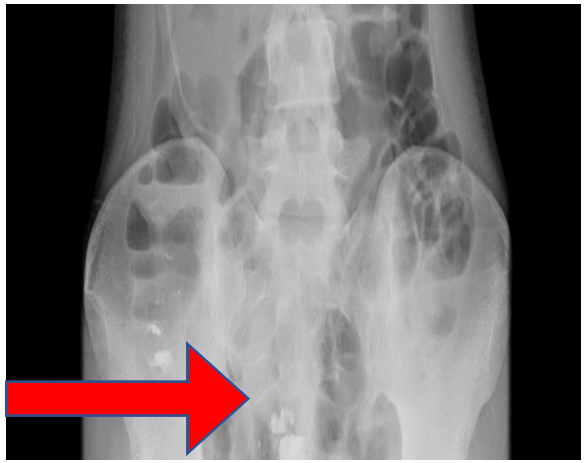
X RAY ERECT ABDOMEN BEFORE AND AFTER



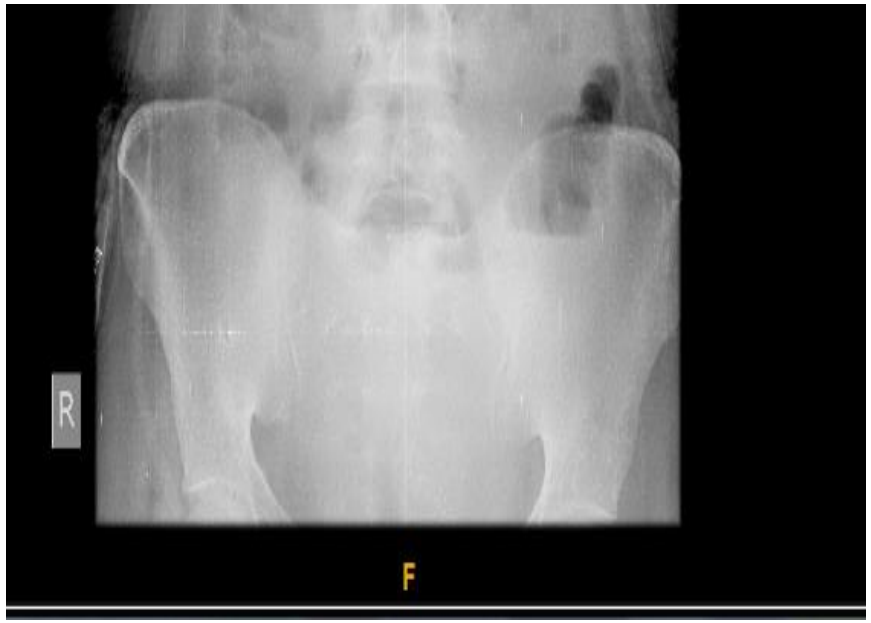
Day 2 for case 1

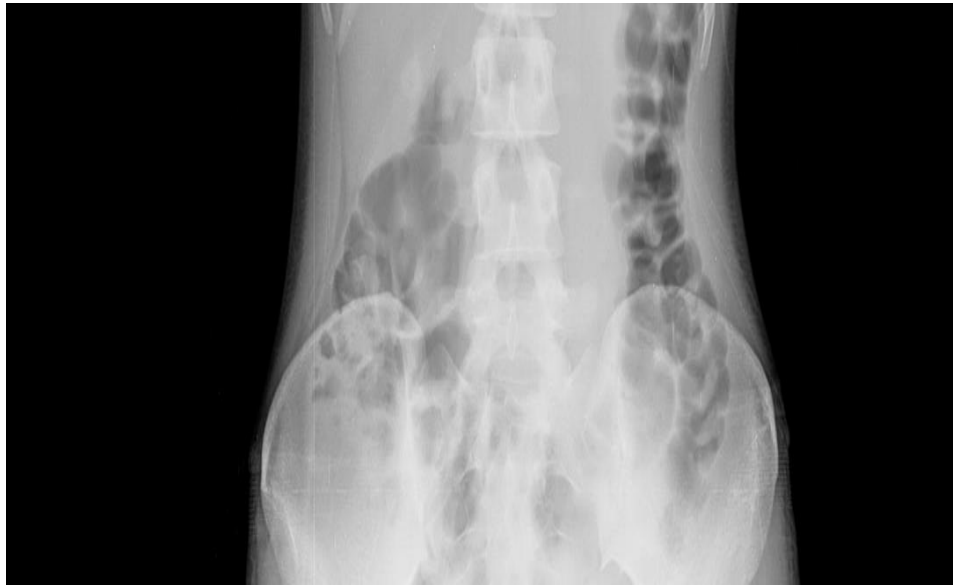
- Purgative ;

polyethylene glycol to clear the bowel of the residual poison



Day 3 for case 2





DISCUSSION

- Zinc phosphide has been used widely as a rodenticide.
- Upon ingestion, converted to phosphine gas into systemic circulation.
- Phosphine causes inhibition of C oxidase, mitochondrial morphology and oxidative respiration are impaired at a cellular level.
- Clinical symptoms are circulatory collapse, hypotension, shock , myocarditis, pericarditis, acute pulmonary edema ,metabolic acidosis, hypocalcemia, hepatotoxicity, thrombocytopenia, acute kidney failure and congestive heart failure
- Liver cell failure is usually seen in the 2nd week and may progress to Fulminant Liver Failure in some patients ,who may then need an urgent Liver Transplant

- Fatal dose 20-40mg/kg body weight
- Mortality rate in various studies is 37% -100%
- There are no antidotes currently known.
- Our first patient developed both Circulatory collapse Respiratory and Heart Failure and Liver Cell failure and had menorrhagia
- Our second patient remained vitally stable ,but developed tetany and had Liver cell Failure
- Both our patients had consumed poison well above fatal dose
- However both our patients recovered well on medical management and are on regular follow up

TAKE HOME MESSAGE

- Start early and give extended administration of N Acetyl cysteine
- Take serial X ray erect abdomen to look for residual poison in intestines in the form of radio opacities and give purgation.
- Transplant Teams to be alerted for a possible requirement of Liver Transplant

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By Zahra

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THANK YOU

A CASE OF PAINFUL SWELLING OF THE LEFT EYE

PRESENTOR : DR. AHSAN FARUQI

UNIT 3

DEPT. OF GENERAL MEDICINE

A 54-year-old male, came with chief complaints of

1) Diminution of vision of Both eyes since childhood
2) Swelling of the left eyelid for 1 month
3) Periorbital pain of the left eye for 14 days.

- Swelling of the left eye was gradually progressive over 1month
- Periorbital pain of the left eye was intense, stabbing type radiating to the retro-orbital region with no aggravating or relieving factors
- Diminution of vision was present in both eyes since childhood gradually progressive in nature.
- There was no history of fever, loss of consciousness & photophobia

PAST HISTORY

- No history of Diabetes, Hypertension, Tuberculosis, or Malignancy.
- No history of trauma
- No Past surgical history.
- No significant personal or family history

GENERAL EXAMINATION

- Conscious, well-oriented to time, place, person
- Afebrile
- Pulse: 80bpm , regular, all peripheral pulses palpable
- BP: 110/70mmhg in the right arm, supine position
- Spo2: 99% on room air
- Bsl Random: 130mg/dl
- No Pallor ,icterus, cyanosis, clubbing, lymphadenopahy, oedema, rash was present

SYSTEMIC EXAMINATION

• CNS EXAMINATION :

Higher Mental Function Examination:

The patient was conscious, oriented to time, place, person

Cranial Nerve Examination :

II:

	LEFT EYE	RIGHT EYE
Visual Acuity	Hand Movement	Perception to light absent
Colour Vision	Could not be assessed	Could not be assessed
Fundoscopy	Pigmentation in a Bone Spicule configuration was present on the mid periphery, Optic atrophy with attenuated vessels.	Pigmentation in a Bone Spicule configuration was present on the mid periphery, Optic atrophy with attenuated vessels.

- III, IV, VI:

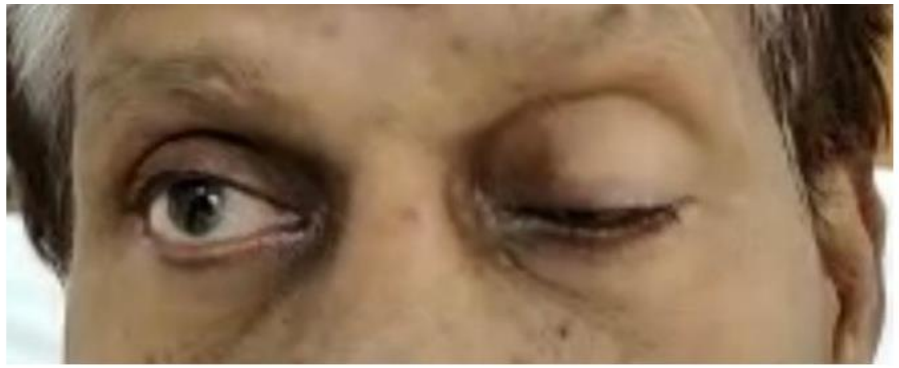
	LEFT EYE	RIGHT EYE
ExtraOcular Muscle Involvement	All Extraocular muscles palsy was noted	No gaze restriction or extraocular muscle involvement was seen
Pupil	4mm	2mm
Nystagmus	Absent	Absent
Ptosis	Complete Ptosis	Absent

- V: Sensation over the face and scalp above the orbit of left side was absent confining to the area supplied by left V1 (Ophthalmic division)

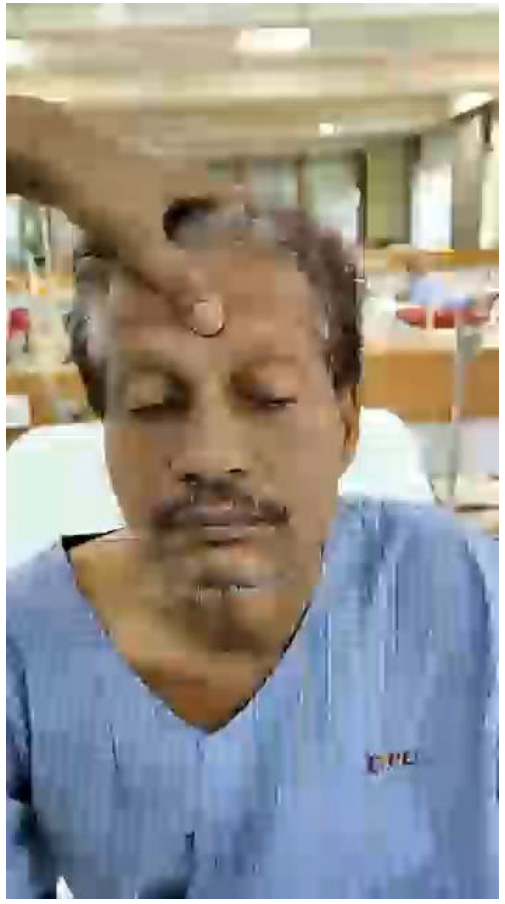
  Corneal sensation of the left eye was absent

- Examination of C.N. I, VII, VIII, IX, X, XI, and XII were normal
- Motor Examination: Power 5/5 in both upper and lower limbs, Normal Tone, Reflexes normal
- Sensory Examination: Normal

- **Cardiovascular System:** S1 S2 present
- **Respiratory System:** Bilateral Normal Vesicular Breath Sounds present
- **Per Abdomen Examination:** Soft , Non Tender, No Organomegaly



Left Eye Complete Ptosis with Left Upper Eyelid Swelling



Video showing normal functioning of right extraocular muscles and complete ptosis and swelling of the left eyelid

DIFFERENTIAL DIAGNOSIS:

- Infections: Mucormycosis, Aspergillosis, Tuberculosis, Bacterial
- Tumours: Pituitary Macroadenoma, Meningioma
- Cavernous Sinus Thrombosis, Cartoid Cavernous Fistula
- IgG4 Disease, Sarcoidosis, Granulomatosis with Polyangitis
- Tolosa Hunt Syndrome

COMPLETE BLOOD	COUNT
Hb:	14.50g/d
TLC	10,900/µL
Platelet count:	3,08,000
PCV	30.80 %,

PERIPHERAL	BLOOD SMEAR
R.B.C.	Mild anisocytosis
W.B.C.	Mild polymorphonuclear leucocytosis
Platelets	Adequate
ESR	15 mm/hr
hsCRP	10 mg/L
Sr.Procalcitonin	0.06
Sr.ACE	20 micrograms/L
KOH Nasal swab	No growth
Blood culture	No growth

LIVER FUNCTION	TEST
Bilirubin-Total	0.84mg/dL
Bilirubin-Conjugated	0.32mg/dL
Bilirubin-Unconjugated	0.52mg/dL
SGOT (AST)	67U/Lt
SGPT (ALT)	25U/Lt
ALP	103U/Lt

RENAL FUNCTION	TEST
Creatinine	0.93mg/dL
Urea	18mg/dL

S. PROTEINS	
Proteins (total)	7.60g/dL
Albumin	4.10g/dL
Globulin	3.50g/dL
Vitamin B12	344.0 pg/mL

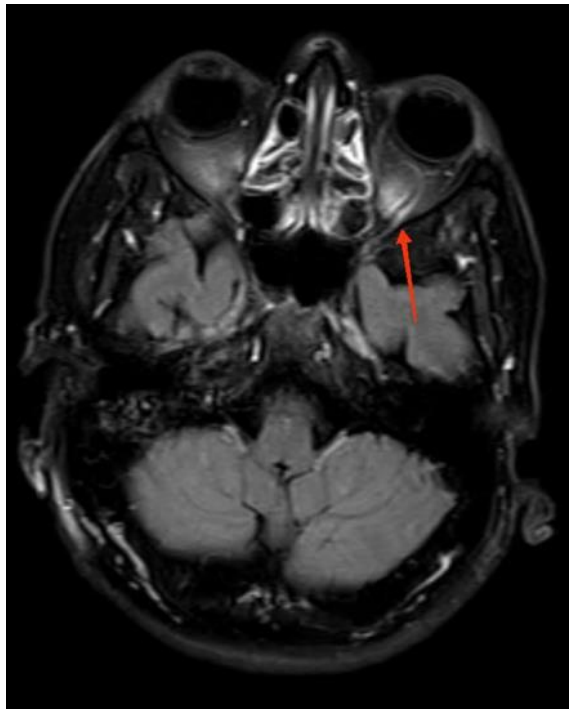
ELECTROLYTES	
Sodium	135.00 mmol/L
Potassium	4.80 mmol/L
Chloride	83.00mmol/Lt
Magnesium	1.80
Calcium	8.90 mg/dL

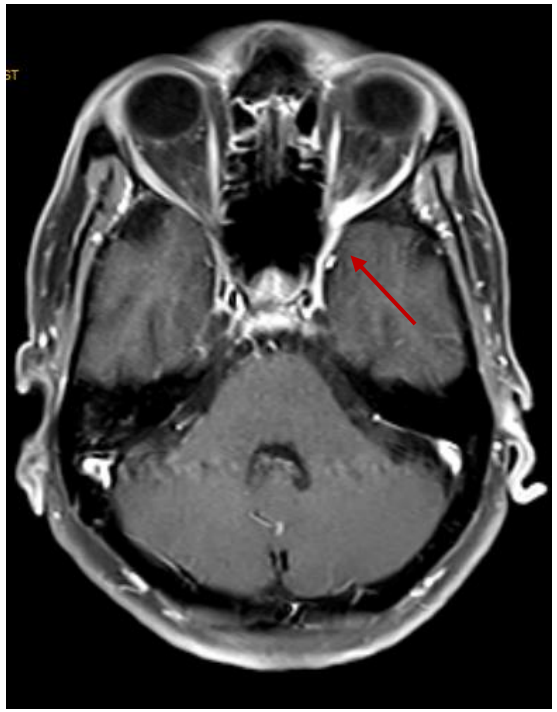
SEROLOGY	
HBsAg	Non-reactive
HCV-Ab	Non-reactive
HIV-Combo	Non-reactive

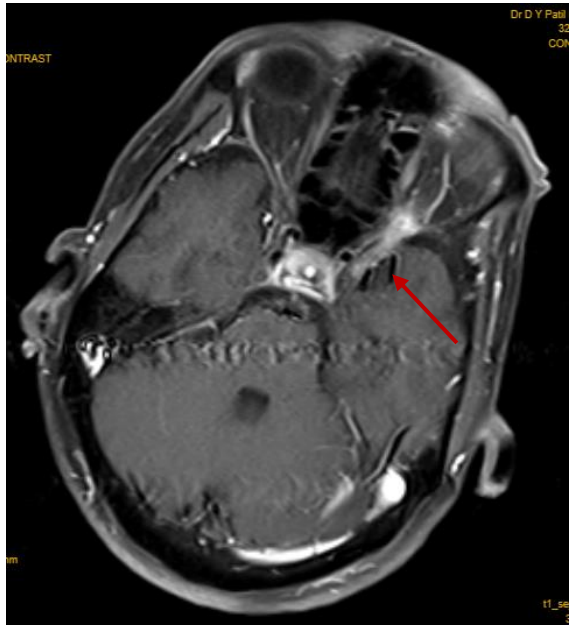
Thyroid Profile	Normal
dsDna	Negative
Sr.Prolactin	Normal
C-ANCA	Negative
COVID RTPCR	Negative
IgE	26 IU/ml

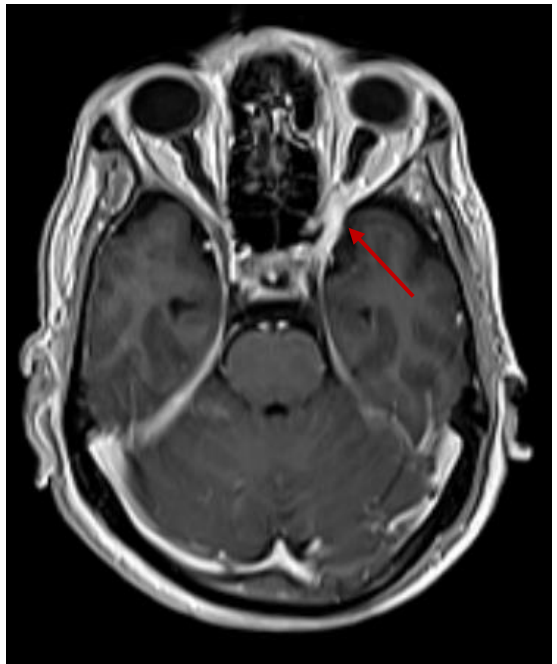
CSF ROUTINE EXAMINATION	
Appearance	clear
Cobweb/Coagulum	Absent
Deposits	Absent
Proteins	29.30
Glucose	60
RBC's	absent
Total Leucocyte Count	2
Neutrophils	0%
Lymphocytes	100%
Mesothelial/Macrophages	0%
Pleomorphic Cells	0%
CSF culture	No growth of organism
CSF CBNAAT	Negative

USG A+P	No Obvious Abnormality Detected
Chest XRay	No Obvious Abnormality
ECG	Normal Sinus Rythm









On MRI Brain & Orbit Contrast Studies:

An Ill-defined soft tissue intensity is noted in the Left orbital apex, superior orbital fissure, and adjacent anterior portion of the left cavernous sinus, abutting the adjacent optic nerve.

It appears isointense on T1WI and iso to hyperintense on T2WI with small focus of diffusion restriction on DWI. The soft tissue shows homogenous post-contrast enhancement.

- Based on MRI findings and negative laboratory investigations, other differential diagnoses were ruled out and the diagnosis of Tolosa Hunt with Bilateral Eye Retinis Pigmentosa was considered

TREATMENT

- The patient was given Injection Methylprednisolone 1gm iv OD for 3 days f/b Oral Prednisolone 60mg OD for 2 weeks
- Partial Resolution of Ptosis and gaze improvement was seen after 3 days of treatment and full resolution post 2weeks of treatment

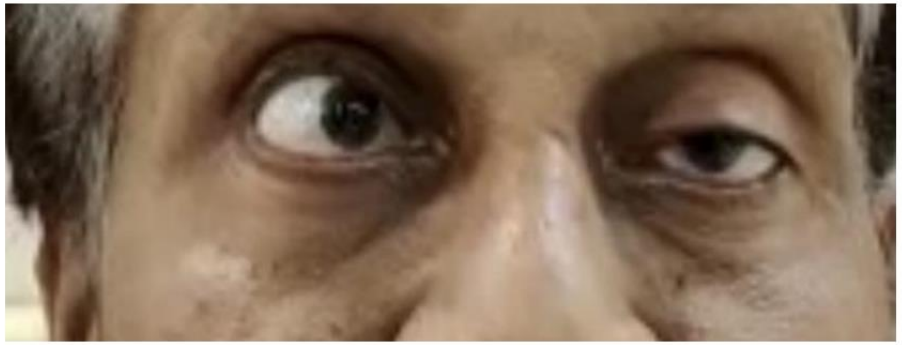


Image showing Left Eye Ptosis resolving, after 3 days of Inj. MPS 1gm iv OD

Video showing Improvement of Ptosis and Extraocular muscles function of the Left Eye

DIAGNOSIS:

- Based on Clinical examination, Negative Laboratory Investigations, MRI findings, Responsiveness to corticosteroid treatment, and excluding other differentials, a diagnosis of **TOLOSA HUNT SYNDROME with BILATERAL EYE RETINITIS PIGMENTOSA** was made

DISCUSSION:

- Tolosa-Hunt syndrome can be seen affecting people of any age from the 1st to the 8th decade of life, with no gender predilection.
- Either side may be affected, with case reports of bilateral simultaneous involvement.
- Most patients complain of pain, which is the main symptom. The pain lasts for an average of 8 weeks if untreated.
- Ocular motor cranial nerve palsies may coincide with the onset of pain or follow it within a period of up to 2 weeks.
- It is usually described as “intense”, “severe”, “boring”, “lancinating”, or “stabbing”.
- It is periorbital/retroorbital in location, frequently extending into frontal, and temporal regions of the face.

- At times, optic nerve dysfunction has been reported with Tolosa-Hunt Syndrome, indicating that the pathological process may involve the orbital apex also. The optic disc might be normal, swollen, or pale in appearance, and visual acuity may be minimal or leading to blindness. Loss of visual acuity is variable and unpredictable and on occasionally be permanent.
- Treatment generally consists of a high dose of corticosteroids.

TAKE HOME MESSAGE:

- Clinicians need to be aware of the different causes of painful ophthalmoplegia, including the less common presentations.

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THANK YOU

AN UNUSUAL CASE OF FEVER WITH RASH

PRESENTOR : DR. HANSINI REDDY

UNIT - 4

DEPARTMENT OF GENERAL MEDICINE

A 19yr old male presented with complaints of

- High grade fever with chills with headache & giddiness since 4 days
- Petechial rash and purpura in both upper limb and lower limbs since 3 days
- 1 episode of **hematemesis** 2 days back
- **Epistaxis** , continuous since 1 day
- Cold and nasal congestion with grade 2 MMRC **breathlessness** since 1 day
- Patient developed **hemoptysis** on 2nd day of admission

- No H/O Burning micturition, chest pain, palpitations, abdominal pain, loose stools, altered sensorium, LOC, seizures, joint pains

Past History:

- No H/O similar complaints of bleeding manifestations
- No H/O blood transfusions, COVID infection or medication intake.
- No Thyroid disorders, tuberculosis

Personal History:

- Mixed diet
- Appetite reduced
- Sleep, Bowel and bladder unaltered
- No addictions

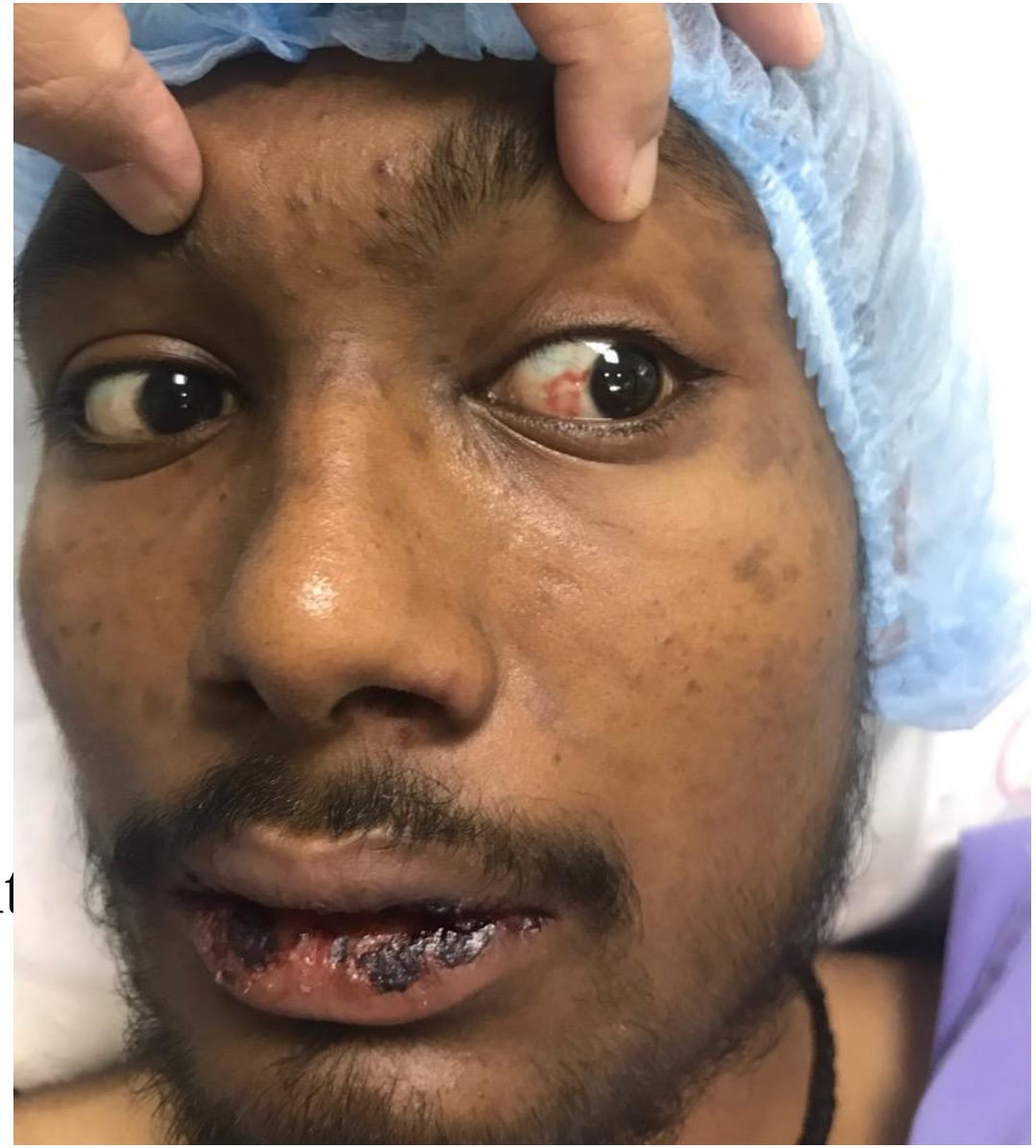
Family history:

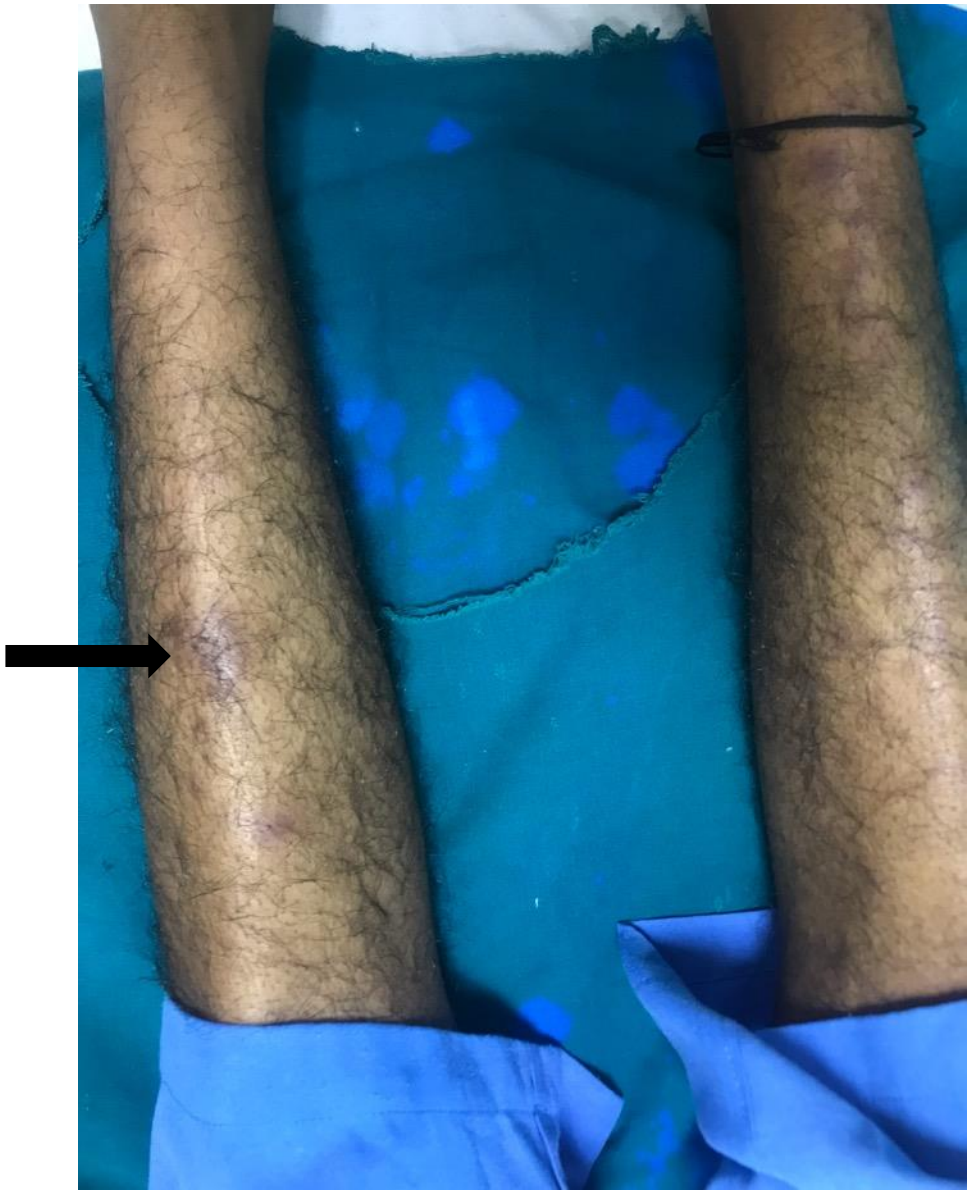
- No significant history

General Examination

- Febrile(101.7F)
- PR: 116/min, regular, peripheral pulsations present
- BP: 110/80mmhg
- RR: 16/ min
- SpO2: 98% @Room air
- Pallor 3+
- No icterus, clubbing, cyanosis, lymphadenopathy, edema
- Sub conjunctival haemorrhages present
- Submucosal bleeding from gums and lips present

Subconjuctival haemorrhages





Palpable purpura

Systemic Examination:

- CVS: S1, S2 +, no added sounds
- RS: vesicular breath sounds present bilaterally. No adventitious breath sounds
- P/A: Soft, non tender . No organomegaly
- CNS: conscious , oriented

WORKING DIAGNOSIS

Due to fever with rash and bleeding diathesis we consider

1) Infectious -

- Dengue fever
- Malaria
- Rickettsial fever
- Brucella
- Leptospira infection
- HIV
- Covid

2)Leukemia

3) Haematological -

- Aplastic anemia
- MAHA
- ITP
- Secondary HLH

4) Autoimmune -

- SLE
- RA
- Sjogrens syndrome
- Still's disease

INVESTIGATIONS

Investigation	Value	Investigation	Value
Hb	4.6	S. Procalcitonin	0.49
TLC	3900	CRP	3.2
Platelet count	20,000	LDH	761
Retic count	10%	Clotting time/bleeding time	WNL
LFT & RFT	WNL	PT-INR	12.1/1.1
HIV/Hbsag/HCV	NR	D-Dimer	1216
RMT/ PS for MP	Negative	Fibrinogen	231
Widal	Negative	Triglycerides	542
Dengue(NS1,IgM)	Negative	PBS	Few schistocytes
Weil felix	Negative	Sputum CBNAAT	Negative
Brucella Ig M	Negative	Blood /urine cultures	No growth
COVID RTPCR	Negative	TFT	Normal

Investigation	Value
Iron	113
Ferritin	884
TIBC	202
Transferin saturation	55.9%
Folic acid	8.5
Vitamin B12	504
Stool occult blood	positive
Stool R/M	WNL
Urine R/M	WNL

- Fundus examination: no retinal haemorrhages
- USG Abdomen: mild hepatomegaly (17cm)
- Chest X-ray and ECG normal
- 2D echo: No RWMA, EF-60%, mild pericardial effusion
- CT brain : normal study

Treatment

DAY 1- DAY 7:

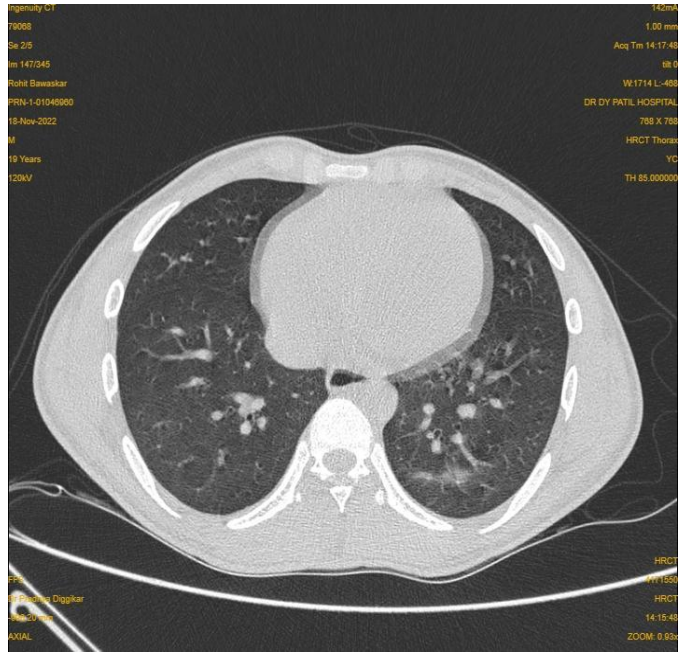
1. T/PR/BP/RR/SPO2 monitoring
2. W/F bleeding, hypotension
3. Inj Ceftriaxone 1gm bd
4. Tab Doxycycline 100 mg bd
5. Total RDP transfusion 16
6. Total PCV transfusion 4
7. IV fluids
8. Inj Tranexemic acid 500mg TDS
9. Inj Ethamlysate 250 mg bd

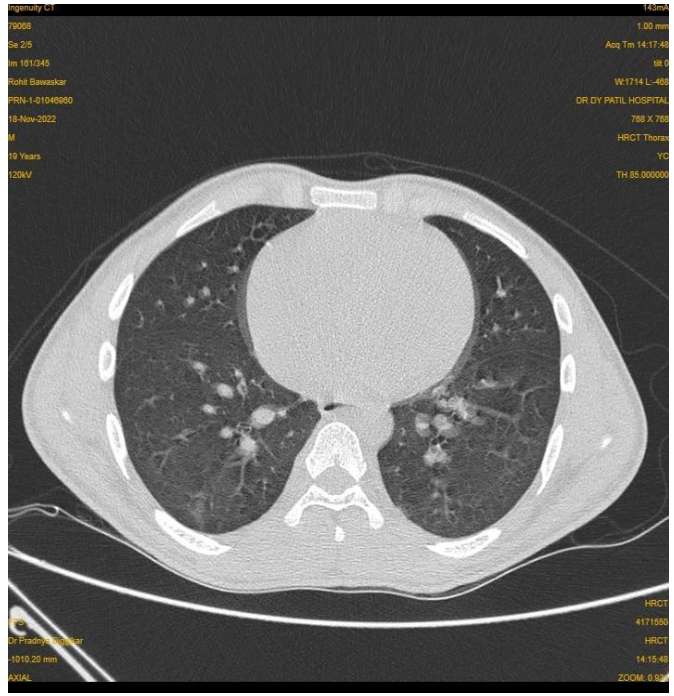
HRCT Thorax

- Multiple areas of patchy subpleural peripheral ground glass opacities are seen

- Centrilobular nodules with tree in bud in posterior segment of lower lobe

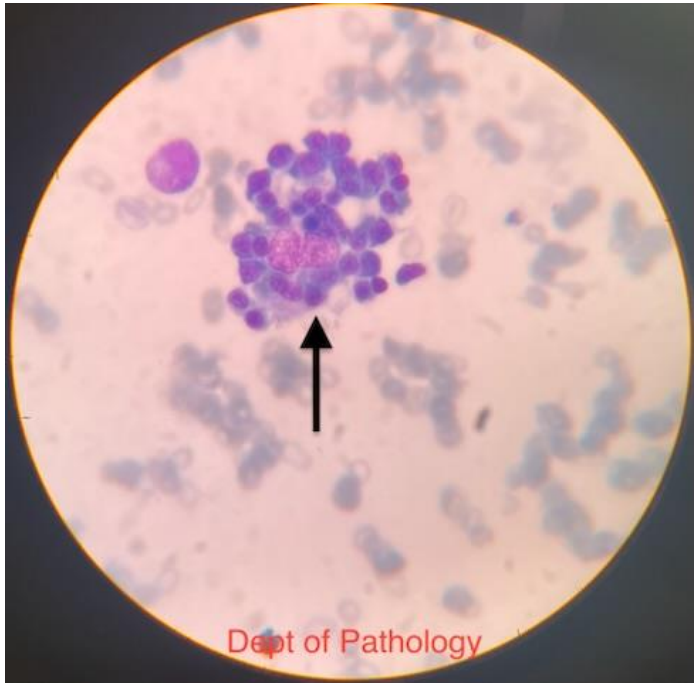
- The above findings suggestive of diffuse alveolar haemorrhages

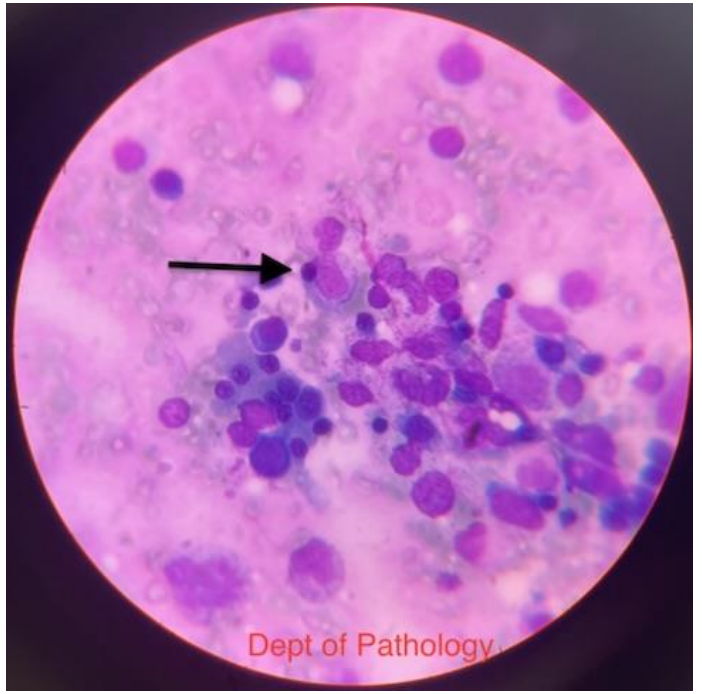




Bone marrow biopsy

- Biopsy shows normal bony trabeculae with few fat spaces.
- Normal hematopoietic cells with erythroid hyperplasia. Megakaryocytes are increased.
- There is evidence of <u>mild hemophagocytosis.</u>
- No evidence of any atypical cells/ granuloma/ fibrosis





Investigation	Value
RA factor	Negative
Direct coomb test	Negative
C3	53mg/dl (decreased)
C4	14 mg/dl (WNL)
ANA by IF	3+ nuclei homogenous
ANA blot	SS-A +ve , Ro- 52 +ve. Ribosomal P +ve, Ku weak positive
Schirmer test	negative
Ds DNA	Positive (78.1)
S. Haptoglobin	WNL
CD 25	Positive

Final Diagnosis

- A diagnosis of Hemophagocytic Lymphohistiocytosis secondary to connective tissue disorder (systemic lupus erythematosus) was made as our patient fulfilled >5 out of 8 diagnostic criteria

TREATMENT on DAY 8:

Hematologist and Rheumatologist was consulted after making a diagnosis of HLH secondary to SLE and pt was advised on :

- Inj Methylprednisolone 1gm IV in 250ml NS for 3 days

Patient was vitally stable & no bleeding manifestations

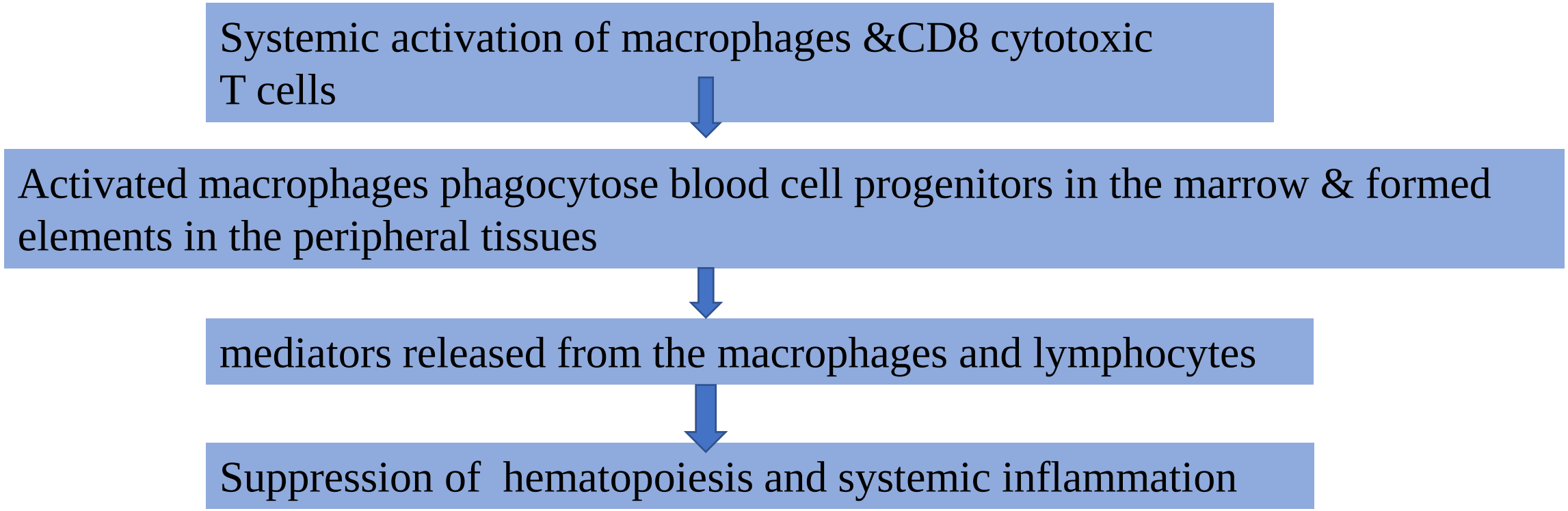
- PR:88/min
- BP: 110/80mmhg
- Hb: 9.6⬆
- TLC: 8900⬆
- Platelet Count : 56000⬆
- Subconjunctival hemorrhage & submucosal hemorrhages resolved. Purpura reduced

Patient was discharged on :

- Tab Prednisolone 50mg od
- Tab Azathioprine 50mg bd

Discussion

- HLH is a reactive condition marked by cytopenias & S/S of systemic inflammation related to macrophage activation
- It may be familial & may present early in life, or sporadic and may affect people of any age



- Most patients present with acute febrile illness associated with **splenomegaly & hepatomegaly**
- Laboratory studies typically reveal pancytopenia and very high levels of plasma ferritin and soluble IL-2 along with elevated LFT and triglyceride levels
- Coagulation profile may show disseminated intravascular coagulation
- If left untreated , might lead to multi organ failure , shock & death
- Treatment involves use of immunosuppressants and mild chemotherapy. The treatment of this condition requires aggressive immunosuppression with either the cytotoxic agent etoposide or anti–T-cell antibodies

- Once remission has been achieved, HSCT should be performed, since it provides the only curative form of therapy.
- Acquired forms of HLH are more commonly observed in adults as a complication of infection(EBV), malignancies or autoimmune diseases(like SLE) or sometimes on its own
- HLH secondary to SLE is a rare clinical entity with an estimated prevalence of 0.9-4.6%. The diagnosis of HLH secondary to SLE is complicated because they both have overlapping symptoms

Revised diagnostic guidelines for HLH

- The diagnosis of HLH is established if one of either 1 or 2 below is fulfilled

1) A molecular diagnosis consistent with HLH

2)diagnostic criteria for HLH is fulfilled (5 out of the 8 criteria below)

- Fever
- Splenomegaly / hepatomegaly
- Cytopenia (>2 of 3 lineages in peripheral blood)
- Hypertriglyceridemia (>265) and/or hypofibrinogenemia (<1.5G/dl)
- Hemophagocytosis in bone marrow , spleen or LN
- Low / absent NK Cell activity
- Ferritin >500mg/L
- Soluble CD 25(soluble IL-2 receptor) >2400U/L

Take home message

- The diagnosis of HLH needs to be considered in the differential diagnosis for any patient presenting with unexplained fever, cytopenia & hepatosplenomegaly
- Mortality in secondary HLH has been reported to vary from 8–22% in rheumatologic HLH to 18–24% in EBV HLH.
- So prompt recognition and timely treatment are crucial to prevent end organ irreversible damage

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THANK YOU

UNUSUAL CASE OF HEPATOMEGALY

PRESENTOR : DR. KALYAN REDDY

UNIT 5

DEPT. OF GENERAL MEDICINE

CASE:

28 year old male presented with complaints of –

- Severe abdominal pain in the right hypochondrium since 4 days
- Jaundice noticed since 4 days
- Vomiting since 2 days
- Disorientation and irrelevant talk since 1 day
- No history of fever, loose stools, abdominal distention
- Non alcoholic
- Patient had similar complaints of abdominal pain, vomiting 6 months back.

CLINICAL EXAMINATION

General examination:

- Pulse -106/min
- Bp -110/70 mm Hg
- Spo2 -98 % on Room air
- Afebrile

- Pallor present
- Icterus present
- No clubbing, cyanosis, lymphadenopathy, edema

Systemic examination:

- **CNS** : Patient was conscious but not oriented to time, place and person

1. Irrelevant talks present
2. Flaps present

- **Per Abdomen**:

1. Liver enlarged
2. Liver span – 20cms
3. Soft in consistency, smooth surface with rounded borders, tender on palpation
4. No evidence of free fluid
5. No other organomegaly

- **CVS, RS : No abnormality detected**

LABORATORY PARAMETERS

HB	8.60gm/dl
TLC	7600
PLATELETS	89000
TOTAL/DIRECT BIL	2.89/1.12mg/dl
SGOT	63 U/L
SGPT	47U/L
ALP	106U/L

S UREA	20
S CREATININE	1.16
NA+/K+/CL-	137/4.20/107
HIV/HBsAG/HCV HEP-E/HEP-A	NON REACTIVE
BSL	92
AMMONIA	304 ug/dl
PT/INR	19/1.56

RADIOLOGICAL INVESTIGATIONS

I. USG Abdomen and Pelvis-

- Gross hepatomegaly [26cms] with multiple cysts of variable sizes largest cyst of 91x77 mm.
- Kidneys normal.

Differential diagnosis:

1)Congenital cysts of liver

2)Polycystic liver disease

3)Hydatid cyst

4)Metastasis in liver

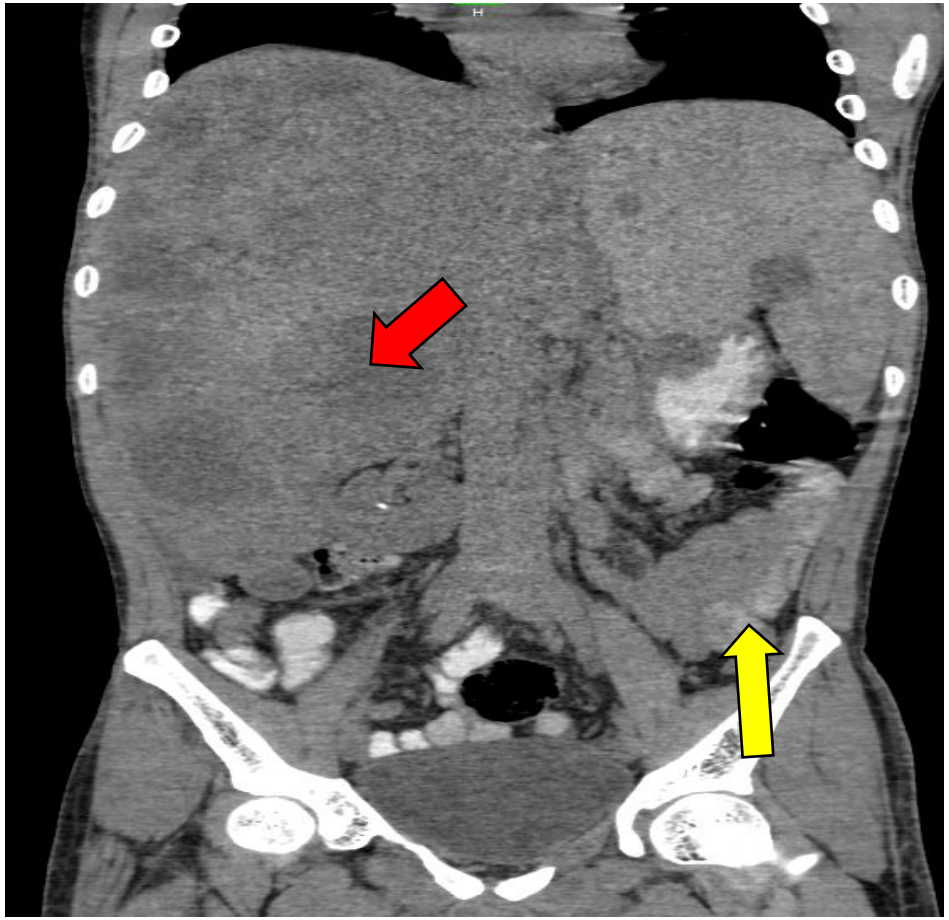


Figure 1

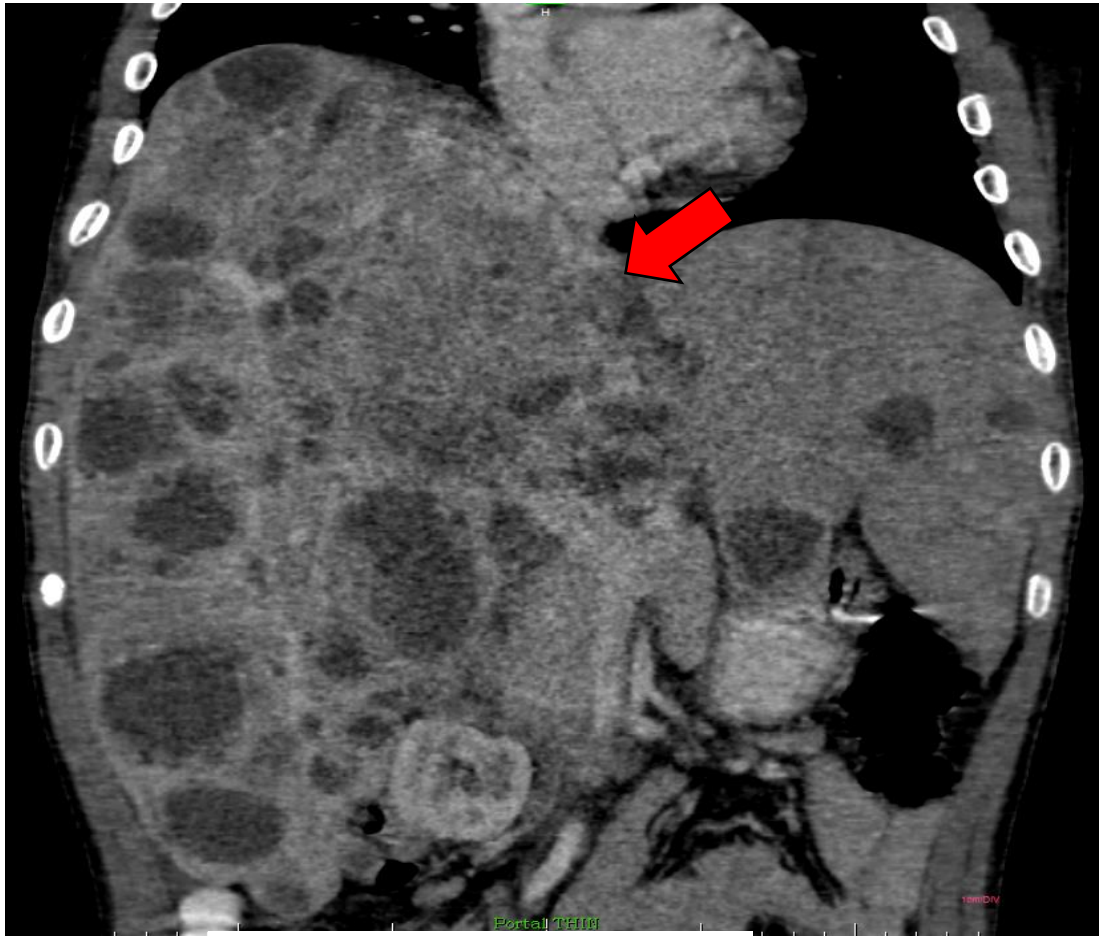


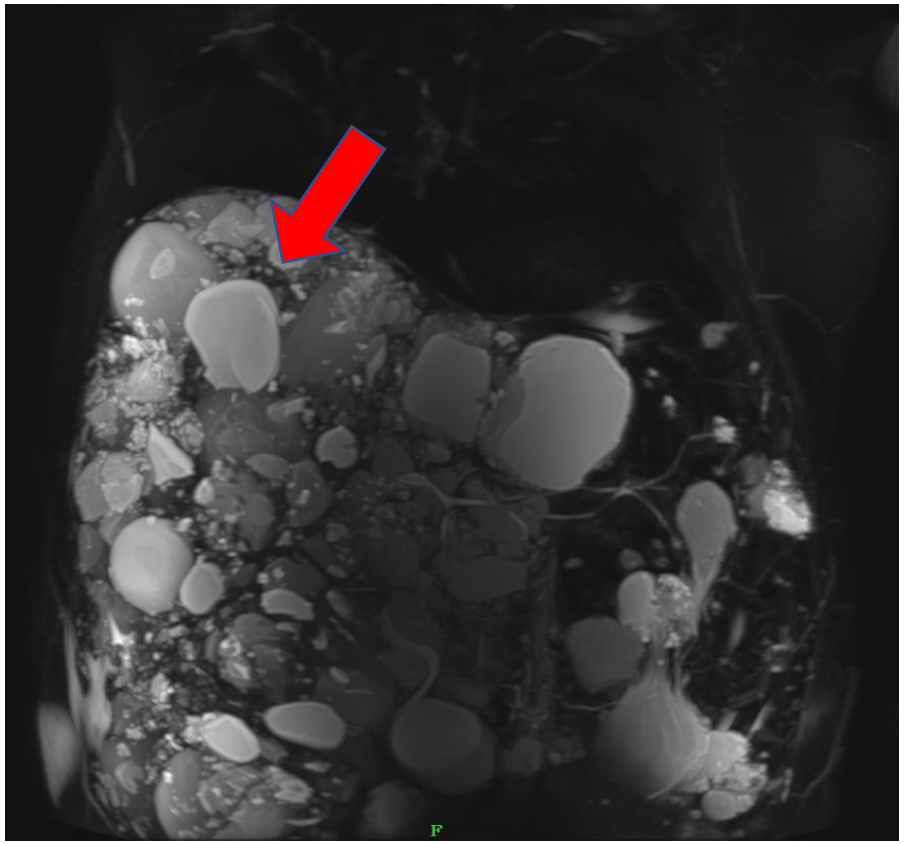
Figure 2

II. <u>CECT ABDOMEN AND PELVIS –</u>

Figure 1 and Figure 2 – (Red Arrow) Gross Hepatomegaly (34cms) with multiple variable sized heterogeneously hypodense cystic lesions and (Yellow Arrow) ,**An ill defined heterogeneously enhancing mass lesion seen in left iliac region in small bowel mesentery likely to be neoplastic.**

III. MRI Abdomen (Plain + Contrast)-

Gross hepatomegaly with multiple variable sized mixed solid-cystic liver lesions, few showing fluid levels and solid enhancing components with mass effect.



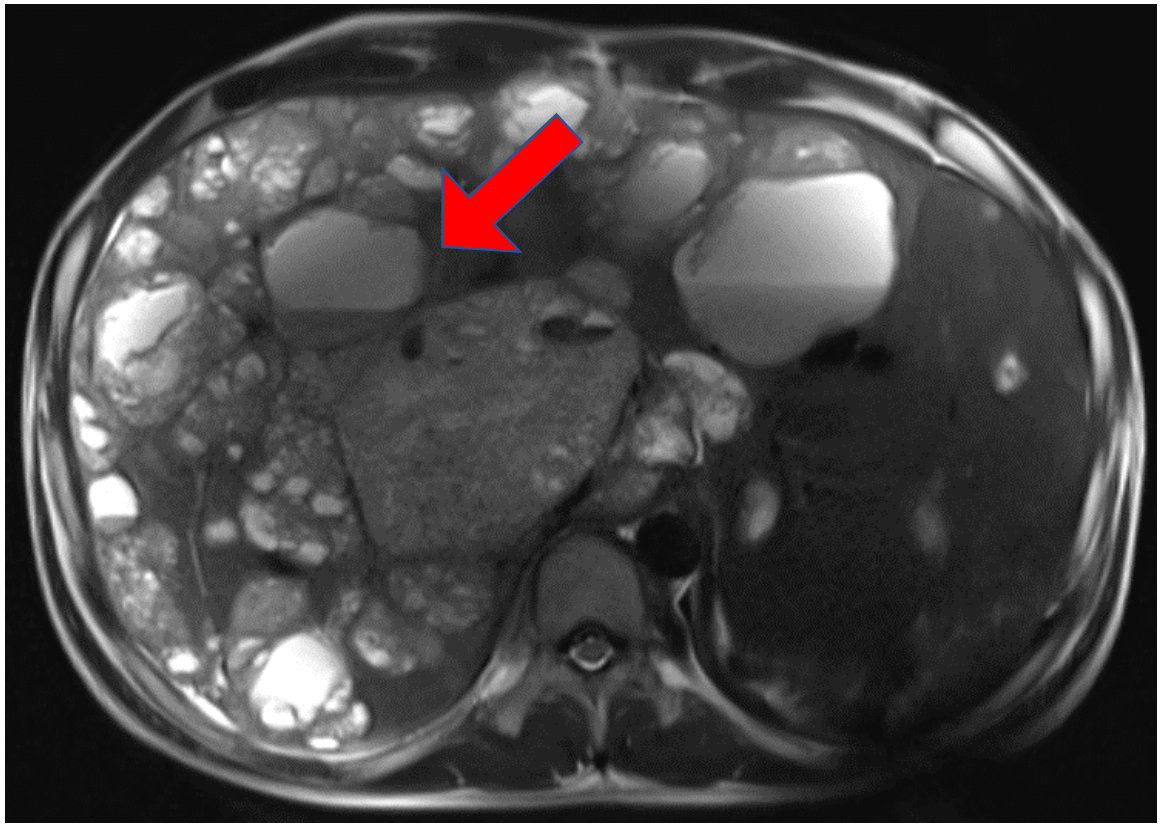
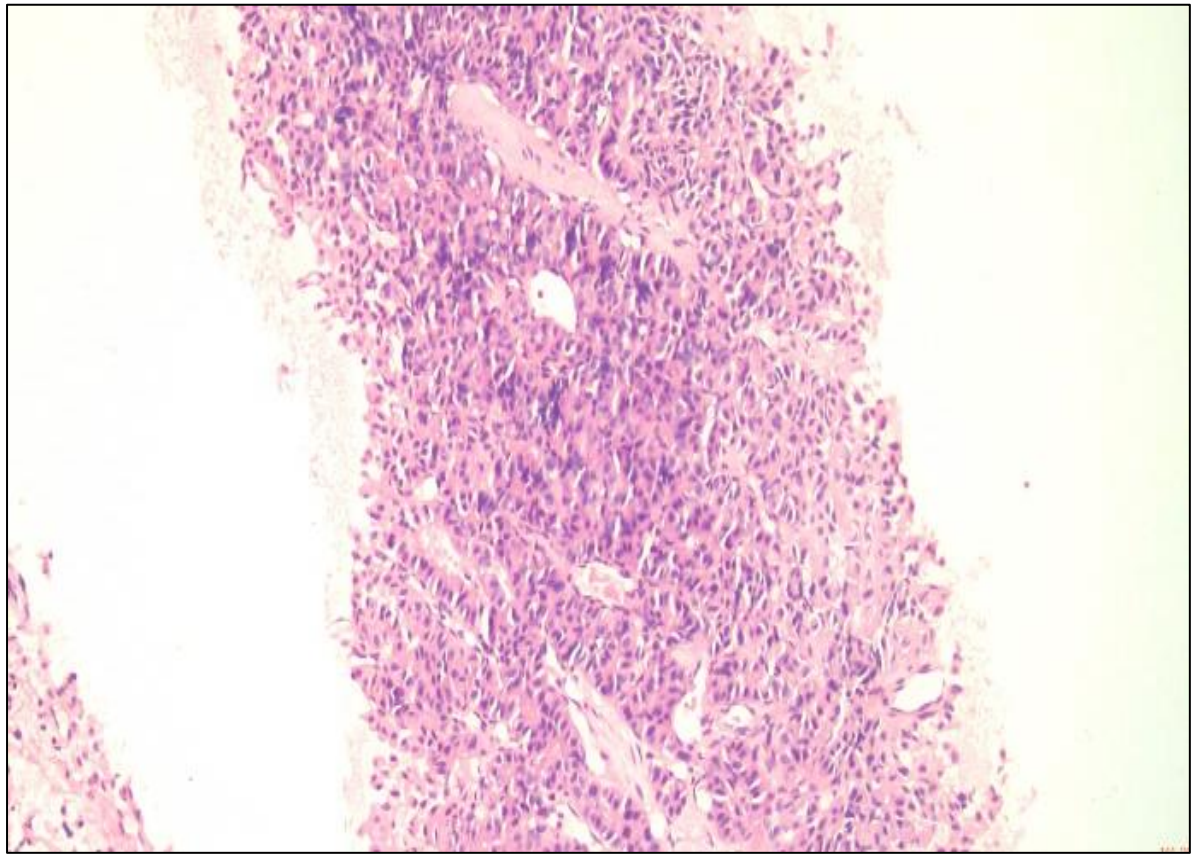
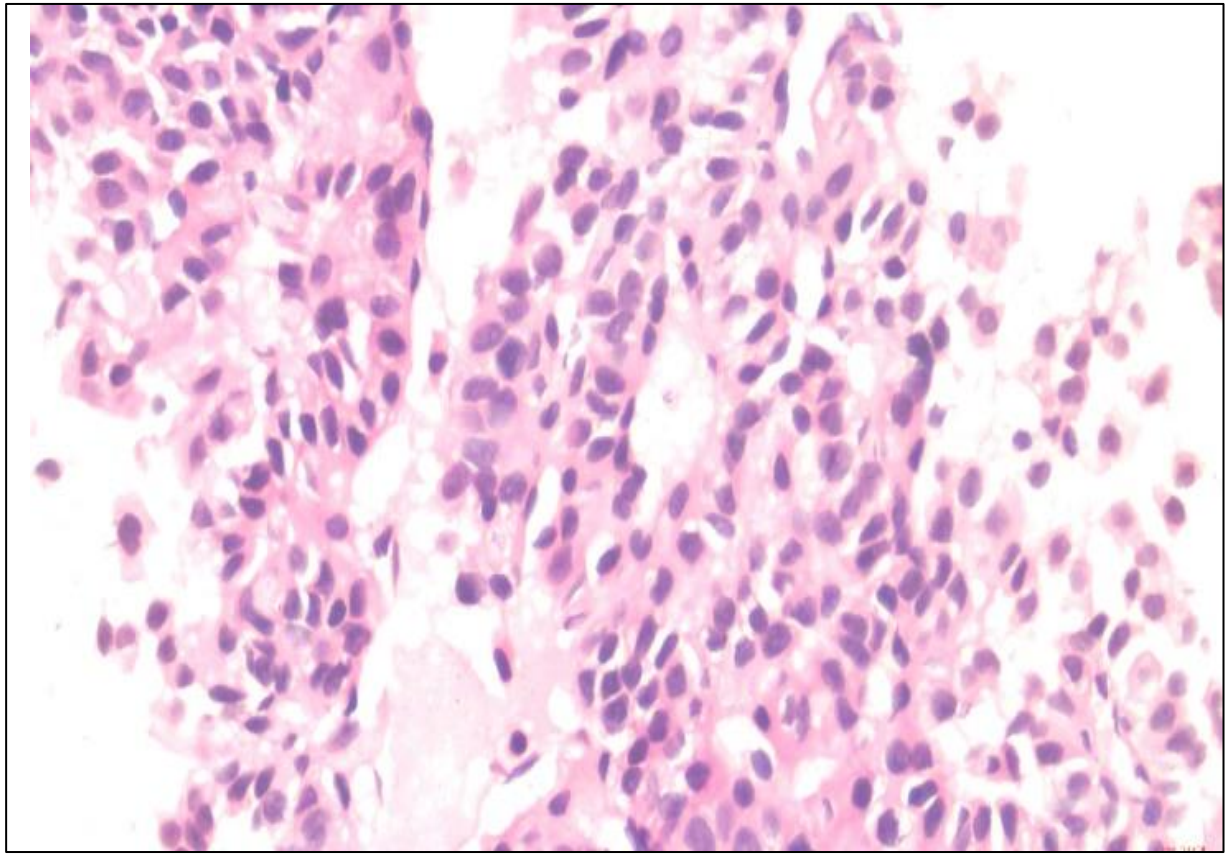


Figure 3 and Figure 4 – Multiple variable-sized solid-cystic lesions replacing liver parenchyma

IV. Liver biopsy – (done after optimization of platelets and PT-INR)



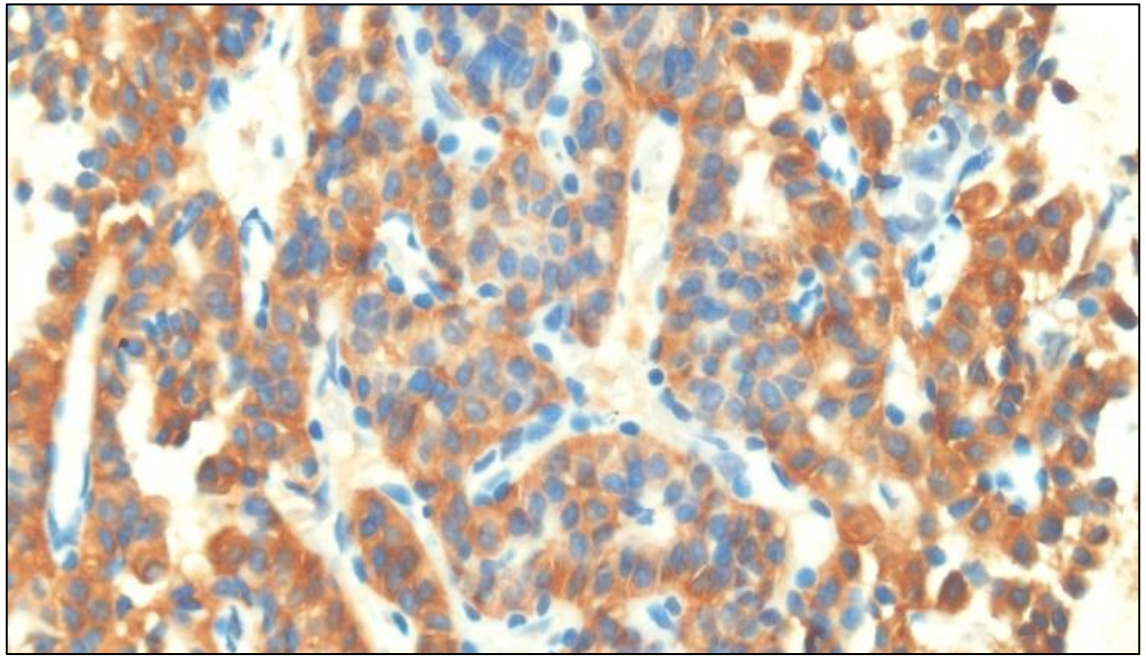
10x section of Liver Biopsy

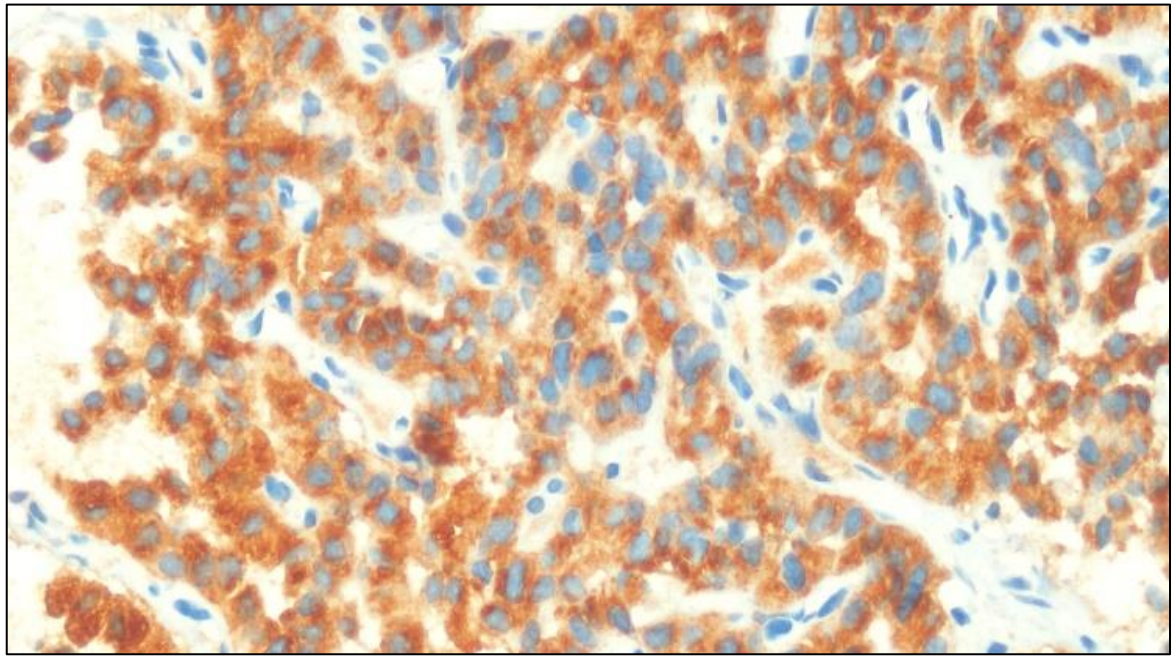


40x section of Liver Biopsy

Microscopic sections from the liver biopsy showed monotonous regular cells with round to oval nuclei, at places showing salt and pepper chromatin and moderate eosinophilic cytoplasm suggestive of well differentiated neuroendocrine tumor.

Special Staining with Chromogranin and Synaptophysin





At higher magnification chromogranin and synaptophysin positivity was noted, multiple tiny tissue cores showing neoplastic cells arranged in cords and trabecular pattern, few foci in solid nests.

V. Special Investigations-

- Serum Chromogranin-A – 4760 ng/ml [Reference value- <108], it is most sensitive marker of neuroendocrine tumor.
- Serum Echinococcus IgG – [0.96] Reference value <9NTU], rules out hydatid cyst.
- Alpha-Fetoprotein – 2.03 ng/ml [Reference value -0 ng/ml to 40 ng/ml], rules out hepatocellular carcinoma.
- Carcinoembryonic antigen –1.55 ng/ml Negative [Reference value 0 ng/ml to 2.5ng/ml].

FINAL DIAGNOSIS

PRIMARY NEUROENDOCRINE TUMOR OF SMALL BOWEL/MESENTERY WITH METASTASIS TO LIVER (MULTIPLE CYSTIC LESIONS)

TREATMENT

Management was as follows –

- INJ CEFTRIAXONE 1GM IV 1-0-1
- INJ PANTOPRAZOLE 40MG IV 1-0-0
- INJ ONDANSETRON 8MG IV 1-1-1
- SYP LACTULOSE 2TBSP 1-1-1
- TAB RIFAXIMIN 550MG 1-0-1
- INJ VITAMIN K 30MG STAT F/B 10MG IV 1-0-0
- IV FLUIDS

Patient was planned for Chemotherapy and Hepatic artery embolization.

DISCUSSION

- Neuroendocrine tumor is a rare tumor of the gastrointestinal system accounting for less than 2% of all GI neoplasms.

- Most neuroendocrine tumors present with secondary metastases to the liver at diagnosis (most common presentation).

- Hepatic artery embolization is frequently done as a palliative technique in patients with hepatic-predominant metastatic NET who are not candidates for surgical resection.

- Young patients with surgically unresectable tumours, hepatomegaly and uncontrollable symptoms, in whom all other therapies have been unsuccessful, may benefit from liver transplantation.

- Immunohistochemistry is performed as the definitive diagnosis for hepatic neuro endocrine tumors.

- It is also associated with immunoreactivity of chromogranin A and Synaptophysin.

TAKE HOME MESSAGE

- Neuroendocrine tumours (NETs) are a rare type of gastrointestinal tumors, often asymptomatic until metastasized.

- In a patient that does not present with symptoms of serotonin hypersecretion syndrome like flushing, diarrhoea and tachycardia, the diagnosis may be missed unless a high index of suspicion is present for Gastrointestinal NETs and their metastases.

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THANK YOU

UNUSUAL PRESENTATION OF LYMPHOMA

Dr Yash Bhimani
Unit 6
Dept. of General Medicine

Case 1

- 70 yrs old male admitted with-
- Precordial chest pain since 1 month
- Breathlessness since 1 month progressed to NYHA class III
- Pedal edema since 12 days.
- No h/o Diabetes mellitus, hypertension, Ischemic heart disease or any other significant disease.

- **General examination**

- Patient was conscious and well oriented to time, place and person.
- Afebrile, Temp – 98.2 F
- P 78/min regular, normal volume tension with all peripheral pulse normal No R-R and RF delay
- BP- 110/80 mmHg in Rt arm in supine position
- RR- 14/min
- Spo2- 98% on RA
- JVP- raised
- Pallor +
- No cyanosis, clubbing, icterus, edema,
- No lymphadenopathy.

- **Systemic examination**

- CVS -Heart sounds were muffled, no murmurs.
- PA- just palpable tender liver
- RS- BAE present with vesicular breathing with B/L basal fine crepitations.
- No obvious abnormality on CNS examination

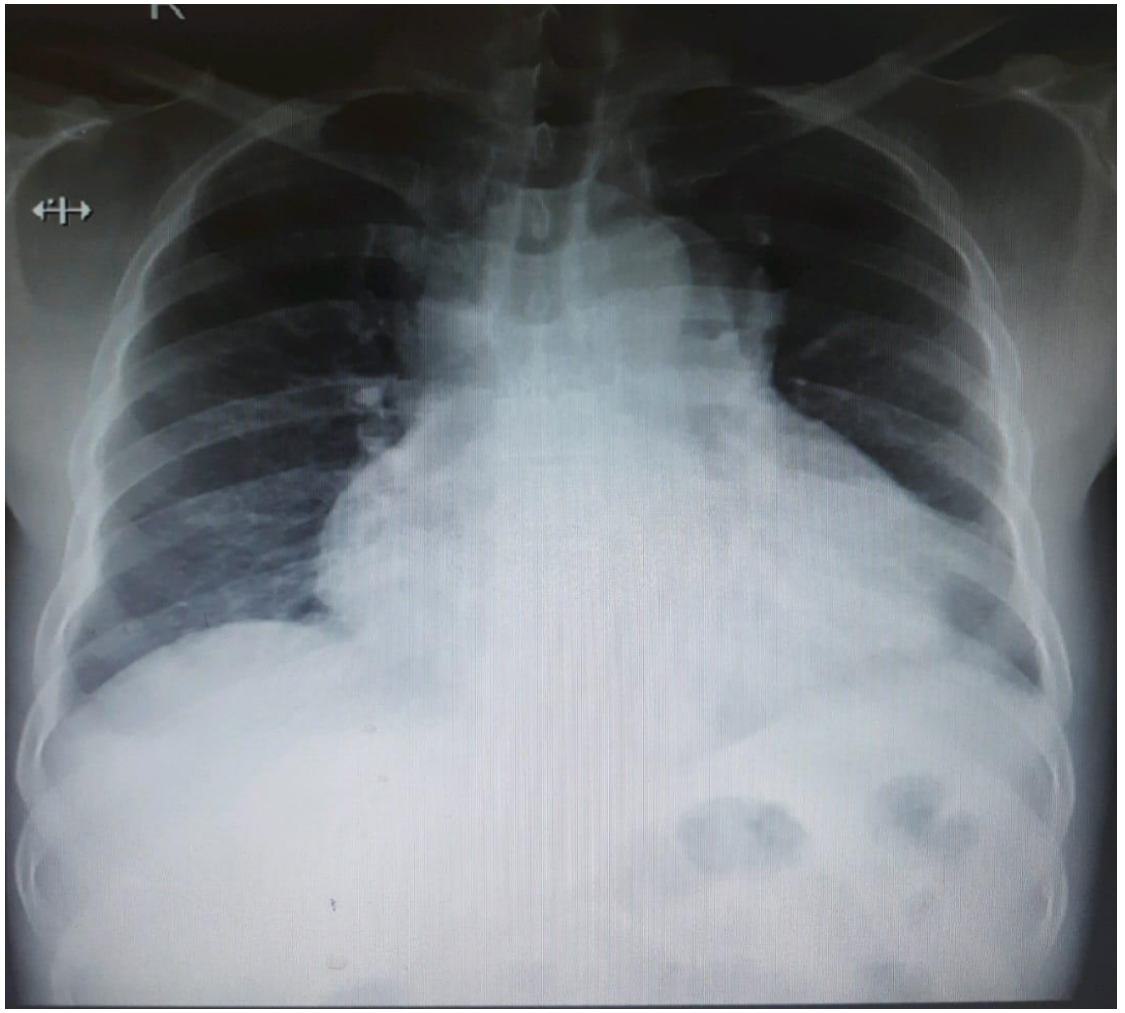
Investigations

Hb	13
TLC	7000
PLT	310000
PCV	31.6
MCV	84.2
Urea	28
Creat	1.06
Total bill.	1.15
Direct	0.48
Indirect	0.67
SGPT	34
SGOT	45
ALP	118

Trop I	27.20
CK MB	17
Pro-BNP	256
Na	137
K	4.50
Cl	102
ESR	44
CRP	5.22

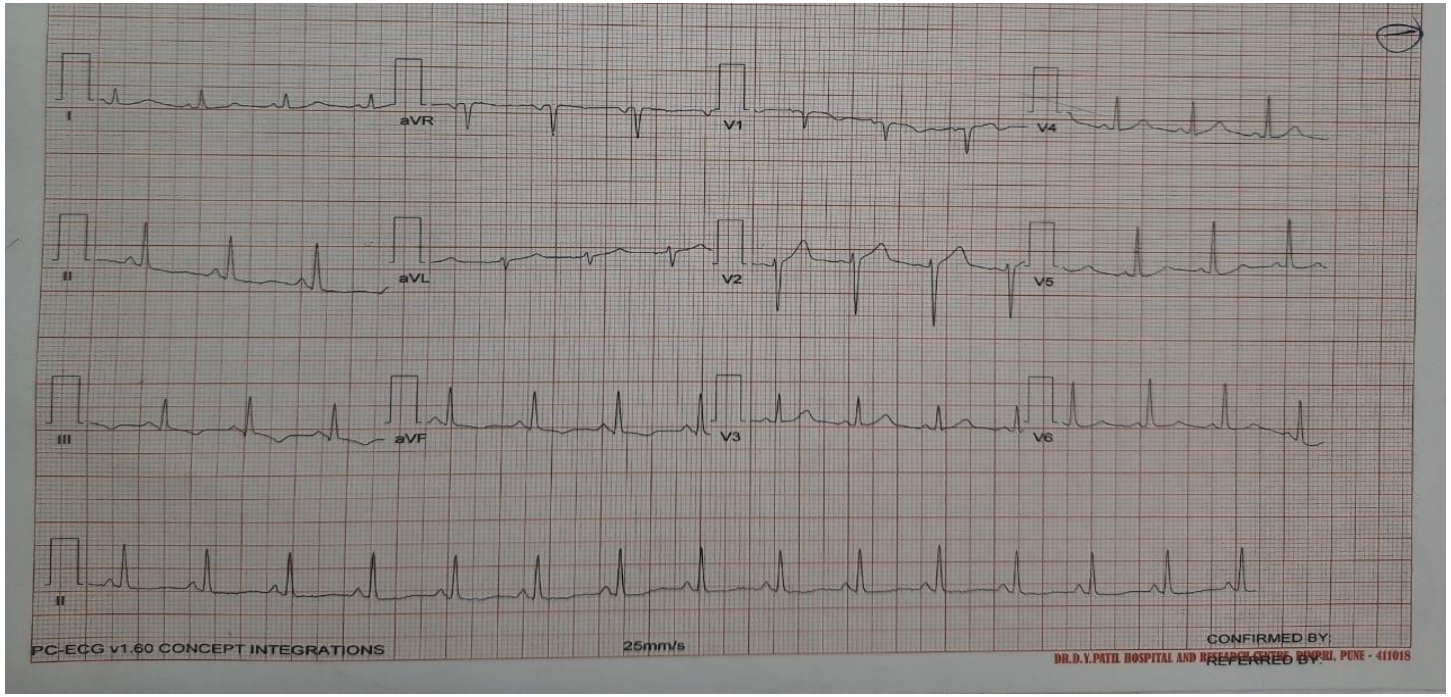
Urine R/M	
Urine R/M	WNL
HbA1c	5.2
PT	P 11.20 C (11.4)
INR	1.13
TFT	Normal
ANA by IF	negative

Chest X-ray



- Chest x ray PA view s/o cardiomegaly with cardio-thoracic ratio (CT ratio) of 65%, mediastinal widening and pulmonary congestion.

- **ECG** was s/o HR of 80 bpm with regular sinus rhythm, with ST-T changes.

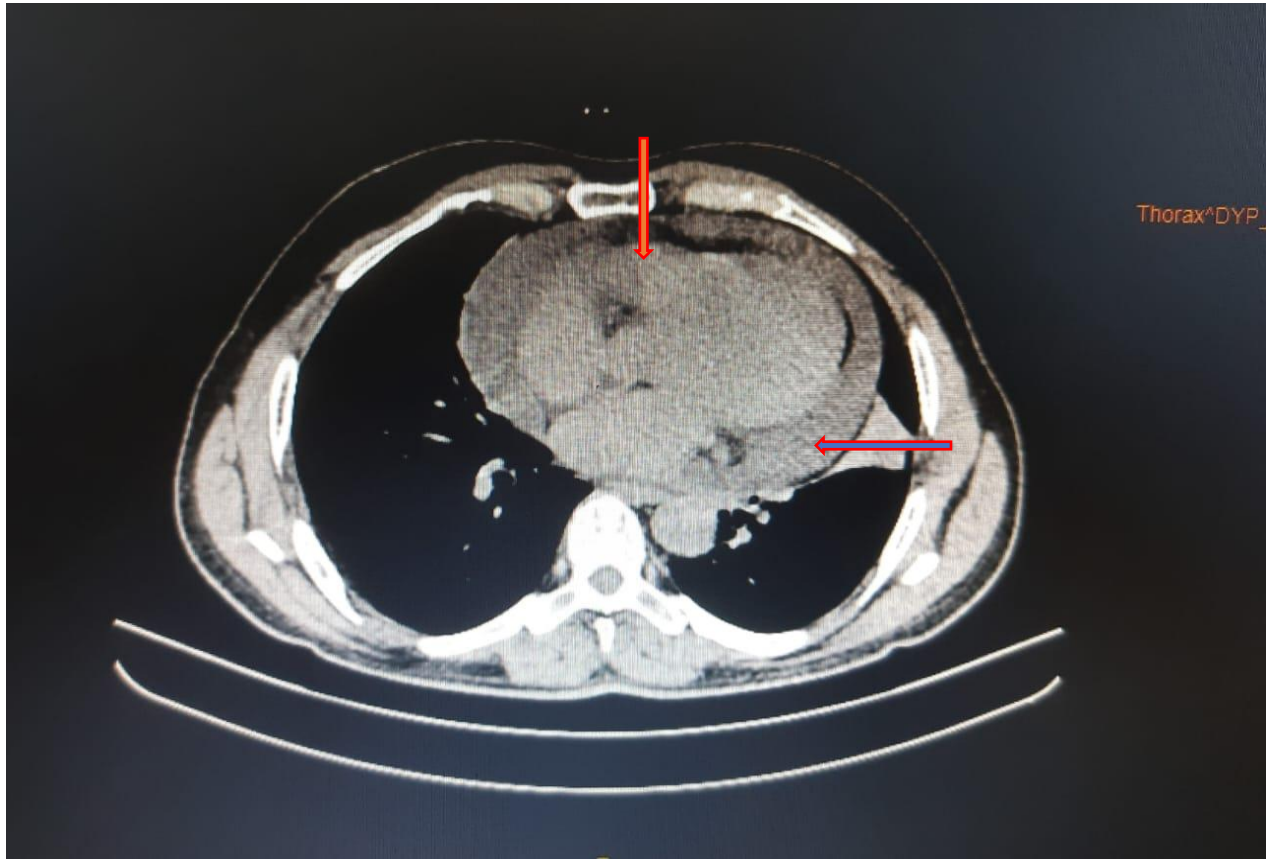


- **2D Echo**
- **Moderate pericardial effusion ,**
- **Posterior to RV- 11mm, posterior to LV- 20mm & posterior to LA- 16mm**
- Grade 1 DD, LVEF- 60%,
- Diuretic therapy was started for CCF and patient was further evaluated.

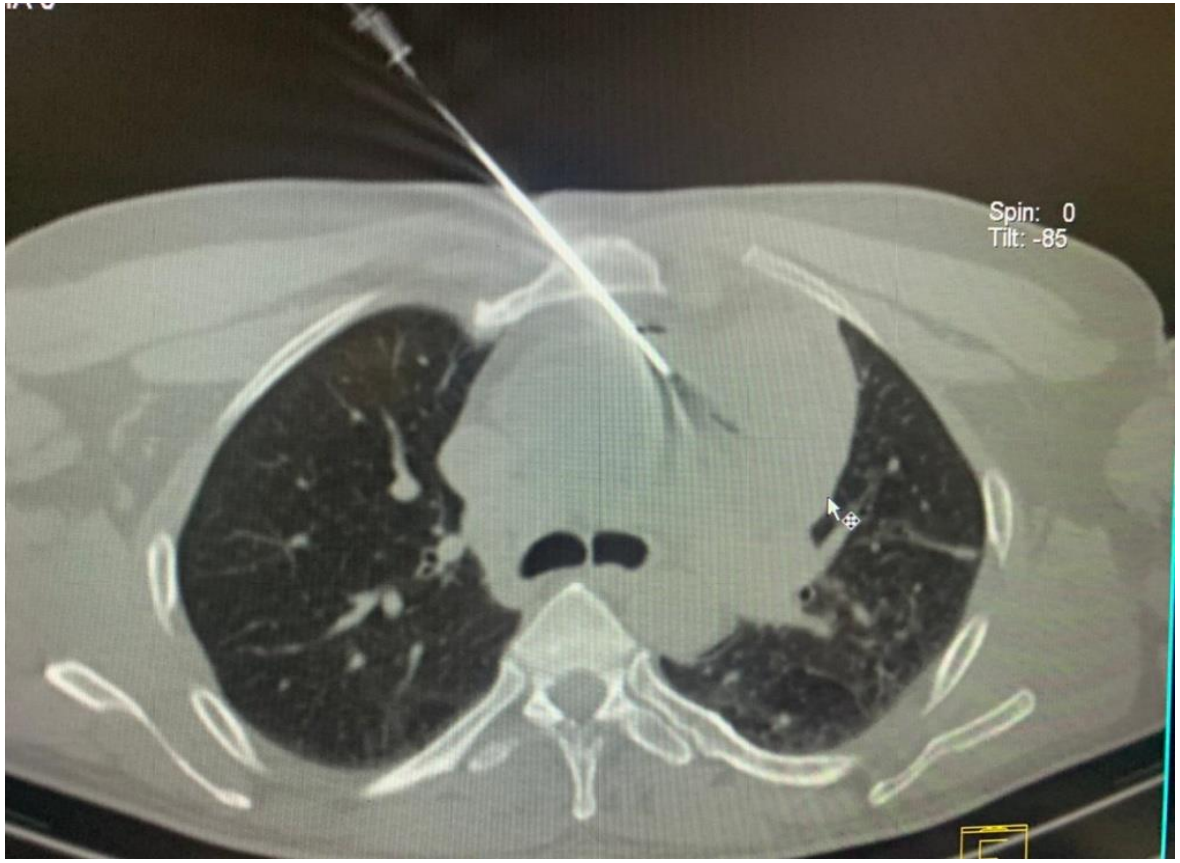
HRCT

- Moderate to gross pericardial effusion.

- Homogenously enhancing mass lesion with epicenter in the left anterior-superior mediastinum.



- Encasing the arch of aorta and extending inferiorly into the middle mediastinum encasing the Ascending aorta, main pulmonary trunk right pulmonary artery and Rt superior pulmonary vein.
- Enlarged LN in pretracheal, paratracheal, pre vascular and aortopulmonary window are seen.

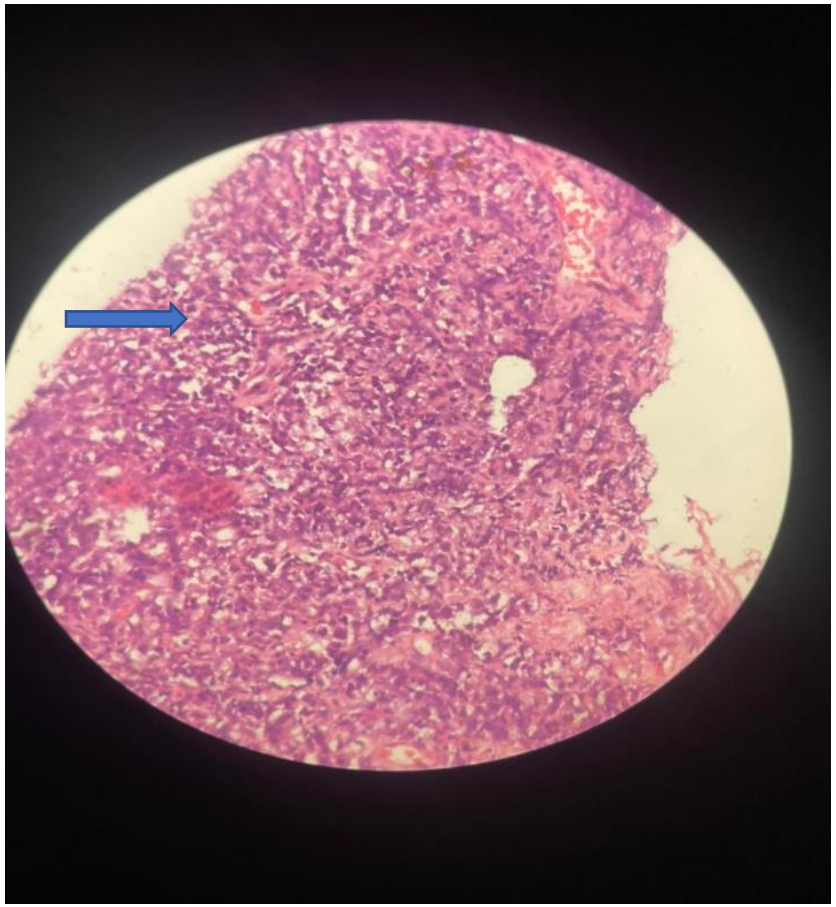


- **For furthur evaluation of Mediastinal mass Tuberculosis/ Lymphoma.**
- CT guided trans-sternal biopsy was taken from the mediastinal mass and sample was sent for the HPE.

Histopathology slides

- HPE of biopsy from the mediastinal mass

- Large cells with irregular nuclear margin and few scattered small lymphoid cells, with some of the cells show large pleomorphic nuclei and pale cytoplasm



➢ s/o Diffuse large B cell Lymphoma

IHC: S/o - CD 20 positive in large cells
- CD 3 positive in background cells
-Ki-67- 80%

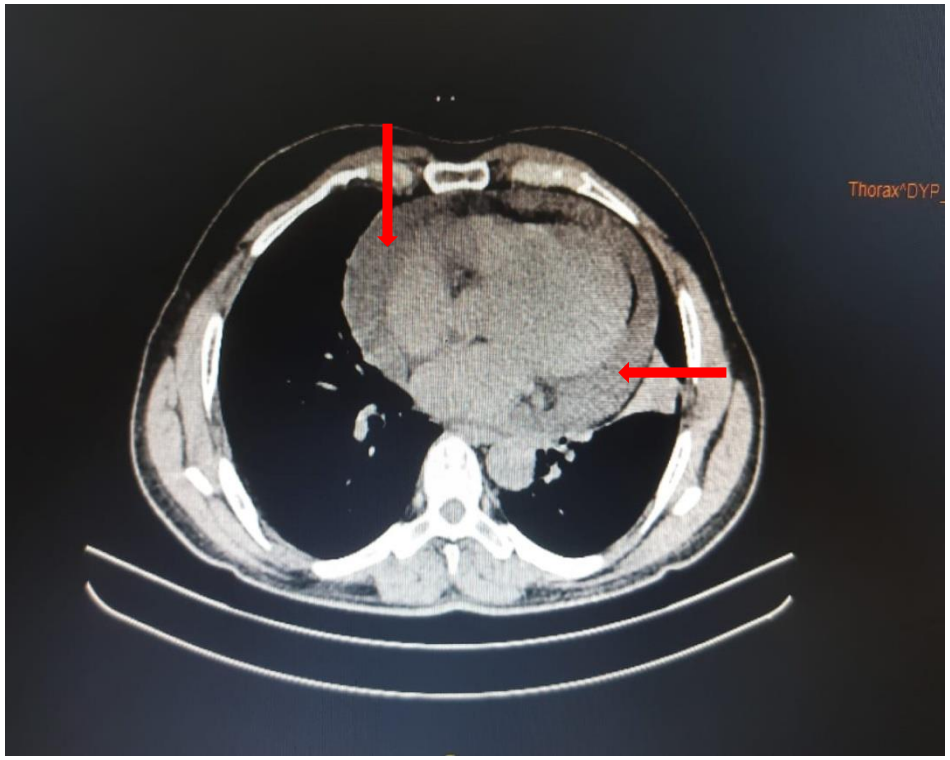
Final diagnosis

Diffuse Large B cell Lymphoma (DLBCL) with pericardial effusion with mediastinal mass.

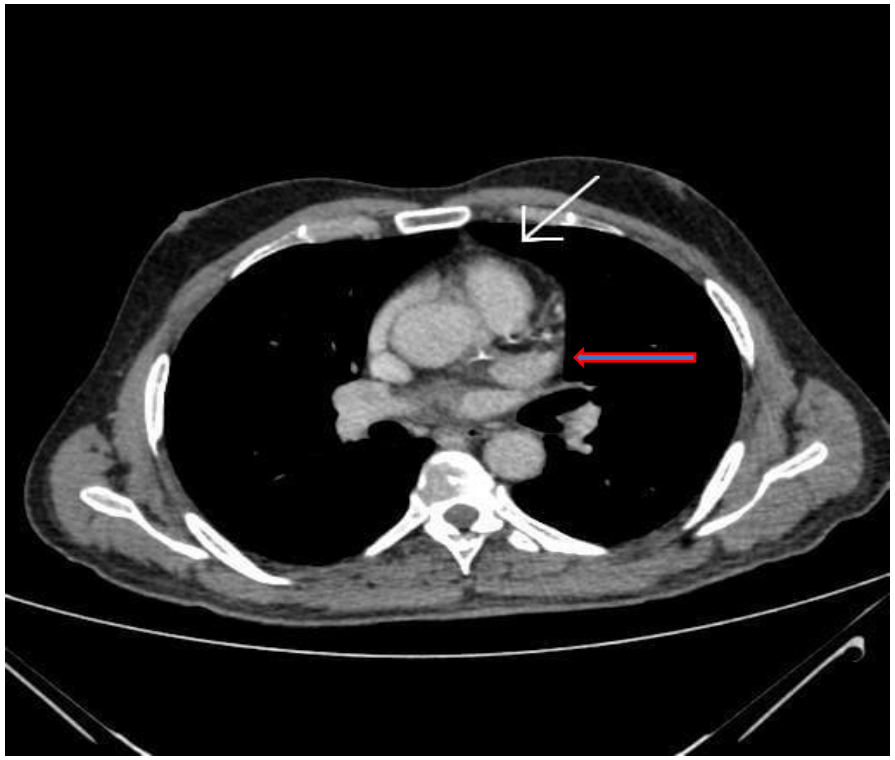
- After the discussion with the Medical oncologist,
- Patient is started on 6 cycles of R-CHOP chemo regimen at an interval of every 21 days.

- **R-CHOP regimen :**
- Inj. Rituximab 500mg iv infusion
- Inj. Cyclophosphamide 900 mg iv infusion
- Inj. Vincristine 2 mg iv push over 10 mins.
- Tab Prednisolone 50 mg BD for 5 days

Mediastinal mass and pericardial effusion on admission



Resolution of mediastinal mass and pericardial effusion after therapy



•Patient is on regular follow up, has completed 6 cycles of chemotherapy, pericardial effusion is resolved and mediastinal mass is also not visualized on follow up HRCT thorax.

Case 2

- 76 yrs old male, Type II DM patient admitted with
  Pain in right hypochondriac region since 12 days,
  High grade fever with chills since 5 days
- Urine R/m s/o 70-80 pus cells.

➢ **Ultrasound suggestive of –**

➢ Few air foci in lower pole calyces-likely s/o B/L **Emphysematous pyelonephritis**.

- Periportal and peripancreatic lymphadenopathy

➢ Inj Piptaz for 21 days and inj Amikacin for 7 days.

➢ Urine C&S E.Coli 1.2 x 10^5

➢ **CECT AP**

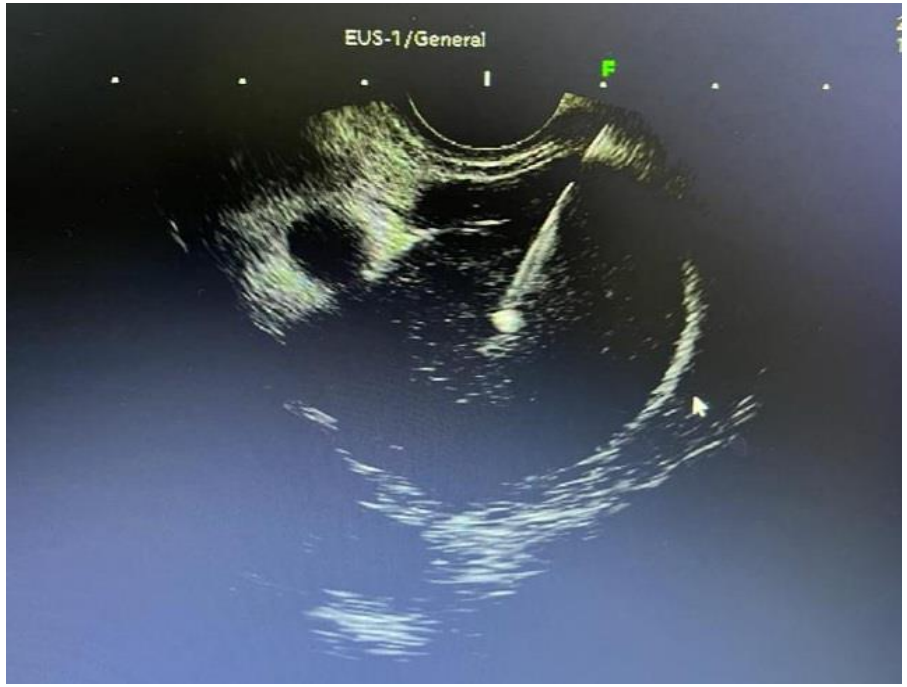
➢ Retro-peritoneal necrotic lymphadenitis in peripancreatic, periportal, paraaortic regeion with largest being **4*5 cm**, with mass effect and compression of lower CBD and mild IHBR dilatation. –

➢ R/o Tuberculosis vs Lymphoma.

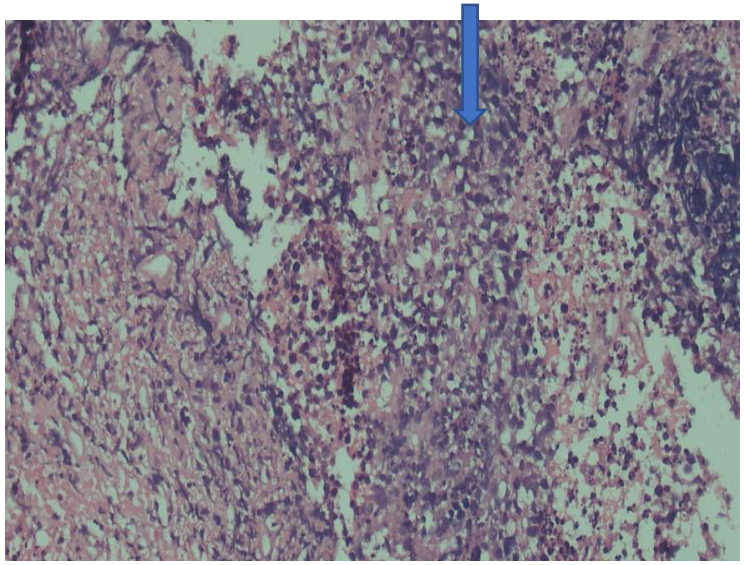
- left renal calculi (**16*11 mm in size**) with air foci in the collecting system- s/o Emphysematous pyelonephritis

Endoscopic USG guided biopsy

EUS showed large necrotic LN between PV and IVC.
Fine Needle Aspiration Biopsy (FNAB) was done and sample was sent for histopathological investigation



HPE- shows a poorly differentiated malignant tumour cells arranged in different sheets. Tumour cells are large in size and have hyperchromatic nuclei, prominent nucleoli and scanty cytoplasm with increased mitoses.
s/o High grade B cell NHL.



Final Diagnosis

High grade B cell Non-Hodgkin's Lymphoma with Emphysematous pyelonephritis with Diabetes mellitus type 2

- After the discussion with the Medical oncologist,
- Patient is advised to complete 6 cycles of R-CHOP chemo regimen therapy at an interval of every 21 days.
- Patient is on regular follow up, has received 5 cycles of chemotherapy out of 6 and is tolerating well.

Discussion

- The term lymphoma identifies a heterogeneous group of biologically and clinically distinct neoplasms that originate from cells in the lymphoid organs.

- A lymph node larger than 1.5 × 1.5 cm that is not associated with a documented infection and that persists longer than 4 weeks should be considered for a biopsy.

- A biopsy should be performed immediately for patients with other findings suggesting malignancy (e.g., systemic complaints or B symptoms, such as fever, night sweats, weight loss)

Usual presentation of patients with Lymphoma

- **Thoracic presentation**

- Cough
- Chest discomfort
- Chest pain
- May be present without symptoms but with an abnormal chest radiograph.

- **Abdominal presentation**

- Chronic pain
- Abdominal fullness
- Early satiety
- Symptoms associated with
  - visceral obstruction
  - acute bowel perforation
  - GI hemorrhage

Unusual presentations of patients with lymphoma

- PMBLs have a female predominance, with median age of 40 years.
- Patient may present with pleural and pericardial effusions.
- Superior vena cava syndrome is a frequent complication.
- An elevated LDH (77%) and B symptoms (47%) are common.
- Relapses occur locally or in extranodal sites, including the liver, the GI tract, the kidneys, the ovaries, and the CNS.
- Patient may present with the renal or any other organ abnormality as a primary presentation

Take home message

- If DLBCL are diagnosed early and treated with R-CHOP regimen, it has 5 years overall survival (OS) rate of 92%, so it’s a highly treatable condition.

- While High grade B cell NHL is having very poor prognosis and if not treated timely can be very fatal.

- Hence there should be high clinical suspicion to diagnose such atypical presentation of NHL, as they are treatable and having good prognosis if treated timely.

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THANK YOU

A CASE OF ACUTE PROGRESSIVE VISION LOSS IN A YOUNG MALE

PRESENTOR : DR. ANIRUDDH WADIVKAR
UNIT – 7
DEPT. OF GENERAL MEDICINE

Clinical History

- 36 year old Male presented with acute onset, progressive loss of vision in both eyes since one week.
- History of intermittent, non-foul smelling, watery loose stools, 4-5 episodes/day for past one month (not investigated for the same).
- No pain, redness, foreign body sensation or watering from eyes.
- No headache or any focal neurological deficits, fever, weight loss or breathlessness.

Alcohol addiction + (20 years, country liquor)

Unsafe sexual practices +

On Examination

- Temperature - Normal
- Pulse – 90/min, regular
- Blood Pressure- 110/70 mmHg
- Saturation – 95% on RA
- Mild pallor present, no icterus, no cyanosis, no clubbing, no lymphadenopathy, no pedal edema.
- On per Oral examination - Candidiasis noted
- RS-NAD CNS-NAD
- PA-NAD CVS-NAD

Ophthalmologic Examination	**Right Eye**	**Left Eye**
Vision	**Perception Of light**	**Perception Of light**
Extraocular Muscle movements	NAD	NAD
Schirmers Test	15mm	12mm
Conjunctiva	NAD	NAD
Cornea	Clear	Clear
Anterior Chamber	Well formed	Well Formed
Iris	NAD	NAD
Pupil	Reactive to light	Reactive to light

Differential Diagnosis

- Central causes - CVA, Multiple Sclerosis, Neuromyelitis Optica
- Drug Induced/Toxin Induced
- Ophthalmologic causes
  - Vasculitis
  - Retinopathy spectrum of disorders
  - CRAO/CRVO
  - Infective causes

Investigations on Admission

Hemoglobin- 10.6 g/dl	CRP- 9
Platelet count -2,34,000	Urine routine and microscopy - normal
Total leukocyte count – 9,000	Stool routine and microscopy - normal
LFT RFT S.Electrolytes-Within Normal Limits	HCV, HBsAg and Serum VDRL- Negative BSL Random-98 mg/dl

- **HIV Serology- POSITIVE**
- **CD4 Count- 12 Cells per cubic millimeter**

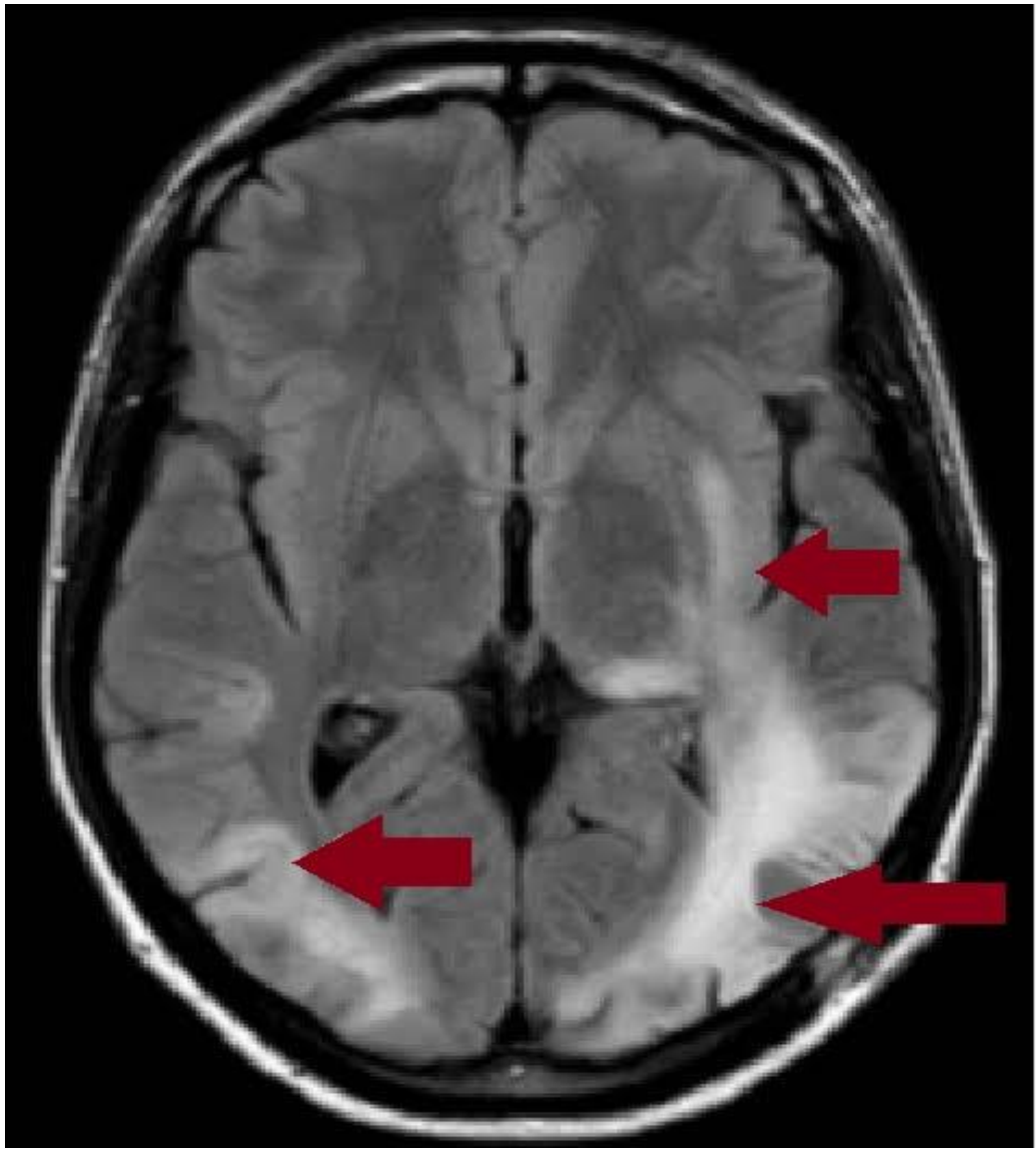
- ECG-Normal Sinus rhythm
- Chest X Ray- No Abnormality detected
- 2D Echo-No abnormality detected
- USG Abdomen and pelvis- No abnormality detected

Differential diagnosis

- Infective causes
  - CytomegaloVirus Retinitis
  - Syphilis
  - Tuberculosis
  - Toxoplasmosis
  - JC virus
- Neoplastic causes
  - Kaposi's Sarcoma
  - HTLV-1 Infection (Human T-Lymphotropic virus-1)
  - Lymphoma
- AIDS associated optic neuropathy

MRI Brain with Orbit Sections (Contrast study) showed

- Ill-defined hyperintensity without significant post contrast enhancement in bilateral occipital and left temporal lobe in the T2 weighted and FLAIR sequence.
- In a known case of HIV positive status these findings were suggestive of **Progressive Multifocal Leukoencephalopathy(PML)** .



CSF Studies	
• CSF Microscopy: • Total Leukocyte count • Red blood cells	 **4 (100% Lymphocytes)** **2 to 3 cells/cu mm**
• Protein • Glucose	**19.1 mg/dL** **53 mg/dL**
• Adenosine Deaminase	2.34 U/L (Negative)
• CSF Culture: • Bacterial • Fungal	 Negative Negative

1. CSF - VDRL	Negative
2. CSF Cryptococcal Antigen	Negative
3. India Ink Staining	Negative
4. Anti-Toxoplasma IgG antibodies	Negative
5. RT-PCR for JC Virus DNA	**Positive**

Final Diagnosis

Newly diagnosed HIV infection (AIDS) presenting as acute painless vision loss due to Progressive Multifocal Leukoencephalopathy (JC Virus infection) with oral candidiasis

- As per the AAN consensus guidelines for diagnosis of PML, our patient had clinical features and MRI features consistent with PML with a positive CSF-PCR assay for JC virus
- Thus a definite diagnosis of PML secondary to JC virus in a newly diagnosed case of HIV infection was made
- Patient was started on TLD regimen (Tab Tenofovir 300 mg + Tab Lamivudine 300 mg + Tab. Dolutegravir 50 mg fixed dose combination once daily) for the same, and is on regular follow up.
- On further follow up the patient's vision improved from perception of light to perception of hand movements.
- Patient was advised to follow up every month but was lost to follow up after 3 months.

Discussion

- JC Virus is a DNA virus belongs to the HPV-2 family.
- Immunocompromised are more prone to JC Virus infection. HIV positive status with CD4 count <100 are more susceptible.
- JC Virus infection is one of the causes of PML. PML has average life expectancy of 6 months to 2 years.
- Blindness in JC virus infection is due to widespread focal demyelination especially in the occipital lobe causing visual symptoms like field defects, homonymous hemianopia and complete blindness.
- There is no specific treatment for JC Virus infection except for introduction of HAART

Take Home Message

- Blindness due to PML as an AIDS defining illness as first manifestation of HIV is rare.
- Thus, progressive deterioration of vision must be evaluated meticulously, especially in immunocompromised individuals, with a high degree of suspicion and consideration for rare presentations and uncommon causes.

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THANK YOU

AN UNUSUAL CASE OF YOUNG GIRL PRESENTING WITH SEIZURE

PRESENTOR : DR. RAMIZ KADIWALA

UNIT - 8

DEPT. OF GENERAL MEDICINE

A 17 year old female born to a second degree consanguineous marriage presented to OPD with

- Generalised Tonic-Clonic seizures with post-ictal confusion one day before.
  - No past history of seizure disorder
  - No history of fever
  - No bowel bladder incontinence
- Complaints of swelling of both the ankle joints for the last 3 years.
  - Associated with dull aching pain that was aggravated upon walking with restriction in movements.
  - No history of trauma, morning stiffness or pain in any other joints.

PAST HISTORY:

- History of bilateral juvenile cataracts detected at 1 year age and underwent surgery for the same.
- H/o poor scholastic performance.
- There was no delay in developmental milestones.
- No comorbidities

FAMILY HISTORY:

- Similar ankle swellings were present in her maternal aunt whose age was 40 years, restricting her daily mobility.
- The aunt also had childhood cataract, unsteady gait and mild cognitive impairment

ON EXAMINATION:

- Patient was conscious, oriented to time, place and person.
- Afebrile
- **Pulse rate-** 80 beats per minute, regular, equal on both sides, no radio-radial and radio-femoral delay. All peripheral pulses were felt.
- **BP-** 100/70 mm of Hg in right upper limb in supine position.
- **RR-**15 cycles per min
- **SpO2-** 98% on room air

- JVP not raised.
- No Pallor, Icterus, cyanosis, clubbing, lymphadenopathy, pedal edema
- Blood Glucose Level – 92 mg/dl

SYSTEMIC EXAMINATION

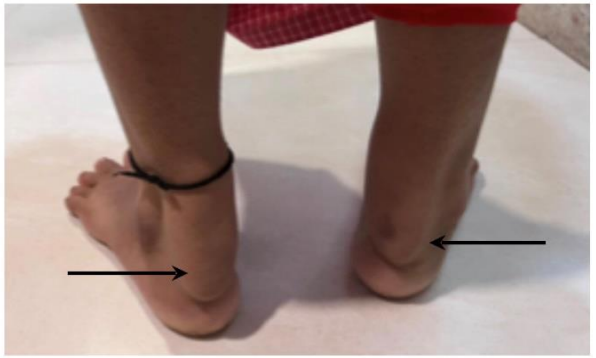
- **CNS-** Conscious, oriented to time, place and person. No motor or sensory neurological deficit.

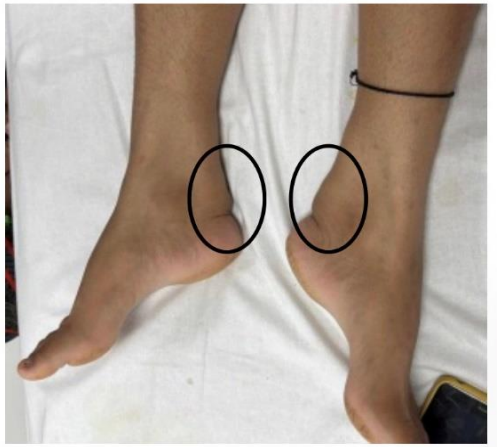
  Higher mental functions- **MMSE score 20/30**

- **CVS-** S1S2 heard, No murmurs
- **RS-** Bilateral vesicular breath sounds, no adventitious sounds.
- **P/A-** Soft, No tenderness, No organomegaly

Local Examination of Ankle joint:

- 3 x 4 cm, firm, non tender nodules
- over the posterior aspect of both the lower limbs.
- Fixed to the underlying Achilles tendon
- Mobile from side to side with normal overlying skin.





Imaging studies

- Radiograph of B/L Ankle joint demonstrated soft-tissue opacity at the posterior aspect of ankle along the lower one-third of Achilles tendon bilaterally with normal osseous structures and joints.
- USG A/P- NAD
- MRI Brain and EEG came out to be normal.

Hb	12.5 gm /dl
TLC	9300 /µl
Platelet	349000 /µl
HCT	40
MCV	90
RDW	19

Total Cholesterol	176 mg/dl
Triglycerides	115 mg/dl
HDL	58 mg/dl
LDL	91 mg/dl
VLDL	27 mg/dl

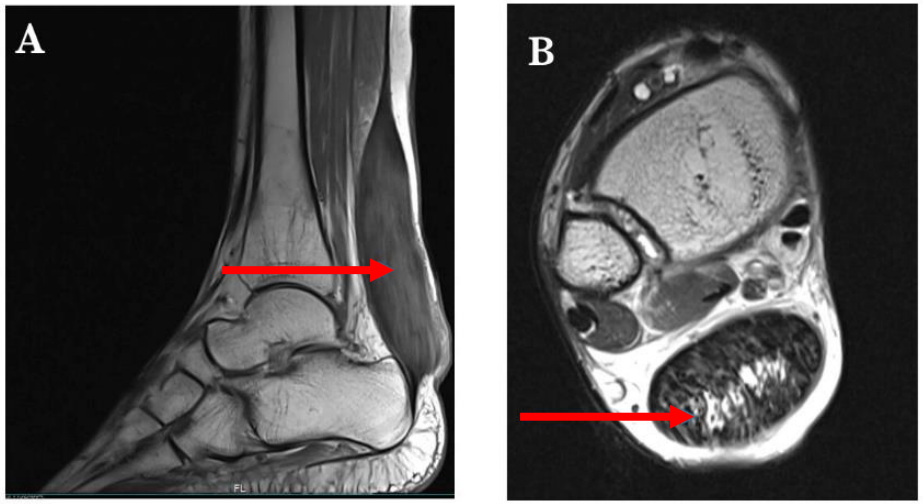
Total bilirubin	1.17 mg/dl
Direct bilirubin	0.4 mg/dl
Indirect bilirubin	0.77 mg/dl
SGOT	10 U/L
SGPT	33 U/L
ALP	46 U/L
Urea	19 mg/dl
Creatinine	0.67 mg/dl

T3	1.43	0.64 – 1.52 ng/mL
T4	7.82	4.87 – 11.72 µg/dl
TSH	2.09	0.35 – 4.94 µIU/ml

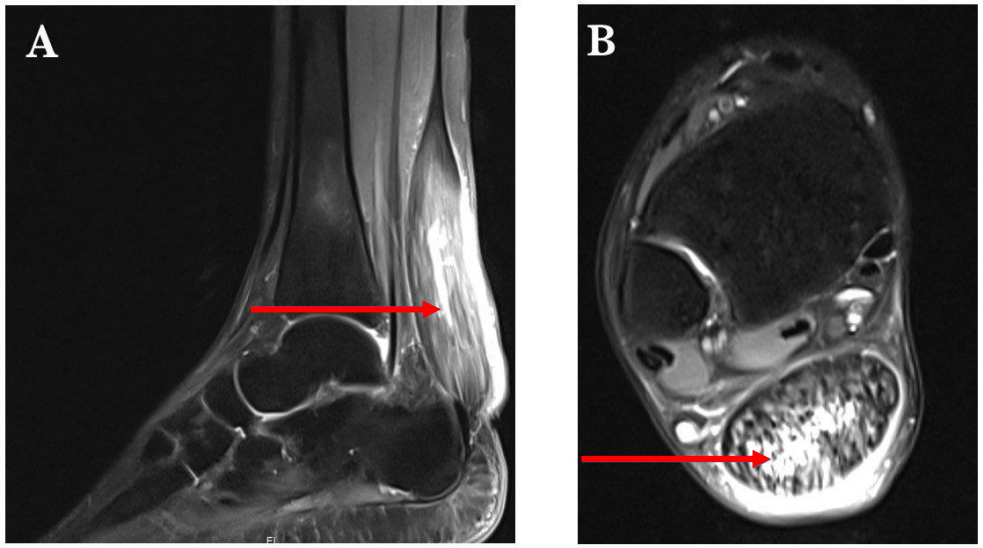
BSL	94 mg/dl
CRP	5 mg/L
ESR	17 mm/hr
HIV, HBsAg, Anti-HCV	Negative

Sodium	136 mmol/L
Potassium	4.6 mmol/L
Chloride	99 mmol/L
Calcium	8.3 mmol/L
Magnesium	1.9 mmol/L

MRI imaging of the ankle was done for better characterization of the swelling which showed a diffuse thickening and enlargement of the distal Achilles tendon with antero-posterior thickness approx 18mm and transverse thickness of 23mm suggestive of Achilles tendon xanthoma.



T1W MRI Ankle



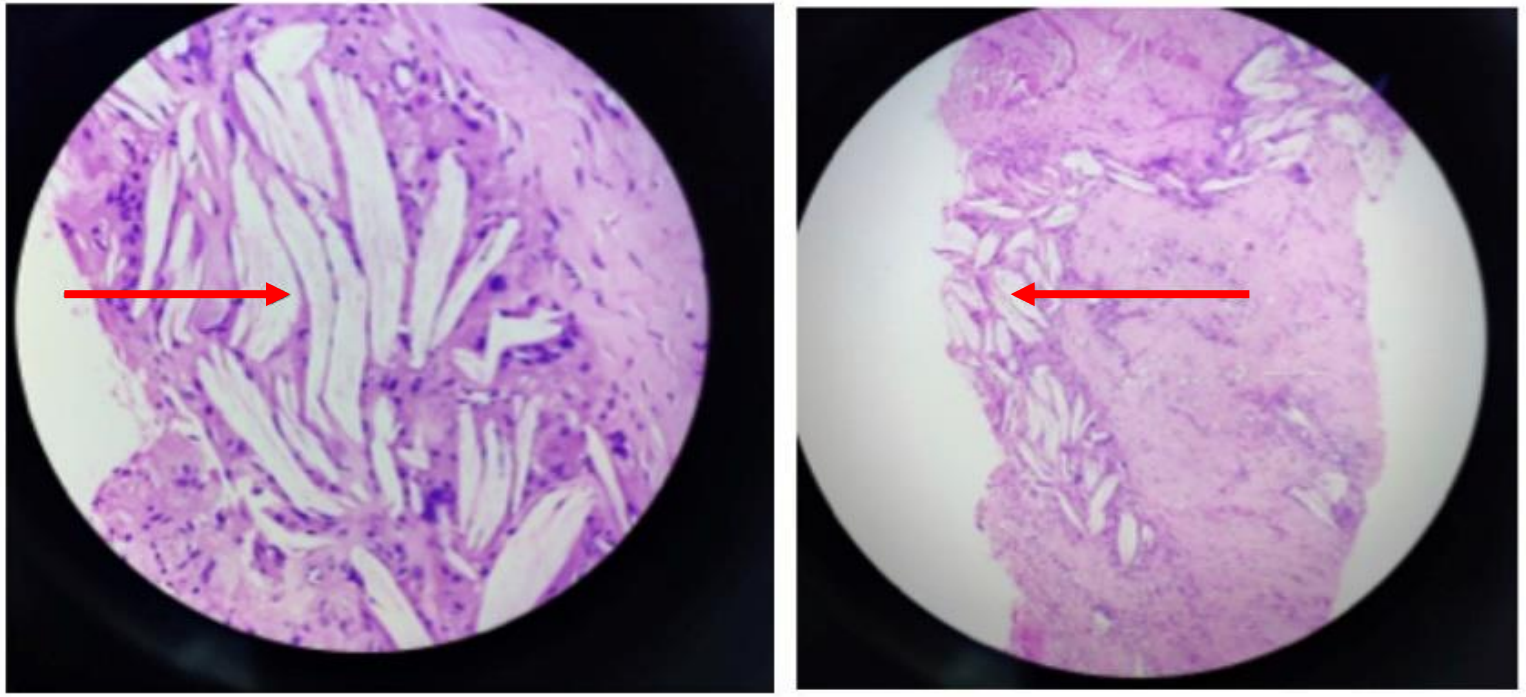
T2W MRI Ankle

Working Diagnosis on presentation:

- A provisional diagnosis of tendon xanthoma was made with a chief differential as Normolipidemic Cerebrotendinous Xanthomatosis considering the history of
    - Seizures
    - Cataract
    - Consanguineous marriage
    - Family history

HISTOPATHOLOGICAL INVESTIGATIONS

Trucut biopsy of the lesion also contributed to our diagnosis showing an abundance of cholesterol clefts along with foamy histiocytes and giant cells on histopathology, suggesting a xanthomatous change.



Genetic Analysis (Clinical exome sequencing)

- A splice donor variant c. 1184+1G>A
- Homozygous in the intron 6

which is observed **in 0.0719% alleles from individuals of gnomAD South Asian background and Novel (not in any individuals) in 1KG All.,** leading to an intolerant loss of function variant in the gene CYP27A1.

This confirmed the diagnosis as Cerebrotendinous Xanthomatosis.

FINAL DIAGNOSIS

Normolipidemic Cerebrotendinous Xanthomatosis

with

- Neurological (Seizures)
- Musculoskeletal (Tendon Xanthoma)
- Ophthalmological (Early onset cataract) manifestations

DISCUSSION

- Cerebrotendinous Xanthomatosis (CTX) is a rare autosomal recessive lipid storage disease first described by Van Bogart et al. in 1937.
- The estimated prevalence of CTX is 3 to 5 per 100,000.
- It is caused due to homozygous or heterozygous mutations in the CYP27A1 gene on chromosome 2q33 that encodes the mitochondrial enzyme sterol 27-hydroxylase responsible for conversion of cholesterol to cholic acid and chenodeoxycholic acid.
- Deficiency of this leads to the accumulation of cholesterol and cholestanol in the lipophilic tissues.
- So, people with mutation for the CYP27A1 gene tends to have a multi-organ involvement such as xanthomas, cataract, a broad spectrum of neurological disorders and psychiatric involvement.

- Most of the patients are diagnosed at a mean age of 32 to 41 years only when the neurologic symptoms appear.
- Xanthomas develop in approximately 70 percent of patients in the second or third decade of the life. They typically form on the Achilles, extensor surfaces of elbow and hand, tibial tuberosity and neck tendons.
- Seizures are reported in approximately 50 percent of patients and can be the presenting symptom.
- The diagnosis is mainly based on clinical findings, biochemical testing for cholestanol levels, histopathology and genetic testing.

Treatment:

- Symptomatic treatment of neurologic and non neurologic manifestations, extraction of cataracts, surgical removal of xanthomas and **oral bile acid supplementation** such as Chenodeoxycholic acid, Ursodeoxycholic acid, Cholic acid or Taurocholic acid **along with statins** can effectively treat CTX.
- Chenodeoxycholic acid 750 mg daily, though expensive, is the preferred treatment of choice for treating neurologic manifestations and improves the neurological symptoms especially when started early.
- Early initiation of treatment prior to the onset of significant symptomatology helps in halting the disease progression and markedly improves the quality of life.

TAKE HOME MESSAGES

- CTX should be considered as a possibility in every person with Achilles tendon swelling and associated neurological symptoms.
- Absence of neurological symptoms at a young age must not rule out the disease as they tend to manifest much later and most often lead to a delay in the diagnosis.
- Carrier testing for at-risk family members and pre-natal genetic testing for CYP27A1 mutation can help in early diagnosis of this condition and prevent permanent neurological damage.

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THANK YOU