AMR :
A Deterrent in Solid Organ Transplant

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Case :

A 45 year old male came to Emergency department with complaints of

- Pain in abdomen - 2 months
- Fever with chills - 1 day

Later he was admitted to Gastroenterology ward, Dr D Y Patil Medical College, Hospital and Research center for further investigations and treatment.

Past History :

- He was a K/c/o alcoholic liver disease since past 20 years.
- He was a K/c/o decompensated liver disease (DCLD) since 2 months.
- H/o ICU admission due to dengue fever with viral cytogenic hepatitis along with h/o blood transfusion one month back.
- He was an established case of pleural effusion as well as pericardial effusion & During Endoscopy, he showed signs of portal hypertension gastropathy and oesophageal varices one month back.

General Examination :

Patient was conscious, cooperative and well oriented to time, place and person.

Bp : 110/70 mmHg

Icterus(eye) : +++

Oedema : B/L pitting pedal edema

Systemic Examination :

- P/A : Distended abdomen. Free fluid present.
- CVS : S_1S_2 heard.
- CNS : NAD
- RS : B/L equal air entry

Lab investigations:

- CBC :

Hb – 7.20g/dL

TLC – 8200 /µL

Neutrophils – 4182/µL

Lymphocytes – 1886/µL

Platelet count – 69000/ µL

- **CRP – 10.20 mg/dL**
- **Procalcitonin – 0.09 ng/dL**
- Ammonia – 43 µg/dL
- Amylase – 31 U/LT
- Lipase – 262 U/L
- HbA1C – 4.10 %

- Liver function test :

Total bilirubin – 23.50 mg/dL
Conjugated - 11.50 mg/dl
Unconjugated -12.00 mg/dL
SGPT- 23 U/Lt
SGOT -43 U/Lt
ALP – 158 U/Lt

- Coagulation profile :

patient- 45 secs
INR – 3.33

Ascitic fluid examination :

Protein – Trace present
Bile pigment – Trace

Plasma Glucose – 124 mg/dL
Total protein – 4.40 g/dL
Albumin – 3.20 g/dL
Globulin – 1.20 g/dL
Albumin-Globulin ratio -2.67
Urea – 18 mg/dL
Creatinine – 1.14 mg/dL
Sodium- 135 mmol/Lt
Potassium – 3.80 mmol/Lt
Chloride – 103 mmol/LT
HIV combo – Non-reactive
HCV- Ab – Non-reactive
HBS-Ag- Non-reactive

- I/v/o fever, Urine culture was also sent before patient was catheterised.

Empirical Treatment –

inj. Meropenem (1 gm) + inj. Teicoplanin (400 mg) – 5 Days

- Next day → discomfort due to ascites

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Therapeutic ascitic tap

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C/s - Negative

MICROBIOLOGY DEPT. Urine Culture Report

Test : Isolation & Antimicrobial susceptibility of aerobic organisms.

Method : Manual.

Specimen : Urine.

Organism : Klebsiella pneumoniae Colony count more than 1,00,000 CFU/ml.

Antimicrobial susceptibility	MIC (µg/ml)	Interpretation
Amp/Sulbactam	>=32	Resistant
Cefepime	>=32	Resistant
Cefoxitin	>=64	Resistant
Ceftazidime+Avibactam	>=16	Resistant
Ceftizoxime	>=64	Resistant
Ceftolozane/Tazobactam	>=32	Resistant
Chloramphenicol	32	Resistant
Colistin	<=0.5	Intermediate
Doxycylcine	4	Susceptible
Levofloxacin	>=8	Resistant
Meropenem	>=16	Resistant
Nitilmicin	>=32	Resistant
Polymyxin B	0.5	Susceptible
Tetracycline	8	Intermediate
Tobramycin	>=16	Resistant

Comment : Carbapenemase Producer. Klebsiella pneumoniae is intrinsically resistant to Ampicillin & Ticarcillin. Kindly correlate clinically.

<End>

- Patient was clinically **asymptomatic** but the culture report turned out to be multi drug resistant *Klebsiella pneumoniae.*

- Later consecutive urine cultures were sent pre-operatively which turned out be ***Negative.***

The Day Of Transplant

Since the patient was a case of - DCLD

Presence of ascites,

B/L pitting pedal oedema

Deranged liver function tests

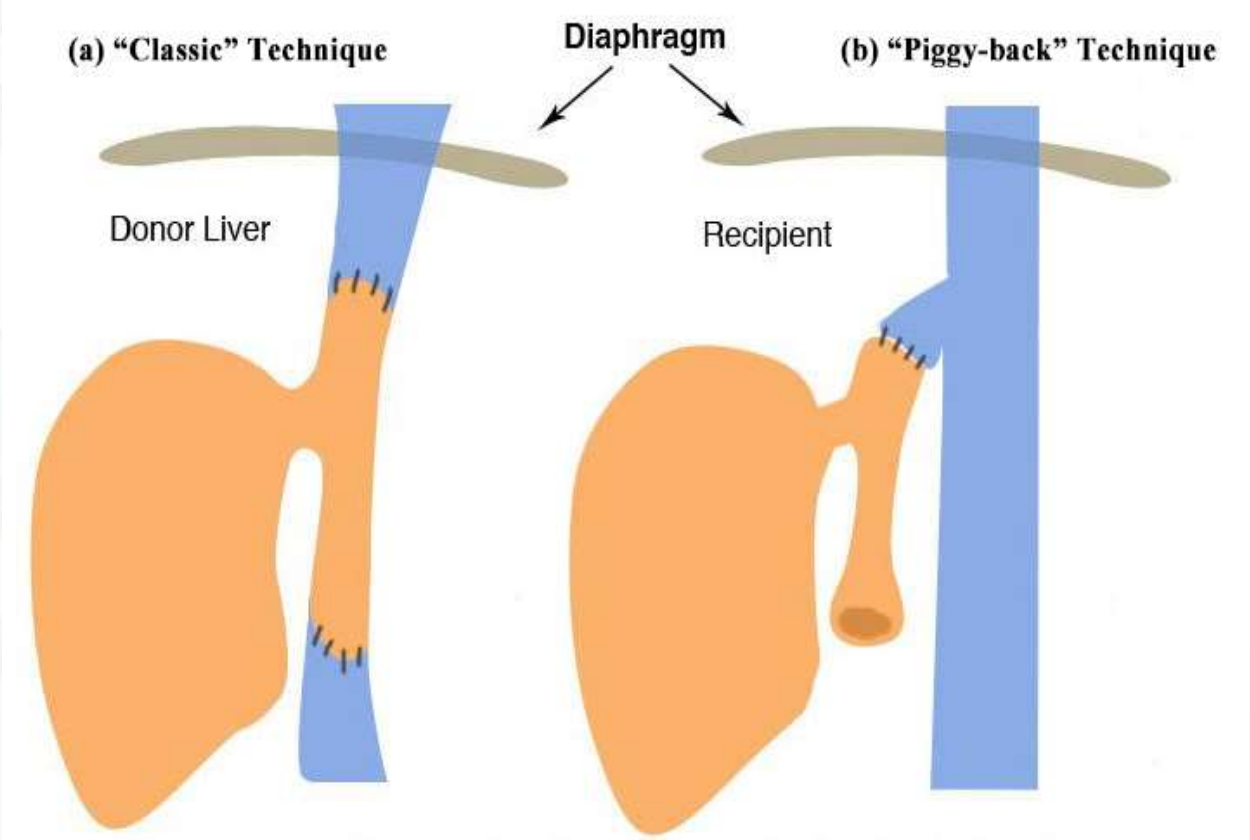
High INR

- He was counselled for the **Cadaveric liver transplant .**
- Consents were taken.
- Patient was haemodynamically stable and all the pre operative evaluation were carried out.

Piggyback Cadaveric Liver Transplant :

- Involves preservation of the recipient retro hepatic inferior vena cava

- Further follow ups-
  - Routine Blood Investigations
  - Inflammatory Markers
  - Liver Function Test
  - Coagulation Profile
  - USG
  - CECT Scan
  - X-ray
  - Liver Doppler



POD 0,

USG Screening Of Abdomen & Pelvis & Transplanted Liver Colour Doppler :

- **Mild hepatomegaly**.
- **Mild splenomegaly**.
- **Mild changes of UTI**
- **Minimal ascites** present.
- **Bilateral pleural effusion** seen, more marked another right side present.
- **SubCutaneous Surgical Emphysema.**

- Inj.Fluconazole (200gm) OD was started along with continuation of Inj. Meropenem (1gm) TID + Inj. Teicoplanin (400mg) OD.

POD1, patient was still intubated, finding were

- P/A : soft
- Right abdominal drain :4000 ml (Dark coloured)
- Left abdominal drain :410 ml
- Urine output :860 ml

- In view of excessive drainage, bleeding and coagulopathy

↓

Re-explore with lavage

- Meanwhile he was stabilized with multiple blood transfusions.
- Patient was started on inj.Polymyxin B (75 mg) + Inj. Micafungin (100 mg) for 5 days.
- Patient was extubated on POD 2 of transplant.

- Patients vitals were stable, gradually ambulatory.

- **POD 4 :** Blood c/s - sterile.

  Step down : Inj.Meropenem (1gm) → Inj. Piperacillin + Tazobactam (4.5 gm) TDS

  Inj. Fluconazole (200mg) → Tab. Fluconazole(200mg)

- **POD 6**, (rt drain 300, Lt-550,u-1760)

  Started on antiviral drug (Tab Valgacel BD (450 mg)) for 14 days

  CMV PCR report : Negative

- **POD 8** – Mild fever (100^0 F) with yellow coloured discharge from suture site.

  Pus swab was taken and sent for C/s.

- **POD 10 : Shivering at night along with Fever (101^0 F), Vomiting, Agitation and Disorientation, later regained consciousness soon after**

BP was fluctuating(84/38 – 130/70 mmHg)

↓ Tacrolimus toxicity ?

Inj.Meropenem (2gm) stat + Therapeutic intervention + Fluid correction

- 3 sets of Blood culture (from central line, right peripheral and left peripheral) were sent for culture and sensitivity.
- 1-3 β-d Glucan and Galactomannan test were ordered.
- His immunological markers were followed on routine intervals along with the radiological investigations.

POD 11 :

Liver Doppler & USG :

Peri- Hepatic SubDiaphragmatic fluid collection

Infra – Hepatic mild fluid collection + soft tissue oedema

↓

Therapeutic aspiration of the localised encysted fluid (115 cc)

↓

Sent for C/s

- He was again started to Inj Meropenem(1 gm) TID

Pus Culture Report

Test : Isolation & Antimicrobial susceptibility of aerobic organisms.
Method : manual culture

Specimen : Swab: surgical site

ZN Stain : No acid fast bacilli seen.

Organism : Klebsiella pneumoniae

Antimicrobial susceptibility	MIC (µg/ml)	Interpretation
Amikacin	32	Intermediate
Amoxycillin/Clavulanic acid	>32	Resistant
Cefepime	>32	Resistant
Cefoperazone/sulbactam	>64	Resistant
Ceftriaxone	>64	Resistant
Cefuroxime	>64	Resistant
Cefuroxime Axetil	>64	Resistant
Ciprofloxacin	>4	Resistant
Colistin	>16	Resistant
Co-Trimoxazole	>320	Resistant
Gentamicin	<=1	Susceptible
Imipenem	4	Resistant
Meropenem	>16	Resistant
Piperacillin/Tazobactam	>128	Resistant
Tigecycline	2	Susceptible

Comment : Gram stain: gram negative bacilli seen. Klebsiella pneumoniae is intrinsically resistant to Ampicillin & Ticarcillin. Carbapenemase producer. Kindly correlate clinically.

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POD 11 :

- C/s report from suture site : *Klebsiella pneumoniae* Susceptible only to Gentamicin and Tigecycline.
- Same Day : All 3 aerobic bottles were flagged **POSITIVE** within a day and were subjected to culture.
- Gram stain : Gram Negative Bacilli

POD 12 :

Oozing was present on the suture site

P/A – Haemorrhagic ascites from main wound

USG – Ascites +

Hb was reduced from 8 to 3 g/dL(even after blood transfusions)

Exploration with evacuation of hematoma and lavage.

POD 12 : Blood culture,

Culture showed : Large

Lactose fermenting

Dome shaped

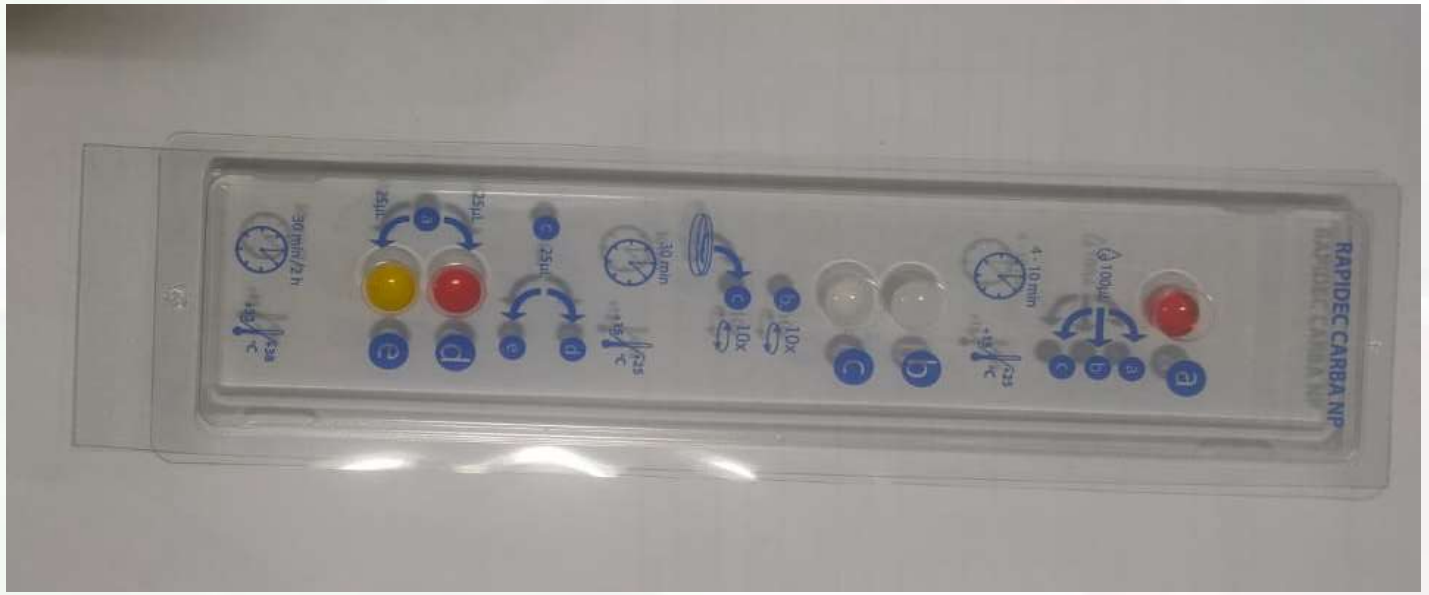
Mucoid colonies

S/O - *Klebsiella pneumoniae*

- *Simultaneously aspirated fluid culture was also performed.*

CARBA-NP :

Within ***2 hours*** it was established that the pathogenic organism is carbapenamase producing strain.



- Patient was escalated from Inj. Meropenem (1gm) to Inj.Ceftazidime-Avibactam (2.5 gm) + Aztreonam (100 mg)
- Patient was also started on inj. Micafungin (110mg) BD for 2 days and (110 gm) OD for 5 days as 1-3 β-d Glucan also showed raised value.

Pus Culture Report

Test : Isolation & Antimicrobial susceptibility of aerobic organisms.
Method : Manual.

Specimen : Pus :

ZN Stain : No acid fast bacilli seen.

Organism : Klebsiella pneumoniae

Antimicrobial susceptibility	MIC (µg/ml)	Interpretation
Amp/Sulbactam	>=32	Resistant
Cefepime	>=32	Resistant
Cefoxitin	>=64	Resistant
Ceftazidime+Avibactam	0.5	Susceptible
Ceftizoxime	16	Resistant
Ceftolozane/Tazobactam	>=32	Resistant
Chloramphenicol	>=64	Resistant
Colistin	>=16	Resistant
Doxycylcine	>=16	Resistant
Levofloxacin	>=8	Resistant
Meropenem	>=16	Resistant
Nitilmicin	>=32	Resistant
Polymyxin B	>=16	Resistant
Tetracycline	>=16	Resistant
Tobramycin	>=16	Resistant
Ceftazidime/Avibactam+Aztreonam Syn	0.5	Susceptible

Comment : Carbapenemase Producer. (Gram stain-gram negative bacilli seen)
Klebsiella pneumoniae is intrinsically resistant to Ampicillin & Ticarcillin. Kindly correlate clinically..

<End>

POD 13 :

- Isolated *Klebsiella pneumoniae* was susceptible to Ceftazidime + Avibactam, Synergy of Ceftazidime + Avibactam & Aztreonam.

- Hence the escalation was justified.

MICROBIOLOGY DEPT. -Culture Report

Test : Isolation & Antimicrobial susceptibility of aerobic organisms.

Method : Bactec FX System

Specimen : Blood: Anaerobic bottle.

Organism : Klebsiella pneumoniae

Antimicrobial susceptibility	MIC (µg/ml)	Interpretation
Amikacin	32	Intermediate
Amp/Sulbactam	>=32	Resistant
Cefepime	>=32	Resistant
Cefoperazone/sulbactam	>=64	Resistant
Ceftazidime+Avibactam	1	Susceptible
Ceftizoxime	16	Resistant
Ceftolozane/Tazobactam	>=32	Resistant
Chloramphenicol	>=64	Resistant
Ciprofloxacin	>=4	Resistant
Colistin	16	Resistant
Co-Trimoxazole	40	Susceptible
Doxycylcine	>=16	Resistant
Gentamicin	<=1	Susceptible
Imipenem	4	Resistant
Meropenem	>=16	Resistant
Nitilmicin	>=32	Resistant
Piperacillin/Tazobactam	>=32	Resistant
Polymyxin B	16	Resistant
Tetracycline	>=16	Resistant
Tigecycline	1	Susceptible
Ceftazidime/Avibactam+Aztreonam Syn	0.5	Susceptible

Comment : Carbapenemase Producer. Klebsiella pneumoniae is intrinsically resistant to Ampicillin & Ticarcillin. Kindly correlate clinically.

<End>

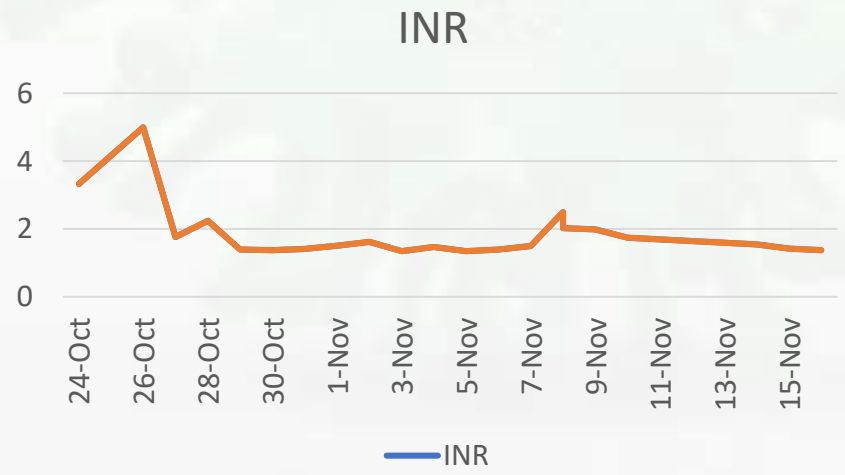
End of Report

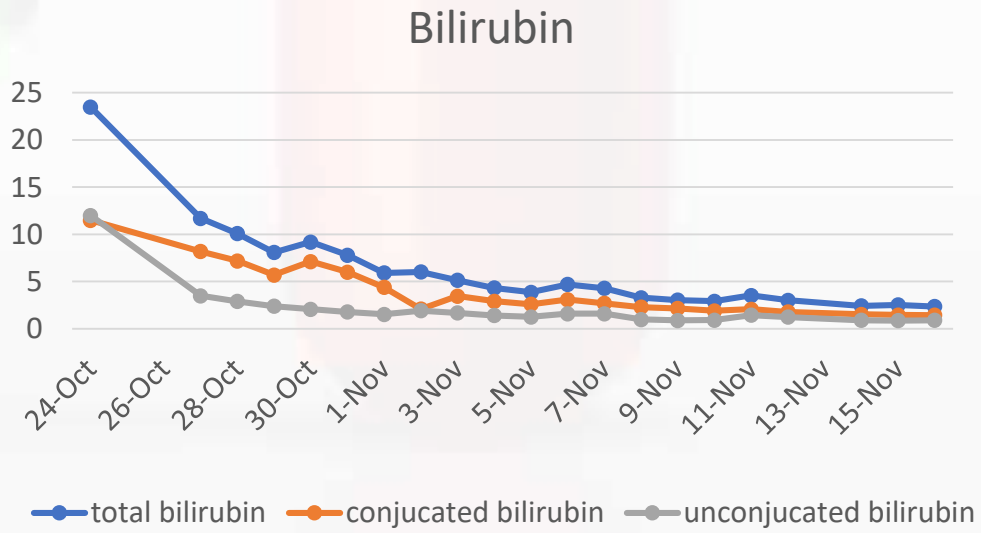
POD : 13

- Patient was started on Inj. Tigecycline based on culture and sensitivity report along with Inj.Ceftazidime + Inj.Avibactam & Inj.Aztreoam
- He was given inj. Tigecycline for 14 days.

Outcome :

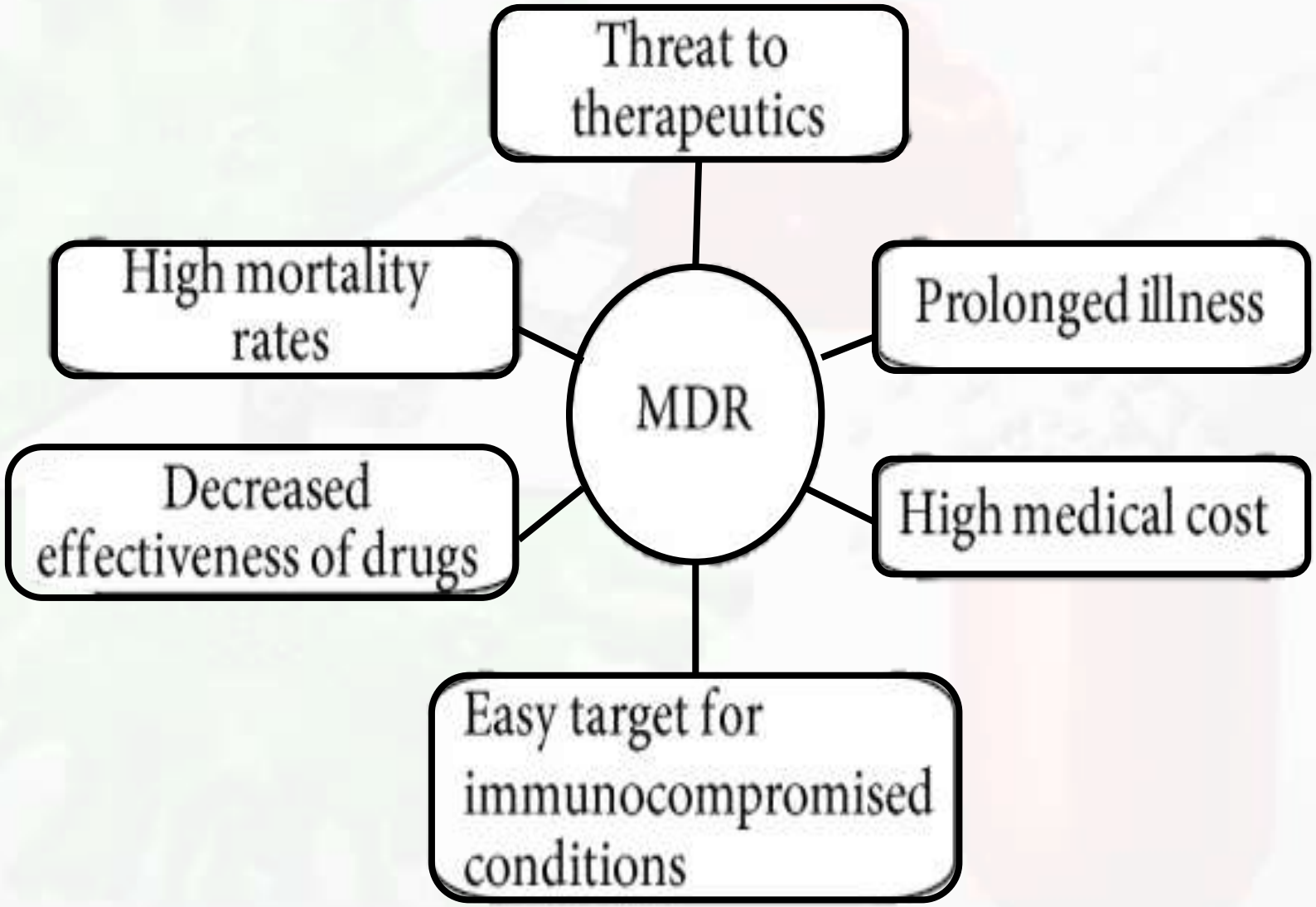
- Patient gradually improved clinically
- Followed up with routine blood investigations : within the normal range.
- Discharged on POD 25.





Discussion :

- Solid organ transplant is best therapeutic option for patient diagnosed with end stage organ diseases. The burden of classical infections related to MDR bacteria especially related to Gram negative bacteria is constantly increasing.
- Over last several decades various MDR pathogens have emerged as a relative cause of infection
- The awareness of this high susceptibility of transplant recipients to MDR related infection challenges the choice of empirical therapy, while the appropriateness can be validated posteriori.
- Excessive use of antimicrobial treatment may contribute to the high mortality due to MDR related infections in transplant recipients especially in case of metallo-β-lactamases.


Threat to therapeutics
High mortality rates
MDR
Prolonged illness
Decreased effectiveness of drugs
High medical cost
Easy target for immunocompromised conditions

Take home message :

- Source control remains an important part of the therapeutic armamentarium.
- Heightened infection control and antimicrobial stewardship initiatives are needed to prevent these infections.
- Targeted therapy should be adjusted according to antimicrobial susceptibility testing and severity of infection.
- Curtail their transmission and limit the evolution of MDR Gram-negative pathogens, especially in the setting of organ transplantation.

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THANK YOU!