Double Trouble: Navigating Dual Positivity in Vasculitis”

CASE HISTORY

- Age: 27 years
- Sex: Male
- Presenting complaints:
  1) Joint pain
  2) Breathlessness

HISTORY

- Apparently well 2 month ago,
  - intermittent arthralgias in the joints of the hands.

    Followed by
    - Involvement of wrists, knees, ankles, and shoulders

  - Associated with early morning joint stiffness.
  - Not associated with skin rash, joint swelling

- One month ago,

- Developed breathlessness, associated with
  - dry cough
  - worsening dyspnea on exertion.
  - one episode of hemoptysis

- No History of fever, Night sweats
- No history of hematuria, decreased urine output
- No history of recent infections
- No history suggestive of urinary tract infections

PAST HISTORY

- History of Renal Calculi- July 2024
  - bilateral renal calculi 2-3mm, non obstructive
  - No treatment taken
- No Known Autoimmune or connective tissue disorder

- No history of
  - Hypertension
  - Diabetes
  - Thyorid disorder

PERSONAL HISTORY

- Non-smoker, occasional alcohol use
- No recreational drug use
- No recent travel or occupational exposures

RECENT MEDICAL HISTORY

- Admitted in local hospital one month back with similar complaints,
  - Treated as pulmonary TB
  - Started on AKT- (HRZE regimen)
  - Taken for 1 week, Discontinued later in view of ?AKT induced hepatitis
- Referred to higher centre
- No history of NSAID/ARB/ACE inhibitor

VITALS

- Vitals:
  - BP: 148/94 mmHg
  - HR: 96 bpm
  - RR: 22/min
  - SpO_2: 92% on room air

EXAMINATION

Height- 160cm, Weight- 42kg,

BSA- 1.37 m^2, BMI- 16.4 kg/m^2

- General:
  - Pale, afebrile, No edema, No icterus

    Skin & Joints: No rash or joint swelling

    No Lymphadenopathy
- Chest: Bilateral fine basal crackles
- CVS: Normal heart sounds
- Abdomen: No organomegaly

INVESTIGATIONS- 13/02/2025

Hemoglobin	**6 g/dL**
WBC	**16800/uL**
Platelets	350,000/ul
Serum Creatinine	**2.44 mg/dL**
Urea	108 mg/dL
Urinalysis	**2+ protein, 20-25 RBC PUS- 6-8 cells, Casts- not detected**
Urine protein/creatinine ratio	**4.17 g/g**
Total Bilirubin	0.32 mg/dl
AST/ALT	23/25

- USG AP-
  - right kidney – 10.9 x 4.9 cm

    left kidney- 11x 6.2cm
  - Raised renal cortical echogencity
  - CMD mantained
  - No calculi, no cysts, no signs of hydroureter, hydronephrosis
- HRCT thorax-
  - B/L lungs- Multiple patchy and confluent areas of consolidation with air bronchogram within and adjacent ground glass opacities, predominantly right upper/lower lobe

Sputum AFB- negative

Sputum CBNAAT – negative

AUTOIMMUNE WORKUP

ANCA (MPO/p-ANCA)	Positive (PR-3 positive, 30.41 AU/mL)
Anti-GBM antibody	Strongly positive (37.34 AU/mL)
ANA/dsDNA	Negative
C3/C4	Normal

TO SUMMARISE

- 27/M
- No comorbidities
- Joint pain, episode of hemoptysis
- Azotemia
- Proteinuria with active urinary sediments
- Anti GBM positive
- ANCA positive (PR-3)

CLINICAL DIAGNOSIS

- Rapidly progressive renal failure with double positive antibody disease

MANAGEMENT

- Steroids-
- IV Methylpredinsolone 500mg IV x 3 days

- Plasmapheresis-

5 sessions done (alternate days)

- Tab Prednisolone 40mg OD

Cyclophosphamide- one dose (Dose-0week)

- Inj Cyclophosphamide 500mg with Inj Mesna given

Patient was discharged and adviced to follow up in OPD after 2 weeks- Plan for 6 doses of CYC 500mg IV every 15 days

Creatinine on discharge – **1.42 mg/dl**

(on admission- 2.44mg/dl)

MEDICATION ON DISCHARGE

- Antiproteinuric- Tab Telmisartan 40mg OD
- Steroid- Tab Prednisolone 40mg OD

2 WEEKS LATER- FOLLOW UP VISIT

Test	Result
Hemoglobin	11.8 gm/dl
Total Leukocyte Count (TLC)	6300/ ul
Platelet Count	232,000/ul
Creatinine	1.12 mg/dl
Urea	36 mg/dl
Sodium (Na^+)	141 mmol/L
Potassium (K^+)	4.43 mmol/l
Urine Routine	Protein 1+, RBC 5-6, Pus 2-3, Casts not detected
Urine Protein Creatinine Ratio (UPCR)	8.51

PATIENT ADMITTED FOR 2ND DOSE

- 2nd Dose of Inj Cyclophosphamide given

- Inj Cyclophosphamide 500mg with Inj Mesna
- Patient discharged in stable state

FOLLOW UP VISITS

Drug Name	March 2025	April 2025	May 2025	Jun2025
Telmisartan (once daily)	40mg	40mg	40mg	40mg
Prednisolone(once daily)	30-20mg	20-10mg	10mg	10mg
Cyclophospha mide (once in 15 days)	500mg (Dose 4week)	500mg (Dose 7week)	500mg (Dose 10week)	500mg (Dose 13week)

FOLLOW UP VISITS

	March 2025	April 2025	May 2025	June 2025
Test	Result			
Hemoglobin	10.7 gm/dl	12.8 gm/dl	13.6 gm/dl	14.9 gm/dl
Total Leukocyte Count (TLC)	6500/ ul	6800/ ul	6700/ ul	8800/ ul
Platelet Count	211,000/ul	205,000/ul	237,000/ul	269,000/ul
Creatinine	1.00 gm/dl	1.02 gm/dl	0.97 gm/dl	1.04 gm/dl
Urea	29 mg/dl	21 mg/dl	31 mg/dl	32 mg/dl
Sodium (Na^+)	136 mmol/L	137 mmol/L	139 mmol/L	139 mmol/L
Potassium (K^+)	4.43 mmol/l	4.05 mmol/l	4.78 mmol/l	4.86 mmol/l
Urine Routine	Protein 1+, RBC 5-6, Pus 2-3, Casts not detected	Protein 2+, RBC 8-10, Pus 6-8, Casts not detected	Protein 2+, RBC 1-2, Pus 1-2, Casts not detected	Protein 3+, RBC 3-4, Pus 1-2, Casts not detected
Urine Protein Creatinine Ratio (UPCR)	6.3	7.2	7	7.25

DISCUSSION

- Small-vessel vasculitis encompasses a group of diseases characterized by necrotizing inflammation of small vessels (i.e., arterioles, capillaries, and venules)
- Pauci-immune small-vessel vasculitides include
  - granulomatosis with polyangiitis (GPA)
  - microscopic polyangiitis (MPA)
  - eosinophilic granulomatosis with poly-angiitis (EGPA)

- Active pauci-immune small-vessel vasculitis is typically associated with circulating antineutrophil cytoplasmic antibody (ANCA), and GPA, MPA, and EGPA
- It is grouped under the term“ **ANCA-associated vasculitis**”

DISCUSSION- WHAT IS DOUBLE POSITIVE DISEASE?

- The incidence of anti-glomerular basement membrane (GBM) disease and ANCA-associated vasculitis (AAV) is less than 2 in million and 20 in million per year, respectively.
- When they occurred together, it is called "**double positive disease**"
- Both may present with life-threatening conditions :
  - rapidly progressive glomerulonephritis (RPGN)
  - alveolar haemorrhage

REMISSION

- Defined as the absence of manifestations of vasculitis and GN (BVAS=0)
- For GN, it is defined as a
  - stable or improved glomerular filtration rate.
  - While hematuria and proteinuria are present at times of active disease and can resolve completely, their persistence does not necessarily imply active

CHOICE OF INDUCTION AGENT- KDIGO 2024

- Induction therapy-
  - Cyclophosphamide+ glucocorticoids
- In 2 RCTs
  - rituximab has been shown to be equally effective in inducing remission as cyclophosphamide.
- Rituximab compared to cyclophosphamide probably makes little or no difference in relapse rate, at 1–6 months

THANK YOU