CLINICOPATHOLOGIC CONFERENCE – DEPT. OF MEDICINE V M UNIT

A 47 years old male admitted on 22/05/2024 with history of hematemesis, melaena and abdominal pain for 3 days.

No H/O fever, NSAID intake, yellowish discoloration of urine, oliguria, abdominal distension, dyspnea, skin rashes, joint pain, weakness of limbs, giddiness, hematuria and epistaxis.

H/O of easy fatigability,

BRIEF PAST HISTORY:

First admission: 2008

Patient was admitted in a private hospital in view of Hematemesis and Melena x 1 day .Patient had H/O NSAIDS intake for epigastric pain .Alcohol history for 3 years and H/O icterus in 2005.

CBC - HB 13.2 g/dl, TC -12000/cu mm, PLT - 29000/cu mm, Bilirubin - 2.5 mg / dl.

UGI Endoscopy showed Erosive esophagitis, Erosive gastritis - ? NSAIDs Induced /? Bleeding diathesis Thrombocytopenia related. After platelet transfusion the platelet count was improved.

SECOND ADMISSION {2014 @ KIMS - 5/11/14 to 9/11/14}

Pt was admitted with C/O Fever with thrombocytopenia .CBC Hb - »13.6 » 10.6 » 11.3 g /dl , TC – 21000» 11400. Platelet count 1.5 Lakh » 20000 .LFT T.B - 2.3 ID - 1.6 mg / dl. AST /ALT / ALP - 38/55/83. RFT Urea-18 mg/dl, serum Creatinine -1.1 mg / dl, PT INR - 1.05 .Urine routine - Plenty of RBCs, 8-10 pus cells

THIRD ADMISSION: {2014 @ KIMS -17/11/14 TO 26/ 11/ 24}

Evaluated for thrombocytopenia

CBC HB - 10.7 g/dl TC - 16200 /cu mm Platelet - 10000 /cu mm Reticulocyte count - 4.3 % Retic index - 2.3. PS - Moderate hypochromic anemia with thrombocytopenia . LFT - TB - 2.3 Direct - 0.7,AST - 38 ALT -55, ALP -83. Urine routine - Plenty of RBCs, occult blood +++. ANA by IF Method – Negative. DCT – Negative. USG Abdomen - Hepatosplenomegaly, Cholelithiasis. Serum Ceruloplasmin - 26.6 {Normal } Serum Ferritin - 829 mg/dl. Bone Marrow Aspiration - Erythroid hyperplasia with normal megakaryocytes. Patient received Steroids for 1 week but No response .ADAMTS 13 Level - ? Low {not documented}

Pt diagnosed as HUS - TTP {Congenital ADAMTS 13 Deficiency}

FOURTH ADMISSION: {Jan 2015 @ CMC Vellore}

C/O Melena and Hematuria X 1 Day - Diagnosed to have TTP{ Based on Evidence of Microangiopathic hemolysis - schistocytes , Increased Indirect hyperbilirubinemia , Thrombocytopenia and deranged renal function and Significant Family H/O TTP in sibling .}

Treated with **Cryosupernatant daily for 6 days**.

Injection Methyl prednisolone 65 mg OD was given for 5 days. The platelet count was improved.

UGI Scopy - Revealed on ulcer Below GE Junction with visible vessel. Hence Hemoclips were applied

Pt was discharged with Tab. Prednisolone 65 mg OD

FIFTH ADMISSION [Feb 2015 @ CMC Vellore }

C/O Hematuria x 2 days. H/O passage of altered blood in stool. Worsened Renal function { non oliguric } with evidence of Hemolysis , and mildly elevated reticulocytes. On tapering the steroids the TTP relapsed. The patient was managed again with cryo and IV steroids. After the treatment hemoglobin, renal function and platelet count became normal.

Patient was advised to continue Cryosupernatant Supplementation at local place. He was on FFP Supplementation along with Dexamethasone whenever the Platelet count falls.

- During the course of illness patient developed secondary hypertension then elevated renal parameters. For hypertension he was on treatment with tablet amlodipine and tablet enalapril.
- Throughout the course of illness he never developed neurological symptoms like giddiness, TIA or focal neurological deficit.
- His renal function was deteriorated over years. On admission he was on CKD stage V with e GFR 14 ml/minute.
- Since November 2023 patient had H/O Melena , Hematochezia , Requiring FFP Transfusion , Dexamethasone Very frequently once in 2 weeks

FAMILY HISTORY

Born to second degree consanguineous marriage.

One brother who has two children. 12 years and 10 years old.

One sister – no children. Had 2 abortions one at 5 months and next on 8 months**.**

She was also diagnosed as TTP at CMC Vellore.

PERSONAL HISTORY; Not a smoker or alcoholic. Consumes mixed diet. Normal bowel and bladder habit.

SYSTEMIC EXAMINATION

CVS – S1 , S2 present. No murmur. RS – Clinically normal. No added sound

Abdomen – soft, bowel sounds +, epigastric tenderness +, no organomegaly.

CNS – Conscious, oriented, no focal neurological deficit.

TREATMENT GIVEN

- NPO
- Ryle's tube aspiration
- IV fluids
- INJ.PANTOPRAZOLE 80mg iv stat f/b 8mg/hr infusion
- Inj. Transexamic acid 500mg iv tds
- Inj. Cefotaxime 1gm iv bd
- T. Amlodipine 5mg 2-0-0
- T. NaHCO3 500mg tds
- T.caco3 300mg 1-0-1
- W/f bleeding manifestations
- I/O chart
- Platelet transfusion

MEDICAL GASTROENTROLOGIST opinion**:**

Diagnosis: Moderate UGI bleed / TTP / jejunal diverticulosis/ CKD / coagulopathy

Advice :- inj . Pantoprazole 80 mg iv stat f/b 8 mg / hr infusion. Adequate hydration. Correction of coagulopathy by FFP/ blood products transfusion. Serial LFT and RFT.

RHEUMATOLOGIST opinion: a case of TTP on treatment.

Advice: AN by IF method

NEPHROLOGIST opinion:

Diagnosis: HT/ TTP/ renal failure – non oliguric / UGI bleed for evaluation

ADVICE T. NaHCO3 1-1-1. 4 units of platelet / 2 units of FFP transfusion. Conservative management. Serial RFT monitoring

To do

1. Peripheral smear with retic count / LDH
2. Anti-factor H Ab testing
3. C3, C4 , genetic study for complement factor gene defect.
4. screening of children for congenital TTP

DAY	1	2	3	4	5
TC	8,500	13200	13500	22,700	15,600
DC	76/14/9	77/14/8	85/9/4	85/8/7	92/5/2
Hb	7.2	6.1	6.7	7.3	5.2
PCV	22.3	25.6	20.5	23.8	14.2
PLT	7000	32000	85000	85000	96000

PT	17.1	18.1	20.8	17.5	19.9
INR	1.3	1.40	1.6	1.35	1.5
APTT	-	24.8	27.7	25.1	26.5

DAY	1	2	3	4
UREA	104	143	107	80
CREATININE	5.0	5.4	4.5	4.3
SODIUM	138	143	148	141
POTASSIUM	4.2	3.6	4.0	3.0

UPPER GI ENDOSCOPY

YEAR	FINDINGS
08-11-2008	Multiple erosions with evidence of recent bleed Mucosa appears black with ulceration and inflammation Duodenum – normal Esophagus- purpuric spots seen in entire length of esophagus
20-12-2008	Grade I reflux esophagitis Stomach – fundus and antrum erosion Duodenum – normal
05-01-2015	SCOPY ELSEWHERE SHOWED A MALLORY WEISS TEAR Esophagus – A few petechial hemorrhages seen in pharynx and esophagus Stomach – two visible ulcers with Fundus – edematous and congested mucosa Body and antrum – few petechial hemorrhages Duodenum – small erosion in posterior wall of D1 TWO HEMOCLIPS APPLIED AT THE BASE OF JUNCTION

GRH	Multiple superficial erosions distributed on fundus, body and maximal antrum with inflamed and thickened mucosa Duodenum – multiple diverticulosis polypoid lesions noted in D1 And D2

USG / CT ABDOMEN

DATE	FINDINGS
27/10/2014	Minimal hepatosplenomegaly Mid diffuse fatty liver Cholelithiasis Increased renal cortical echoes
18/11/2014	Normal size kidney with CMD maintained
26/03/24	Fatty liver. Cholelithiasis. Bilateral grade II MRD Jejunal diverticulitis
31/03/24 MRCP abdomen	Acute edematous pancreatitis Multiple calculi in gall bladder Mild hepatomegaly

PERIPHERAL SMEAR AND BONE MARROW BIOPSY

19/11/2014	P Smear anisopoikilocytosis, with normocytic polychromastic cells Fragmented RBCs Occasional normoblast WBC shift to left Platelet reduced
19/11/2014	Bone marrow erythroid hyperplasia normal megakaryocytes
GRH	Microcytic hypochromic anemia[few schistocytes seen with neutrophilic leukocytosis and thrombocytopenia

OTHER INVESTIGATIONS

DATE	TEST	RESULT
29-05-2015	**Serum C3** **Serum C4**	**84.30 (90-140)** **26.20 (10-40)**
25-10-2014	ANA	Negative
18/11/2014	Hb A1C	4.6%
	BLOOD GROUP	O POSITIVE

DATE	WBC COUNT	PLATELET	Hb gm/dl	LDH IU/L	Blood urea	Serum creatinine
O7/11/2008	12000	29000	15.5			
26/10/2014	12700	9000	14.6		38	1.32
20/11/2014	6300	11000	8.1			
22/11/2014	5100	22000	5			
24/11/2014	7400	1.45 L	8.6			
20/01/2015	16600	2.27 L	13.7	478		
27/01/2015	16500	62000	13.6			
06/02/2015	15200	1.5 L	13.7			
25/02/2015		2L				
02/01/2023	14000	50000	11.7		52	1.3
04/01/2023	13800	1 L	10			
26/03/2024	11500	85000	7.7		41	3.0
30/03/2024	12000	48000	7.9		70	3.9
05/04/2024	7500	2 L	6.6			

DISCUSSION

1. Discussion on thrombotic microangiopathy – congenital
2. Congenital TTP Vs. congenital a-HUS
3. Etiopathogenesis of erosive gastritis and other GI complications
4. Pathogenesis of hypertension and CKD
5. Further workup on this patient
6. Discussion on other specific treatment
7. Genetic counselling