Introduction:

The rise of multidrug-resistant (MDR) Gram-negative bacteria has ushered in a renewed reliance on polymyxins, particularly polymyxin B and colistin, as essential antibiotics in the modern armamentarium. These agents, initially discovered in the mid-20th century and later relegated due to toxicity concerns, have found a second life in critical care, where the treatment of infections caused by carbapenem-resistant *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* leaves few other viable options. Despite their efficacy against these formidable pathogens, polymyxins are notorious for their adverse effects, most commonly nephrotoxicity and neurotoxicity, which have been well-documented in the literature(1). Optimal dosing and dose adjustments in renal failure patients are essential for achieving the best outcomes and minimizing toxicity(2).

However, respiratory complications such as acute respiratory failure—particularly when directly attributable to polymyxin therapy—are relatively rare and underreported. Given that polymyxins can impair neuromuscular transmission and disrupt membrane integrity, there is a plausible mechanistic link between their use and the onset of respiratory failure. Such an adverse event poses a significant challenge in critically ill patients, where the balance between treating severe infections and avoiding iatrogenic harm becomes exceedingly important.

In this report, we describe the case of a critically ill CKD patient who developed acute respiratory failure after the initiation of polymyxin therapy and had multiple episodes of extubation failure. This case serves as a reminder of the potential for polymyxin-induced respiratory toxicity, a phenomenon that may be under recognized in the critical care setting. We explore the clinical course, diagnostic approach, and management strategies that were employed underlie this adverse effect. Through this report, we aim to shed light on the need for high vigilance and prompt recognition of respiratory complications in patients receiving polymyxin, particularly in the intensive care unit (ICU), where the margin for error is very thin.

Case Report:

A 34 year-old male, a known case of CKD on maintenance dialysis for the past 3-4 months, was admitted to our ICU on 29/07/2024 with complaints of fever, cough, and shortness of breath for 2-3 days.

On admission, the patient was febrile, tachypneic, and required supplemental oxygen. He was immediately transferred to the semi-ICU for further evaluation. Chest X-ray showed

right-sided consolidation, and laboratory investigations revealed significant leukocytosis with a total leukocyte count (TLC) of 20,310 cells/µL. Inj Cefoperazone and sulbactum 1.5gm BD started with tab clarithromycin.The patient underwent hemodialysis same day of admission, but his respiratory status did not improve. His antibiotic therapy was escalated to iv meropenem, and sputum samples were sent for gram stain and culture sensitivity testing the next day. The patient's oxygen requirements was still high and xray didn't show much improvement and his respiratory status did not improve.His TLC continued to rise, reaching 39,990 cells/µL after two 3 days of starting iv meropenem.Suspecting a MDR pathogen, colistin was added as empirical therapy which later on became the directed therapy as sputum culture revealed MDR *Klebsiella pneumoniea* susceptible to only polymyxin. A bolus dose of 9MIU was given followed by 3MIU iv bd which was later reduced to 3MIU iv OD.The patient suddenly became drowsy, hypoxic, and developed bradycardia along with hypotension on the next day early in the morning. He was immediately intubated and placed on mechanical ventilation. Over the next several hours, his condition stabilized, fully conscious,oriented without any vasopressor support.He was successfully extubated by the evening of the same day.

The patient again became progressively drowsy with bradycardia and hypotension, necessitating reintubation the same day at night. His consciousness and hemodynamic status improved following intubation, and vasopressors were weaned off by the evening. This time he was kept on mechanical ventilator for two more days and was again extubated ,and kept on minimal oxygen support After a brief period of stability, the patient developed drowsiness, bradycardia, and hypotension again shortly after extubation, prompting another reintubation.

Metabolic causes of weaning failure were also excluded. Neurologist consultation was taken who asked to continue the same as he was stable maintaining on T piece moving all 4 limbs actively. Given the recurrent episodes of respiratory failure following particularly with drowsiness, bradycardia and hypotension, the possibility of colistin-induced respiratory paralysis was considered. Colistin was discontinued, and the patient was started on ceftazidime-avibactum as culture results confirmed the presence of MDR *Klebsiella pneumoniea*.

After two days, the patient was fully conscious, off vasopressors, and successfully extubated for the third time. He was maintained on 4 liters of oxygen via face mask and closely observed for reintubation. This time, he maintained adequate oxygenation without the need for further respiratory support.

The patient was later shifted out of the ICU after two days of stable respiratory and

hemodynamic parameters.

INVESTIGATIONS:

INVESTIGATION REPORT

Vikash Binayak Hospital

Patient Name	: [redacted]	Lab ID No.	: 15146
Gender/ Age	: Male / 34Y 3M 4D	Patient ID No.	: 2361 / 24-25 (IPD)
Consultant Dr.	: Dr. Basanta Kumar Pradhan	Registered On	: 29/07/2024 01:21 PM
Referred By	: Self	Collected On	: 03/08/2024 02:07 PM
Ward / Bed	: Icu_2 / 9	Reported On	: 03/08/2024 02:46 PM
UHID No.	: 8353		

BIOCHEMISTRY

TEST DESCRIPTION	RESULT	REFERENCE RANGE/UNITS
Procalcitonin(PCT)-Serum	34.18	<0.50:Low risk of sepsis 0.50-2.00:Borderline risk >2.00:High risk of severe sepsis/septic shock ng/ml

Note :
For diagnostic purpose, the result should always be interpreted in conjunction with patient's medical history as several non-infectious causes can also elevate Procalcitonin levels
Comments
Procalcitonin (PCT) is a prohormone expressed by neuroendocrine cells (C cells of thyroid, pulmonary and pancreatic tissues) present in very low levels in healthy individuals. Measurement of PCT can be used as a marker of severe sepsis and generally grades well with the degree of sepsis. Evidence is emerging that PCT levels can reduce unnecessary
antibiotic prescribing in lower respiratory tract infections.
Increased Levels
* Infectious – Bacterial infections leading to Septic shock / Severe sepsis, Community acquired respiratory tract infections & Ventilator induced pneumonia
* Non Infectious – Severe Cardiogenic shock, organ perfusion anomalies, Small cell lung cancer or Medullary C-cell carcinoma of thyroid, major trauma, surgical intervention & severe burns, treatment which stimulate the release of pro-inflammatory cytokines & Neonates (<48 hrs. after birth)
Clinical Use
* As a prognostic marker to support outcome prediction in sepsis patients.
* As an indicator of severity and major complications in acute pancreatitis.
* As a guide for the necessity of antibiotic therapy and to monitor success of treatments in patients suffering from community-acquired respiratory tract infections or ventilatorinduced pneumonia.
Fluorescence Immunoassay

End Of Report

chandrasekharputel
Lab Incharge

Dr . Ghanashyam Meher
MD pathology
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INVESTIGATION REPORT

(13)

Vikash Binayak Hospital

Patient Name	:	Lab ID No.	: 14961
Gender/ Age	: Male / 34Y 3M 4D	Patient ID No.	: 2361 / 24-25 (IPD)
Consultant Dr.	: Dr. Basanta Kumar Pradhan	Registered On	: 29/07/2024 01:21 PM
Referred By	: Self	Collected On	: 03/08/2024 08:08 AM
Ward / Bed	: Icu_2 / 9	Reported On	: 03/08/2024 09:11 AM
UHID No.	: 8353		

RFT PROFILE
BIOCHEMISTRY

TEST DESCRIPTION	RESULT	REFERENCE RANGE/UNITS
CREATININE-SERUM	4.36	0.6-1.3 mg/dl

Comments:
Creatinine is the catabolic product of creatinine phosphate which is used by the skeletal muscle.
The daily production depends on muscular mass and it is excreted out of the body entirely by the kidneys.
Elevated levels are found in renal dysfunction, reduced renal blood flow (shock, dehydration, congestive heart failure) diabetes acromegaly. Decreased levels are found in muscular dystrophy.

ELECTROLYTES - SERUM

Sodium-Na+	139.76	136-146 mmol/L
Potassium-K+	3.34	3.5-5.1 mmol/L
Chloride-Cl-	100.10	94-110 mmol/L
BLOOD UREA	79.88	12-50 mg/dl

Comments:
Urea is the end product of the protein metabolism. It is systhesised in the liver from the ammonia produced by the catabolism of amino acids.
It is transported by the blood to the kidneys from where it is excreted.
Increased levels are found in renal diseases, urinary obstructions, shock, congestive heart failure and burns.
Decreased levels are found in liver failure and pregnancy.

URIC ACID - SERUM	4.67	3.5-7.2 mg/dl

Uric acid is the final product of purine metabolism in humans. The major causes of hyperuricemia are increased purine synthesis, inherited metabolic disorder, excess dietary purine intake, increased nucleic acid turnover, malignancy, cytotoxic drugs, and decreased excretion due to chronic renal failure or increased renal reabsorption. Hypouricemia may be secondary to severe hepatocellular disease with reduced purine synthesis, defective renal tubular reabsorption, overtreatment of hyperuricemia with allopurinol, as well as some cancer therapies (eg. 6-mercaptopurine).
(Modified Uricase)

End Of Report

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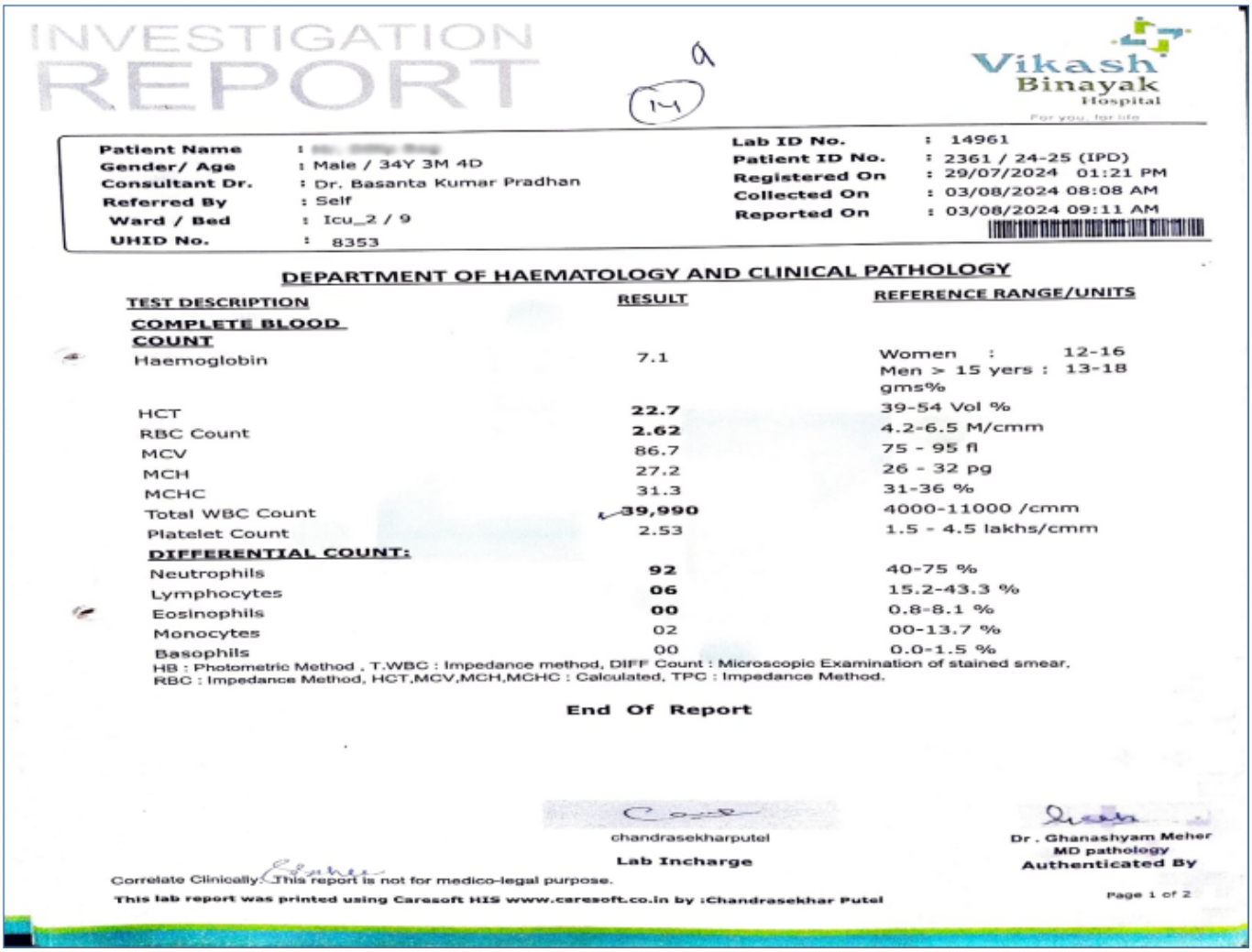

INVESTIGATION REPORT

Vikash Binayak Hospital

Patient Name	:	Lab ID No.	: 14961
Gender/ Age	: Male / 34Y 3M 4D	Patient ID No.	: 2361 / 24-25 (IPD)
Consultant Dr.	: Dr. Basanta Kumar Pradhan	Registered On	: 29/07/2024 01:21 PM
Referred By	: Self	Collected On	: 03/08/2024 08:08 AM
Ward / Bed	: Icu_2 / 9	Reported On	: 03/08/2024 09:11 AM
UHID No.	: 8353		

DEPARTMENT OF HAEMATOLOGY AND CLINICAL PATHOLOGY

TEST DESCRIPTION	RESULT	REFERENCE RANGE/UNITS
COMPLETE BLOOD COUNT		
Haemoglobin	7.1	Women : 12-16 Men > 15 yers : 13-18 gms%
HCT	**22.7**	39-54 Vol %
RBC Count	**2.62**	4.2-6.5 M/cmm
MCV	86.7	75 - 95 fl
MCH	27.2	26 - 32 pg
MCHC	31.3	31-36 %
Total WBC Count	**39,990**	4000-11000 /cmm
Platelet Count	2.53	1.5 - 4.5 lakhs/cmm
DIFFERENTIAL COUNT:		
Neutrophils	**92**	40-75 %
Lymphocytes	**06**	15.2-43.3 %
Eosinophils	**00**	0.8-8.1 %
Monocytes	02	00-13.7 %
Basophils	00	0.0-1.5 %

HB : Photometric Method , T.WBC : Impedance method, DIFF Count : Microscopic Examination of stained smear.
RBC : Impedance Method, HCT,MCV,MCH,MCHC : Calculated, TPC : Impedance Method.

End Of Report

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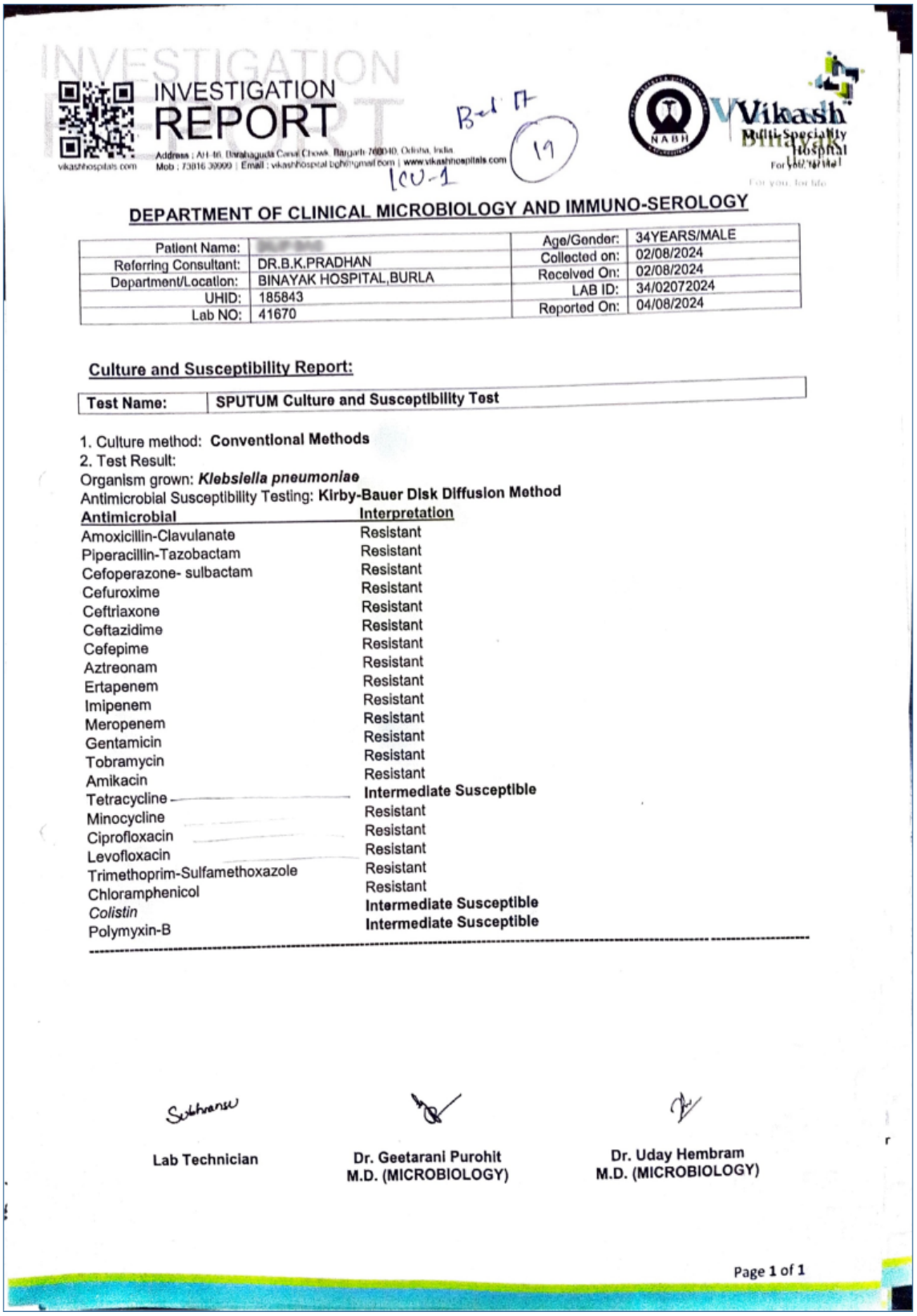

INVESTIGATION REPORT

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Mob : 73816 39999 | Email : vikashhospital.bgh@gmail.com | www.vikashhospitals.com

Bed 17
ICU-1

Vikash Multi Speciality Hospital
Binayak

DEPARTMENT OF CLINICAL MICROBIOLOGY AND IMMUNO-SEROLOGY

Patient Name:	[redacted]	Age/Gender:	34YEARS/MALE
Referring Consultant:	DR.B.K.PRADHAN	Collected on:	02/08/2024
Department/Location:	BINAYAK HOSPITAL,BURLA	Received On:	02/08/2024
UHID:	185843	LAB ID:	34/02072024
Lab NO:	41670	Reported On:	04/08/2024

Culture and Susceptibility Report:

Test Name:	SPUTUM Culture and Susceptibility Test

1. Culture method: **Conventional Methods**
2. Test Result:

Organism grown: ***Klebsiella pneumoniae***

Antimicrobial Susceptibility Testing: **Kirby-Bauer Disk Diffusion Method**

Antimicrobial	Interpretation
Amoxicillin-Clavulanate	Resistant
Piperacillin-Tazobactam	Resistant
Cefoperazone- sulbactam	Resistant
Cefuroxime	Resistant
Ceftriaxone	Resistant
Ceftazidime	Resistant
Cefepime	Resistant
Aztreonam	Resistant
Ertapenem	Resistant
Imipenem	Resistant
Meropenem	Resistant
Gentamicin	Resistant
Tobramycin	Resistant
Amikacin	Resistant
Tetracycline	**Intermediate Susceptible**
Minocycline	Resistant
Ciprofloxacin	Resistant
Levofloxacin	Resistant
Trimethoprim-Sulfamethoxazole	Resistant
Chloramphenicol	Resistant
Colistin	**Intermediate Susceptible**
Polymyxin-B	**Intermediate Susceptible**

Lab Technician

Dr. Geetarani Purohit
M.D. (MICROBIOLOGY)

Dr. Uday Hembram
M.D. (MICROBIOLOGY)

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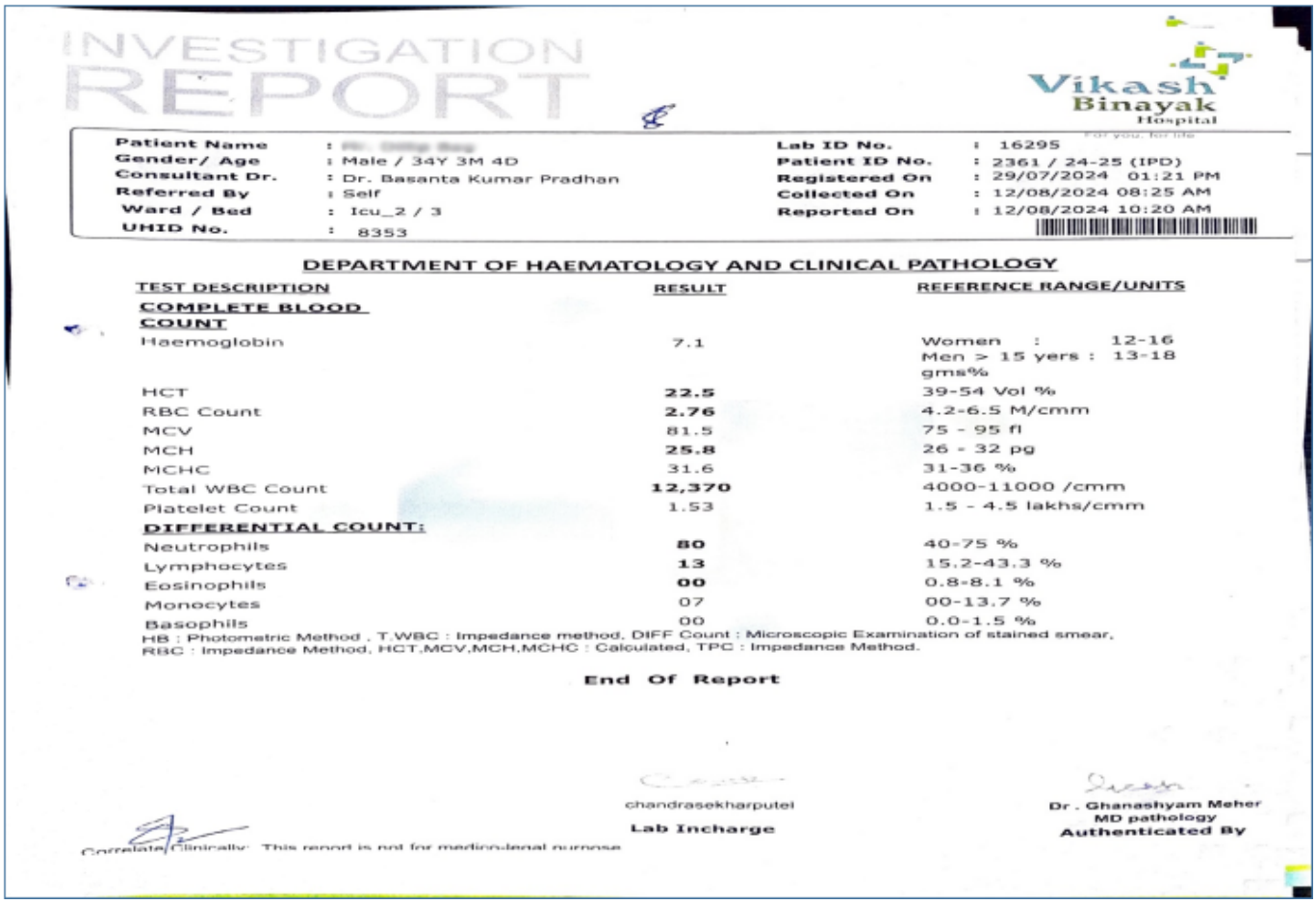

INVESTIGATION REPORT

Vikash Binayak Hospital

Patient Name	:	Lab ID No.	: 16295
Gender/ Age	: Male / 34Y 3M 4D	Patient ID No.	: 2361 / 24-25 (IPD)
Consultant Dr.	: Dr. Basanta Kumar Pradhan	Registered On	: 29/07/2024 01:21 PM
Referred By	: Self	Collected On	: 12/08/2024 08:25 AM
Ward / Bed	: Icu_2 / 3	Reported On	: 12/08/2024 10:20 AM
UHID No.	: 8353		

DEPARTMENT OF HAEMATOLOGY AND CLINICAL PATHOLOGY

TEST DESCRIPTION	RESULT	REFERENCE RANGE/UNITS
COMPLETE BLOOD COUNT		
Haemoglobin	7.1	Women : 12-16 Men > 15 yers : 13-18 gms%
HCT	**22.5**	39-54 Vol %
RBC Count	**2.76**	4.2-6.5 M/cmm
MCV	81.5	75 - 95 fl
MCH	**25.8**	26 - 32 pg
MCHC	31.6	31-36 %
Total WBC Count	**12,370**	4000-11000 /cmm
Platelet Count	1.53	1.5 - 4.5 lakhs/cmm
DIFFERENTIAL COUNT:		
Neutrophils	**80**	40-75 %
Lymphocytes	**13**	15.2-43.3 %
Eosinophils	**00**	0.8-8.1 %
Monocytes	07	00-13.7 %
Basophils	00	0.0-1.5 %

HB : Photometric Method , T.WBC : Impedance method, DIFF Count : Microscopic Examination of stained smear, RBC : Impedance Method, HCT,MCV,MCH,MCHC : Calculated, TPC : Impedance Method.

End Of Report

chandrasekharputel
Lab Incharge

Dr . Ghanashyam Meher
MD pathology
Authenticated By

Correlate Clinically. This report is not for medico-legal purpose

INVESTIGATION REPORT

Vikash Binayak Hospital

Patient Name	:	Lab ID No.	: 16464
Gender/ Age	: Male / 34Y 3M 4D	Patient ID No.	: 2361 / 24-25 (IPD)
Consultant Dr.	: Dr. Basanta Kumar Pradhan	Registered On	: 29/07/2024 01:21 PM
Referred By	: Self	Collected On	: 13/08/2024 07:37 AM
Ward / Bed	: Icu_2 / 3	Reported On	: 13/08/2024 08:41 AM
UHID No.	: 8353		

RFT PROFILE
BIOCHEMISTRY

TEST DESCRIPTION	RESULT	REFERENCE RANGE/UNITS
CREATININE-SERUM	**4.85**	0.6-1.3 mg/dl

Comments:
Creatinine is the catabolic product of creatinine phosphate which is used by the skeletal muscle.
The daily production depends on muscular mass and it is excreted out of the body entirely by the kidneys.
Elevated levels are found in renal dysfunction, reduced renal blood flow (shock, dehydration, congestive heart failure) diabetes acromegaly. Decreased levels are found in muscular dystrophy.

ELECTROLYTES - SERUM

Sodium-Na+	138.30	136-146 mmol/L
Potassium-K+	4.12	3.5-5.1 mmol/L
Chloride-Cl-	102.50	94-110 mmol/L
BLOOD UREA	**95.06**	12-50 mg/dl

Comments:
Urea is the end product of the protein metabolism. It is systhesised in the liver from the ammonia produced by the catabolism of amino acids.
It is transported by the blood to the kidneys from where it is excreted.
Increased levels are found in renal diseases, urinary obstructions, shock, congestive heart failure and burns.
Decreased levels are found in liver failure and pregnancy.

URIC ACID - SERUM	5.46	3.5-7.2 mg/dl

Uric acid is the final product of purine metabolism in humans. The major causes of hyperuricemia are increased purine synthesis, inherited metabolic disorder, excess dietary purine intake, increased nucleic acid turnover, malignancy, cytotoxic drugs, and decreased excretion due to chronic renal failure or increased renal reabsorption. Hypouricemia may be secondary to severe hepatocellular disease with reduced purine synthesis, defective renal tubular reabsorption, overtreatment of hyperuricemia with allopurinol, as well as some cancer therapies (eg. 6-mercaptopurine).
(Modified Uricase)

End Of Report

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MD pathology
Authenticated By

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Discussion:

This case of a 34 year-old male CKD patient on maintenance dialysis with recurrent respiratory failure presents important learning points regarding the management of multidrug-resistant (MDR) infections and the complications associated with polymixin particularly in critically ill patients.

Chronic kidney disease (CKD) patients on maintenance dialysis are highly susceptible to infections due to impaired immunity, frequent hospitalizations, and the presence of vascular access for hemodialysis, which acts as a potential source for infection. In this case, the patient presented with fever, cough, and shortness of breath, initially suggestive of community-acquired pneumonia. The rapid progression of his condition, coupled with

imaging showing right-sided consolidation and a markedly elevated white blood cell count (TLC > 39,990 cells/µL), indicated a severe infectious process likely exacerbated by his underlying comorbidities.

Managing MDR infections is very challenging. This patient was eventually diagnosed with MDR *Klebsiella* pneumoniea infection found in his sputum culture only susceptible polymyxin group of antibiotic.No susceptibility test was done for ceftazidime avibactam combination.Early empirical therapy with broad-spectrum antibiotics like Meropenem was warranted, given the patient's clinical condition and suspected bacterial pneumonia. However, the persistent worsening of the patient's clinical status, despite broad spectrum antibiotic coverage, raised the suspicion of an MDR pathogen, prompting the addition of Colistin, as an empirical therapy a last-line antibiotic often reserved for its bacteriocidal effect against MDR Gram-negative organisms.

Colistin, a polymyxin group of antibiotic, is frequently used for MDR Gram-negative infections treatment. Despite its efficacy against organisms like *Klebsiella pneumoniea, Acinetobacter baumanii*, it carries significant toxicity, particularly in patients with renal dysfunction. Colistin-induced nephrotoxicity is well documented, but this case illustrates another less recognized complication—colistin-induced neuromuscular blockade and respiratory paralysis(1). Neurotoxicity rates have remained low in most studies, ranging from around 0% to 5% of patients(3,4).The mechanism of colistin associated neurotoxicity is a noncompetitive myoneuronal presynaptic blockade of acetylcholine release to the synaptic gap.

The patient experienced recurrent episodes of respiratory failure with associated bradycardia and hypotension, necessitating multiple reintubations. After the third extubation attempt failed, it became evident that these recurrent episodes were unlikely to be related to the underlying infection or sepsis. Instead, they were more consistent with colistin-induced respiratory paralysis, a rare but serious adverse effect. Colistin can cause dose-dependent neuromuscular blockade, especially in patients with preexisting renal dysfunction, leading to respiratory muscle weakness or paralysis(4,6). Given that this patient was on maintenance dialysis and had impaired renal clearance, even the adjusted doses of colistin may have contributed to the drug's accumulation and subsequent toxicity.

The clinical pattern of initial improvement following extubation, followed by rapid deterioration with drowsiness, bradycardia, and hypotension, points towards neuromuscular dysfunction rather than a purely infectious or hemodynamic cause. The decision to stop colistin and switch to ceftazidime-avibactum combination, following the identification of MDR Klebsiella pneumoniea , marked a pivotal point in the patient's recovery. This switch

allowed for continued effective antimicrobial therapy while avoiding the neuromuscular complications associated with colistin.

The decision to intubate and subsequently wean critically ill patients requires careful consideration of both the underlying disease process and potential complications of treatment. In this case, each extubation attempt was followed by reintubation due to rapid respiratory decompensation, highlighting the need for vigilance in patients at risk for drug-induced respiratory paralysis. Balancing early extubation with the risks of premature respiratory failure is essential in ICU settings, particularly in patients with complicating factors like colistin use or CKD.

This case underscores the importance of antibiotic stewardship, especially when managing patients with MDR infections. While colistin remains a vital antibiotic for certain resistant organisms, its use must be weighed against the potential for serious toxicities, particularly in patients with renal impairment.Loading dose of colistin recommended in critically ill patients might lead to serious neurotoxicity, especially in patients with severe renal impairment(6)

Also we have to be aware that concomitant use of other neurotoxic drugs like aminoglycosides, corticosteroids,muscle relaxant increases the neurotoxicity.The successful management of this patient hinged on early recognition of the adverse effects of colistin, timely discontinuation of the drug, and the introduction of Ceftazidime-Avibactam, which provided adequate coverage for MDR *Klebsiella pneumoniea* while avoiding further neuromuscular complications.

Conclusion:

The case highlights several important aspects of ICU management, including the challenges in treating MDR infections, the risks associated with colistin use, and the complexities of mechanical ventilation in critically ill patients. Colistin-induced respiratory paralysis is a rare but life-threatening complication, particularly in patients with CKD. Early identification and appropriate management, including switching antibiotics, can significantly improve outcomes.

Reference:

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2. Dr. Raghvendra Singh

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