A Rare Complication in a Case of MDR Tuberculosis

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Clinical Course

MAY 2016

- 28 year old lady, housewife; presented with:

1. Fever
2. Cough with expectoration
3. Loss of appetite

} x 3 weeks

- Chest Radiograph suggestive of ? Pulmonary Tuberculosis
- Chest X Ray/Sputum Report and other treatment records not available

? CLINICALLY DIAGNOSED PULMONARY TUBERCULOSIS

- Started on Non Programmatic Anti Tubercular Treatment by Private Practitioner in Osmanabad

- Completed Treatment for 6 months (Nov 2016) With poor drug compliance

- Apparent good response after treatment

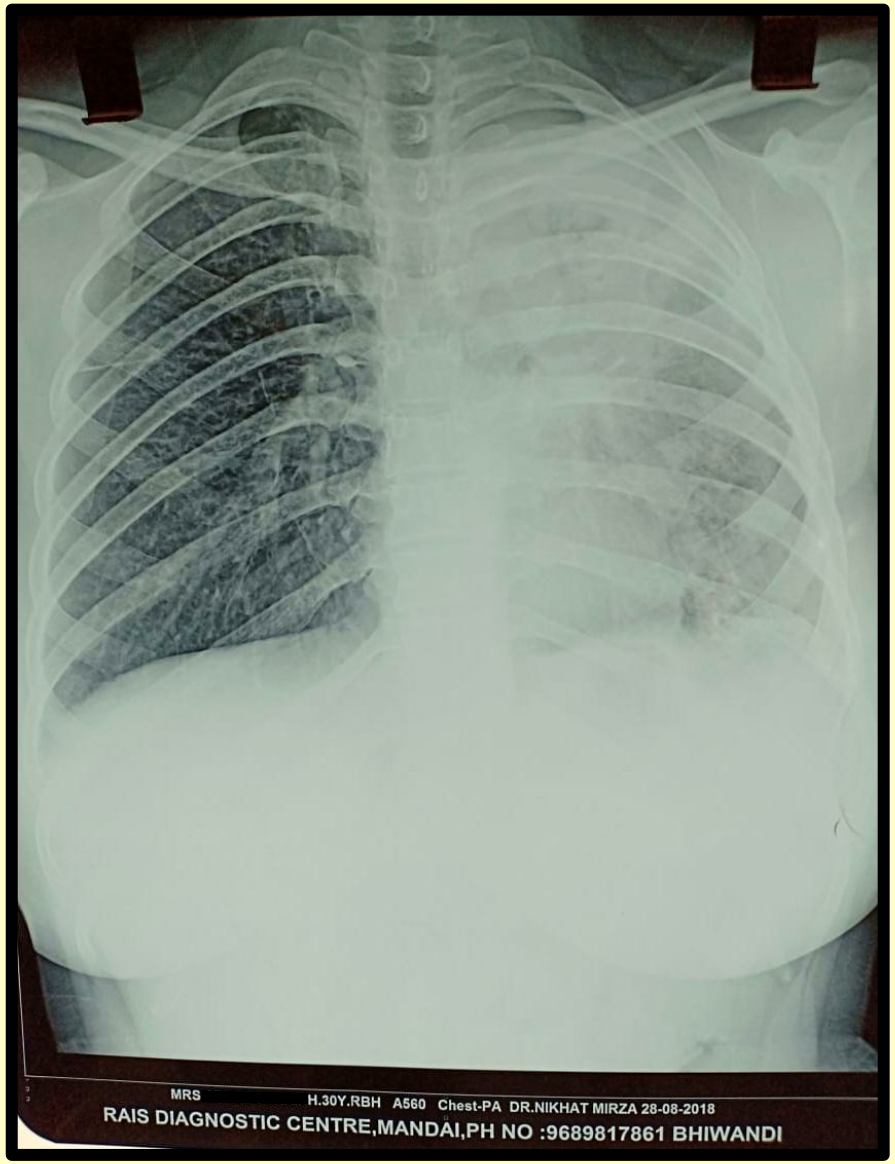
- No Follow Up Done after completion of ATT

AUGUST 2018

- Asymptomatic from Nov 2016 till July 2018
- Fever, Cough, Loss of appetite X 4 weeks

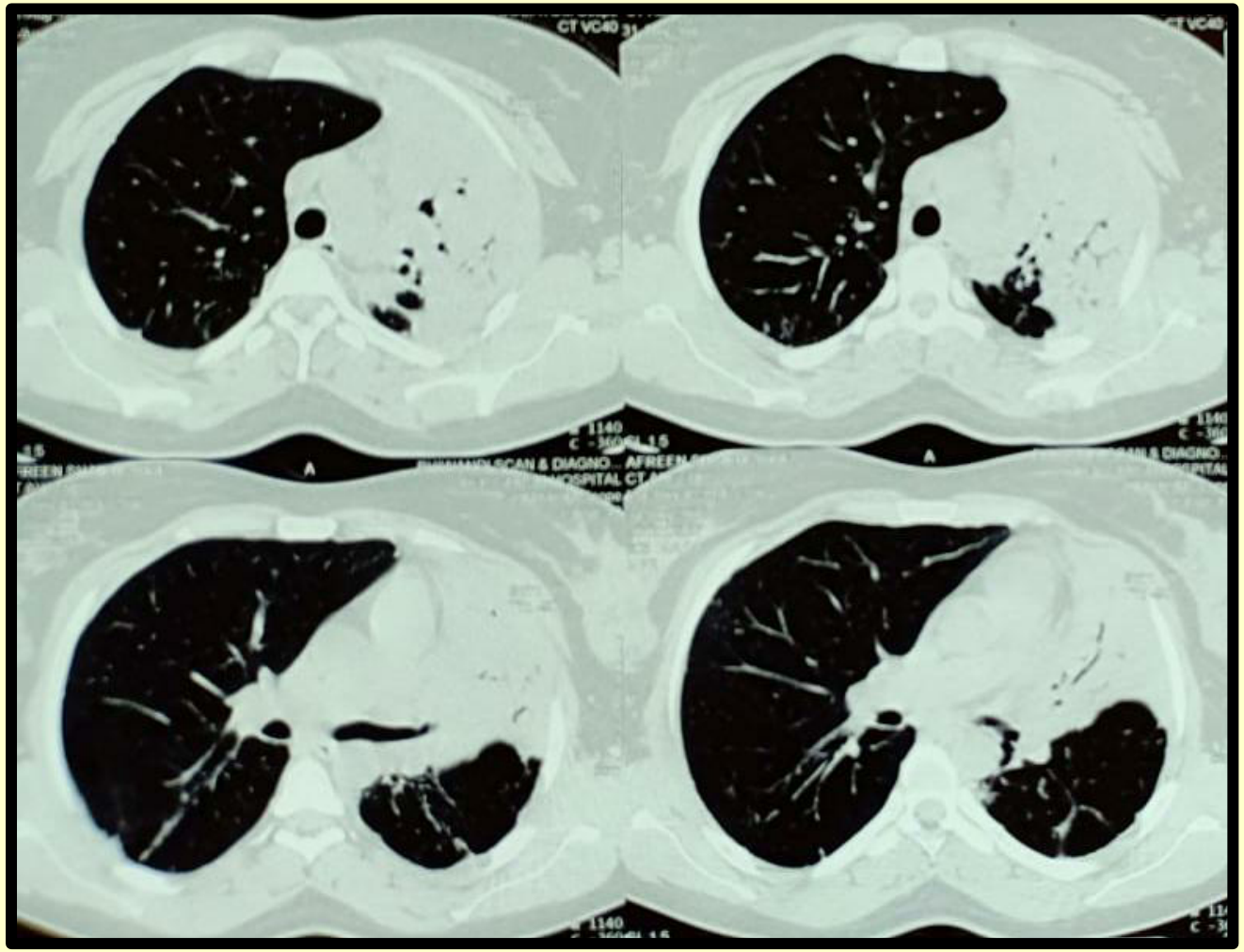
Sputum ZN (17/9/18)	: Sputum AFB 1 +
Sputum CBNAAT (1/10/18)	: Rifampicin Resistant M. Tb

MDR TUBERCULOSIS



AUGUST 2018

Inhomogeneous opacity occupying Left hemithorax predominantly upper zone with air bronchogram sign s/o consolidation with collapse



AUGUST 2018

HRCT Thorax:
Inhomogeneous opacity in Left Apical region with air bronchogram sign s/o consolidation with collapse

Started on DOTS CATEGORY IV on 01/10/18 (weight corrected)

TAB. LEVOFLOXACIN 500 mg OD (A)
INJ. KANAMYCIN 500 mg OD (B)
TAB.ETHIONAMIDE 500 mg OD (C)
TAB. CYCLOSERINE 500 mg OD (C)
TAB. ETHAMBUTOL 750 mg OD (D1)
TAB.PYRAZINAMIDE 1200 mg OD (D1)

Group	Class of drugs		Drugs
Group A	Fluoroquinolones		Levofloxacin
			Moxifloxacin
			Gatifloxacin
Group B	Second-line injectables		Kanamycin
			Amikacin
			Capreomycin
Group C	Other core second-line agents		Ethionamide/Prothionamide, Cycloserine/Terizidone, Linezolid, Clofazimine
Group D	Add-on agents	D1	Pyrazinamide
			Ethambutol
			High-dose isoniazid
		D2	Bedaquiline
			Delamanid
		D3	P-aminosalicylic acid
			Imipenem-cilastatin
			Meropenem
			Amoxicillin-clavulunate
			Thioacetazone

DECEMBER 2018

PRESENTED IN OUR CASUALTY WITH:

(After 2 months of DOTS CAT IV)

- Tingling sensation in bilateral upper & lower limbs } x 4 weeks
- Weakness in all 4 limbs L/L > U/L

No history of :

1. Trauma or fall
2. Seizures in the past
3. Fever with URTI preceding to the episode
4. No Bowel/Bladder symptoms

DECEMBER 2018

ON ADMISSION

- Conscious, Oriented
- Pallor Present
- Spine Examination: NAD
- Vitals:
  - Pulse Rate : 90 bpm
  - Blood pressure : 110/70 mmHg
  - Respiratory Rate : 22 cycles/min
  - SpO_2 : 94 % on room air

ON ADMISSION

- R/S : Left supra scapular tubular bronchial breath sounds heard with crepitations
- CVS : S1, S2 heard; No murmurs
- P/A : Soft, Non Tender; No organomegaly

ON ADMISSION

- CNS

  - Higher function : Normal

  - Cranial Nerves : No involvement

  - Motor:

    Tone : Hypotonia in all 4 limbs

    Power : 3/5 in B/L upper limbs; 2/5 B/L lower limbs

    Reflexes : Superficial & Deep present B/L

  - Sensory : Normal in B/L all limbs

CHOVSTEKS' SIGN & TROUSSEAU'S SIGN POSITIVE

ON ADMISSION: 29/12/2018

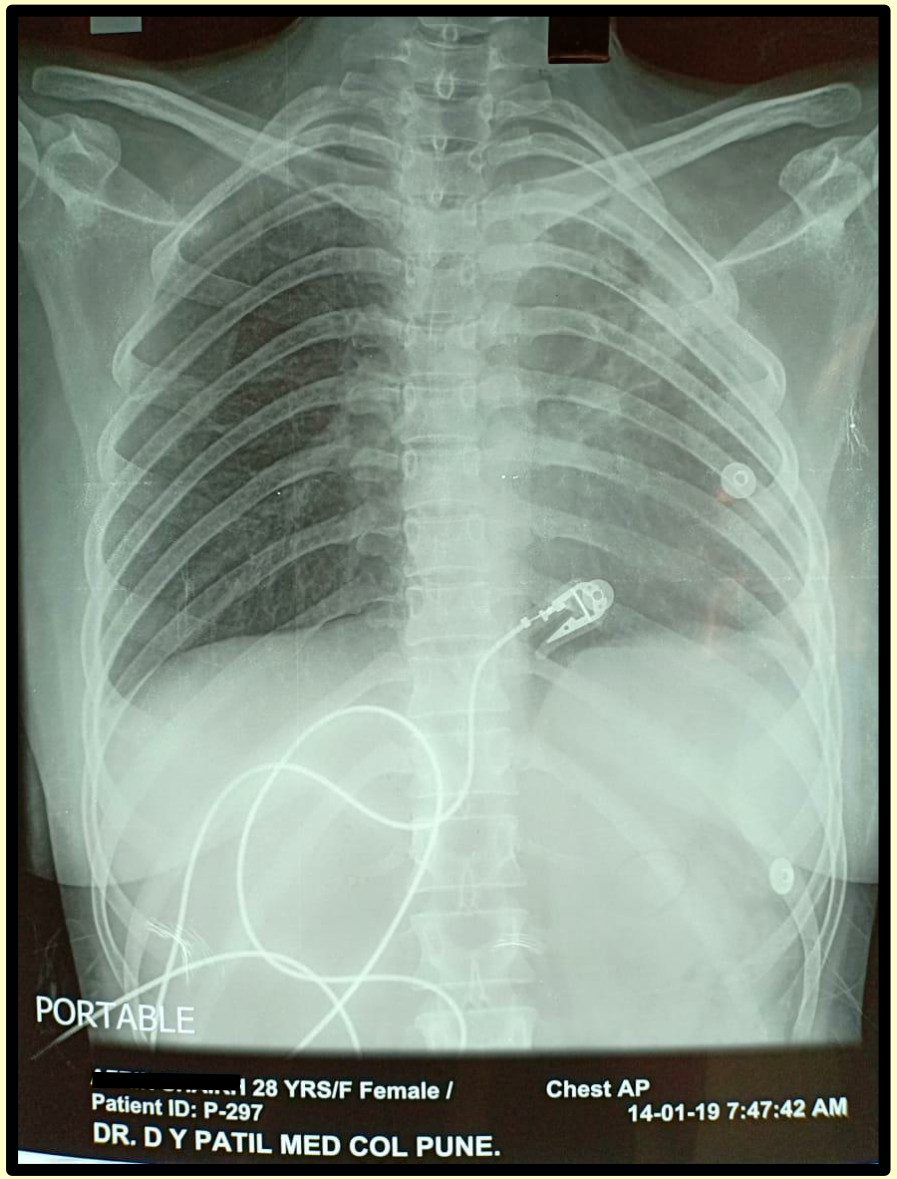
Hb	8.2 ↓	Urine Routine	WNL, No casts
TLC	13000	Se Na^+	144
Platelets	2.2 lacs	Se K^+	2.0 ↓
PBS	Microcytic Normochromic	Se Ca^{2+}	3.7 ↓
Blood Urea	46 ↑	Ionized Ca^{2+}	0.94 ↓
Se Creat.	1.9 ↑	Se Mg^{2+}	1.4 ↓
LFT	WNL	Se Cl^-	87 ↓

ON ADMISSION: 29/12/2018

ABG ON ROOM AIR

pH	7.53
PaO_2	92.6
$PaCO_2$	38.1
HCO_3^-	30.1
SO_2	97%

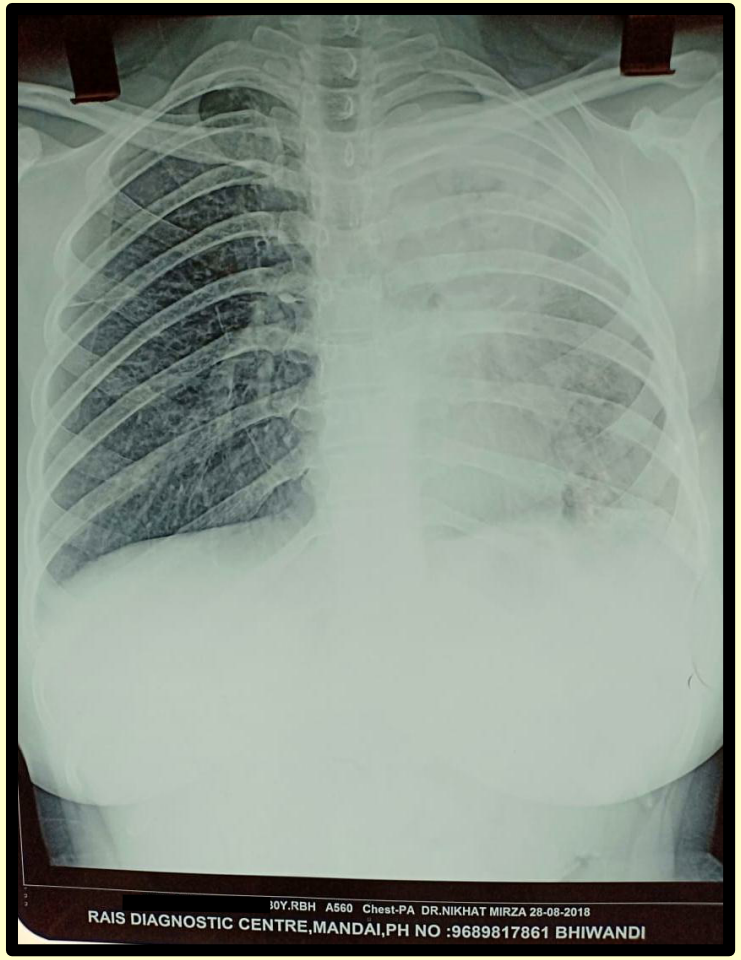
Uncompensated
Metabolic Alkalosis
With mild hypoxemia



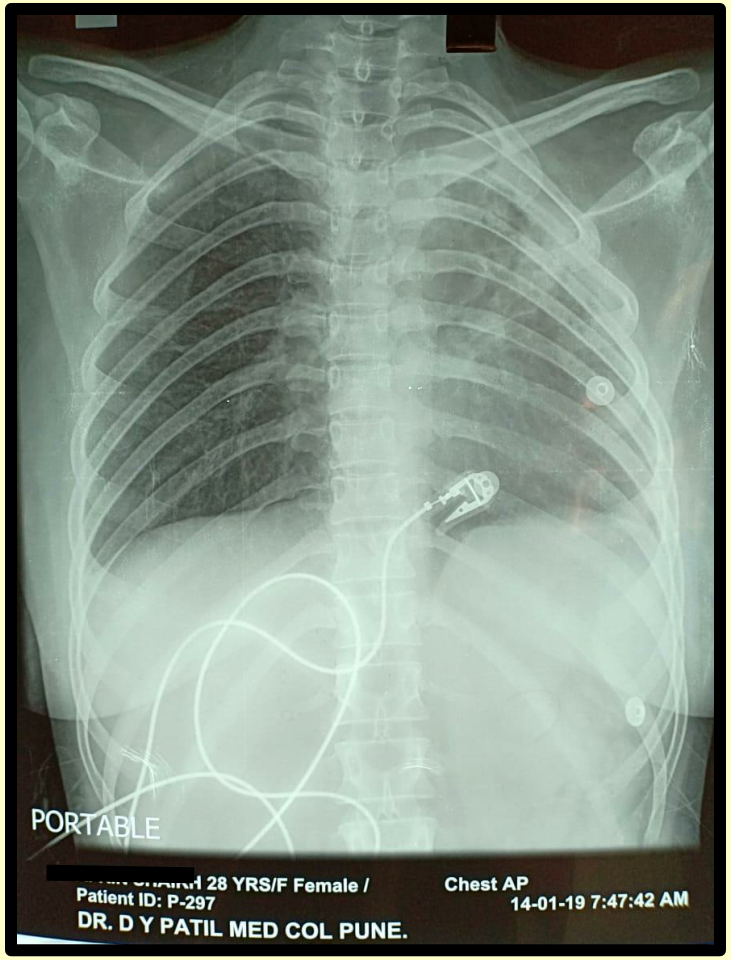
JANUARY 2019

Inhomogeneous opacity in Left Hemithorax with air bronchogram s/o consolidation with Left C/P angle blunting s/o ? Left pleural effusion with ? Few fibrotic residual lesions in Left upper zone

AUGUST 2018



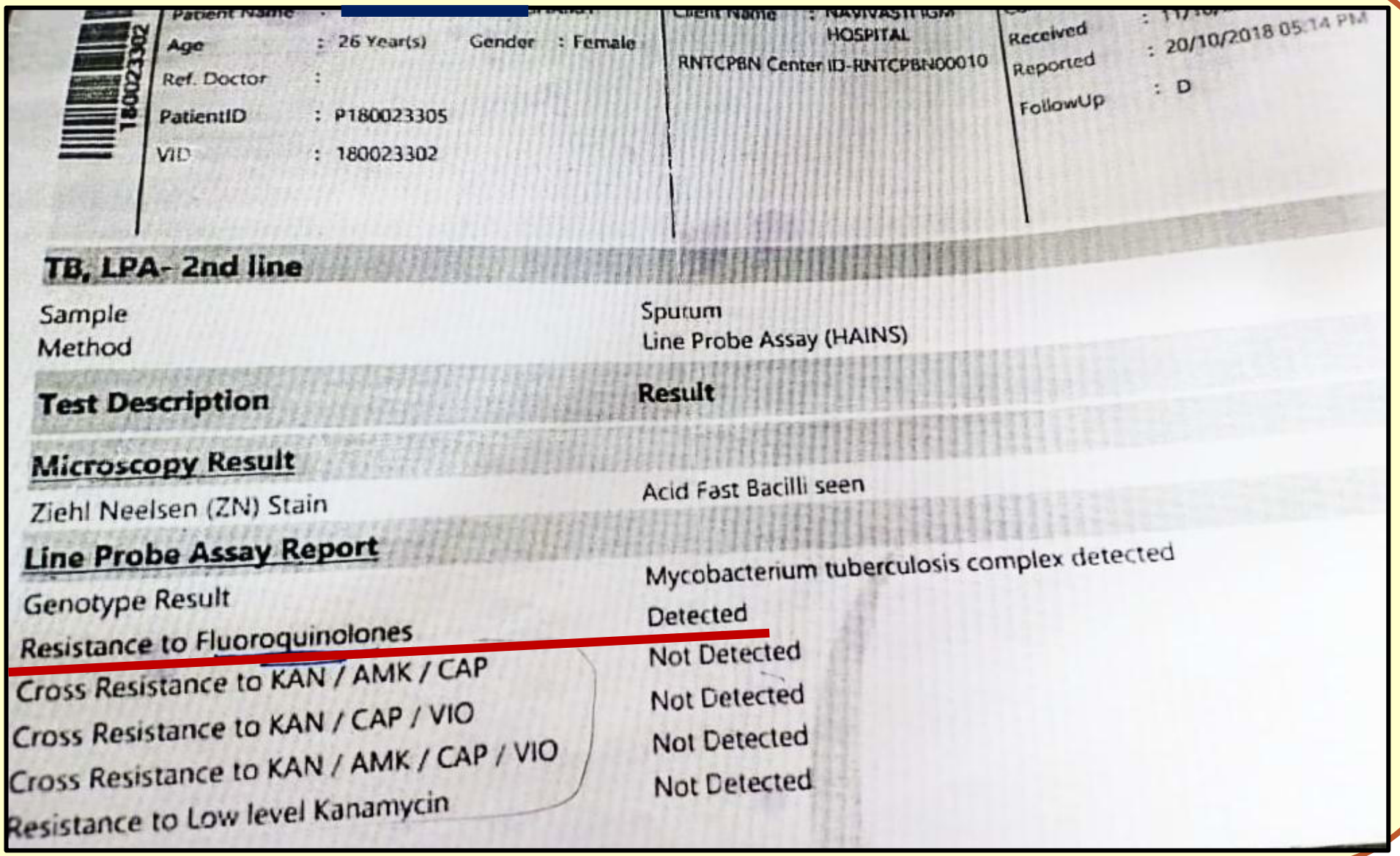
JANUARY 2019



Line Probe Assay with 2nd line DST (sent on 10/10/2018)

- **FLUOROQUINOLONE RESISTANCE : PRESENT**
- **2ND LINE AMINOGLYCOSIDE RESISTANCE: NOT DETECTED**

PRE XDR TUBERCULOSIS



Patient Name : [redacted]
Age : 26 Year(s) Gender : Female
Ref. Doctor :
PatientID : P180023305
VID : 180023302
Client Name : NAVIVASTHGM HOSPITAL
RNTCPBN Center ID-RNTCPBN00010
Received :
Reported : 20/10/2018 05:14 PM
FollowUp : D

TB, LPA- 2nd line

Sample	Sputum
Method	Line Probe Assay (HAINS)

Test Description	Result
Microscopy Result	
Ziehl Neelsen (ZN) Stain	Acid Fast Bacilli seen
Line Probe Assay Report	
Genotype Result	Mycobacterium tuberculosis complex detected
Resistance to Fluoroquinolones	Detected
Cross Resistance to KAN / AMK / CAP	Not Detected
Cross Resistance to KAN / CAP / VIO	Not Detected
Cross Resistance to KAN / AMK / CAP / VIO	Not Detected
Resistance to Low level Kanamycin	Not Detected

05/01/2019

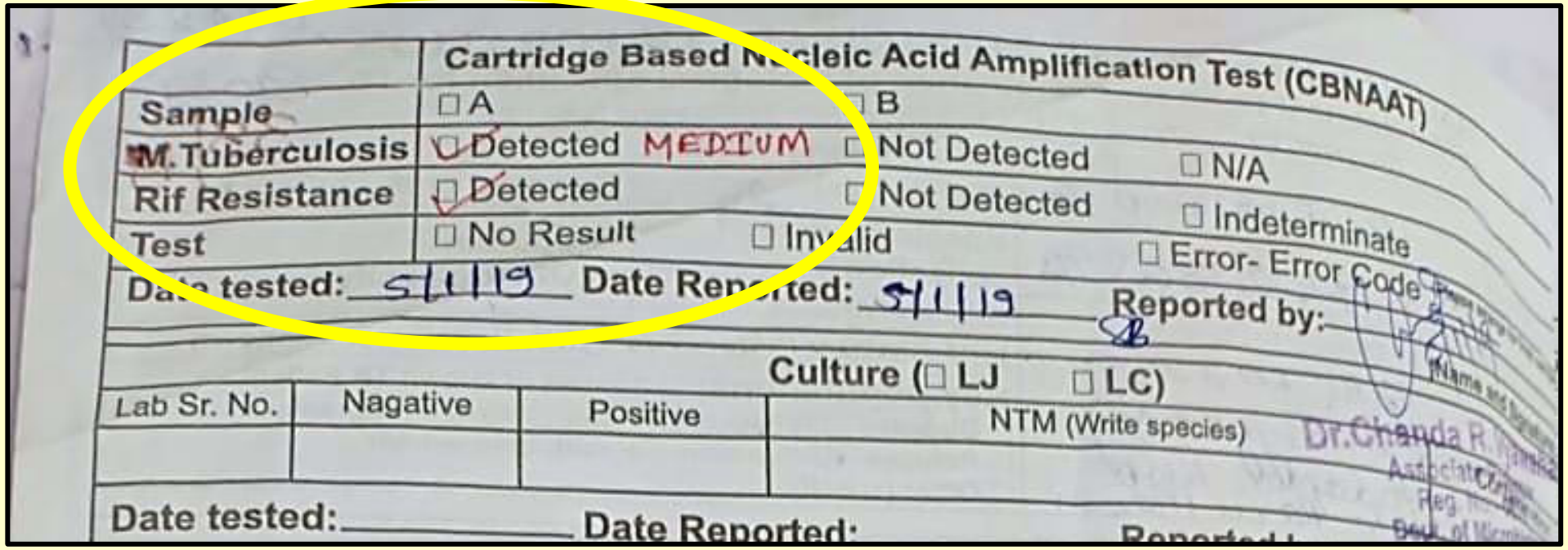
Sputum MGIT c/s (sent on 01/10/18): No Growth ??!!

FIRST CULTURE NEGATIVE!!!

Despite Sputum Smear Positivity and adequate clinico-radiological evidence.

05/01/2019

- Sputum ZN : Negative
- Sputum Genexpert: Rifampicin Resistant



Cartridge Based Nucleic Acid Amplification Test (CBNAAT)

Sample	☐ A	☐ B	
M.Tuberculosis	☑ Detected MEDIUM	☐ Not Detected	☐ N/A
Rif Resistance	☐ Detected	☐ Not Detected	☐ Indeterminate
Test	☐ No Result	☐ Invalid	☐ Error- Error Code

Date tested: 5/1/19 Date Reported: 5/1/19 Reported by:

Culture (☐ LJ ☐ LC)

Lab Sr. No.	Nagative	Positive	NTM (Write species)

Date tested: Date Reported:

Dr.Chanda R

NEUROLOGY CONSULT DONE

- Provisional Diagnosis: Dyselectrolemia under evaluation (Hypokalemia, Hypocalcemia)

- Potassium & Calcium supplementation BOTH intravenous & oral started with frequent ECG & lab monitoring.

NEPHROLOGY CONSULT DONE

- Provisional Diagnosis: ?Drug Induced Nephrotoxicity
- Patient continued on DOTS Cat IV with Renal Dose Modification
- Potassium & Calcium supplementation BOTH intravenous & oral started with frequent ECG & lab monitoring.

PROVISIONAL DIAGNOSIS

1. Aminoglycoside induced Nephrotoxicity (AIN)
2. Dyselectrolemia under evaluation

FURTHER WORK UP

- <u>USG Abdomen/Pelvis:</u>
  Normal Study; Renal size, shape, echogenicity normal

- 24 hr Urine Sodium : 88.0 (40 – 220 mEq/L)
- 24 hr Urine Potassium : 20.8 (20 – 40 mEq/L)
- 24 hr Urine Calcium : 98 ↓ (100 – 250 mEq/L)
- Se. Vitamin D Level : 15.8 ↓ (25 – 80 ng/ml)
- Thyroid function test :T3 - 1.0/ T4 – 6.9/ TSH – 15.3 ↑
- Se. Parathyroid hormone :125 ↑ (10 – 65 ng/ml)

INJ. KANAMYCIN WAS DISCONTINUED

- Inj. Kanamycin was replaced with Tab. Linezolid
  (from WHO Group C 2nd Line ATT drugs)
- Intra venous & Oral Potassium & Calcium supplementation was continued.

Patient improved symptomatically & gradual improvement in lab parameters was seen over 2 weeks.

ON DISCHARGE: 01/02/2019

Hb	9.1	Se Na^+	142
TLC	12800	Se K^+	4.0
Platelets	2.4 lacs	Se Ca^{2+}	8.7
Urea	19	Ionized Ca^{2+}	1.2
Se Creat.	0.93	Se Mg^{2+}	1.9
LFT	WNL	Se Cl^-	96

SALIENT FEATURES – Present Case

HYPOKALEMIA

HYPOMAGNESEMIA

HYPOCALCIURIA

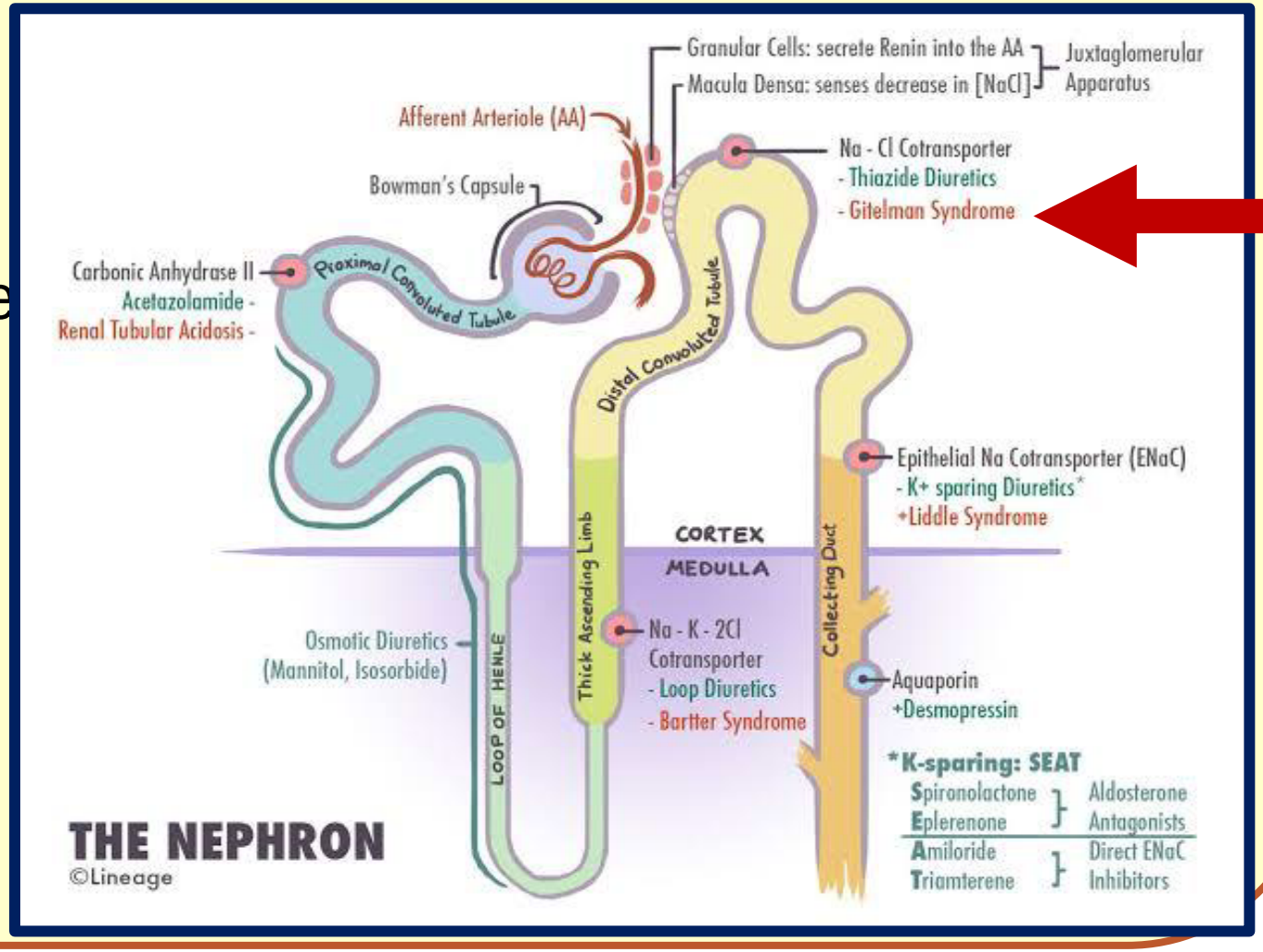
PERSISTENT METABOLIC ALKALOSIS

GITELMAN- LIKE SYNDROME

with ? Pre-XDR Pulmonary Tuberculosis

DISCUSSION

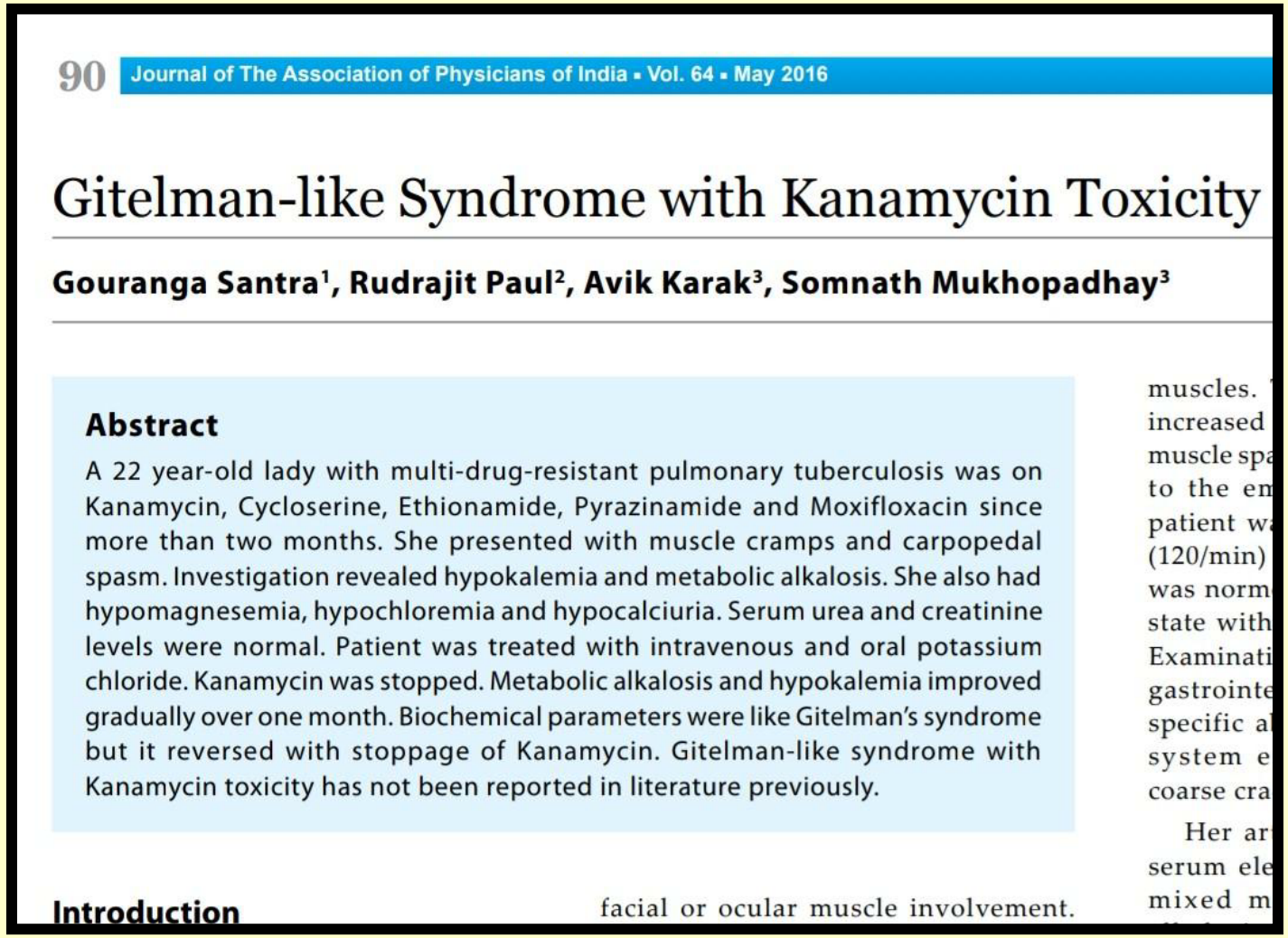
- Gitelman's Syndrome (GS) is a rare genetic renal disease due to mutations in the thiazide sensitive Na^+-Cl^- co-transporter in the DCT.
- Characterised by hypokalemia, hypomagnesemia, metabolic alkalosis and hypocalciuria.



DISCUSSION…contd.

Hypokalemia & Hypomagnesemia have been reported with aminoglycoside toxicity but a full- blown GS like episode as in our patient is rare.

Exact mechanism of biochemical alteration in Gitelman-like syndrome is still unknown.



Gitelman-like Syndrome with Kanamycin Toxicity

Gouranga Santra[1], Rudrajit Paul[2], Avik Karak[3], Somnath Mukhopadhay[3]

Abstract

A 22 year-old lady with multi-drug-resistant pulmonary tuberculosis was on Kanamycin, Cycloserine, Ethionamide, Pyrazinamide and Moxifloxacin since more than two months. She presented with muscle cramps and carpopedal spasm. Investigation revealed hypokalemia and metabolic alkalosis. She also had hypomagnesemia, hypochloremia and hypocalciuria. Serum urea and creatinine levels were normal. Patient was treated with intravenous and oral potassium chloride. Kanamycin was stopped. Metabolic alkalosis and hypokalemia improved gradually over one month. Biochemical parameters were like Gitelman's syndrome but it reversed with stoppage of Kanamycin. Gitelman-like syndrome with Kanamycin toxicity has not been reported in literature previously.

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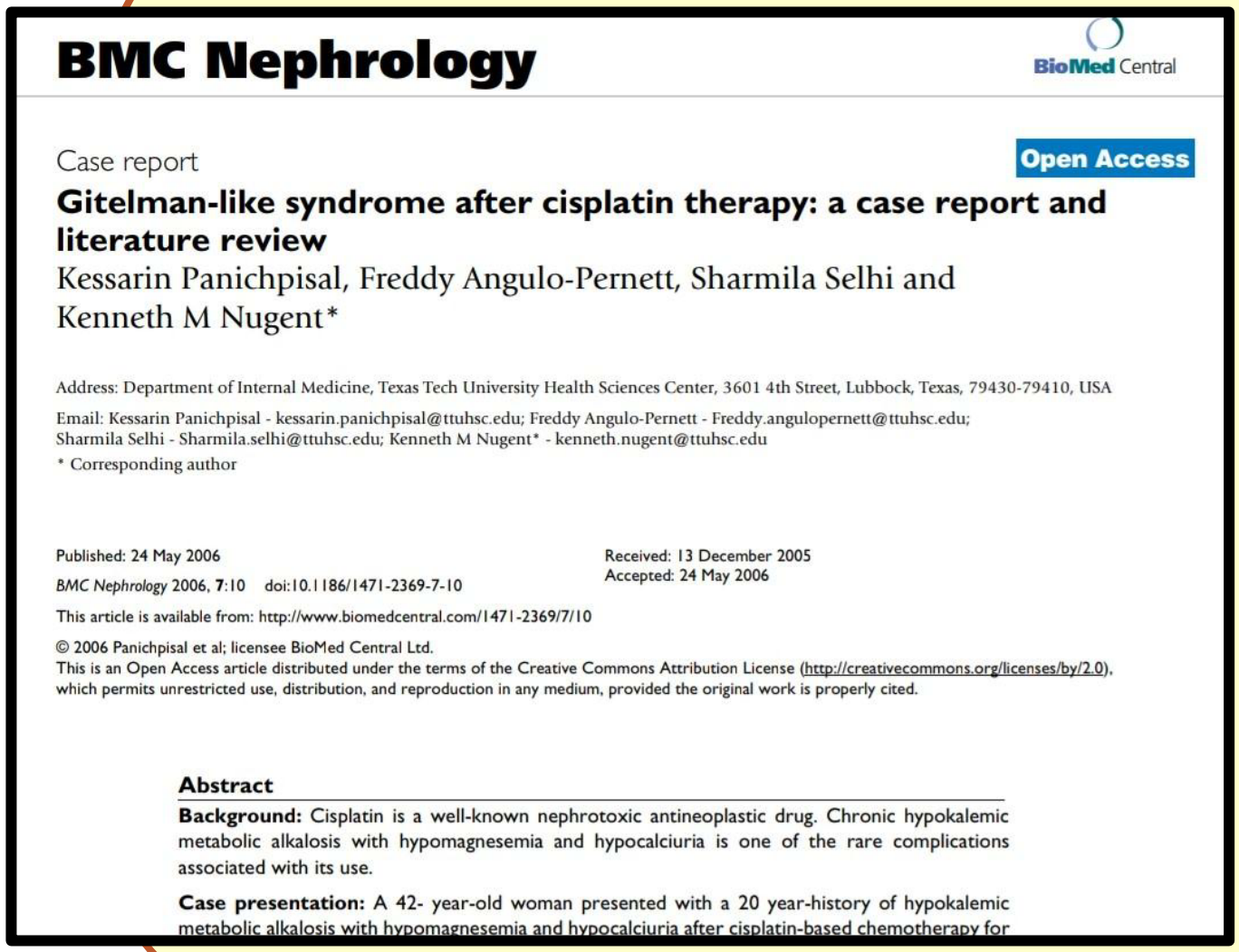
Introduction

facial or ocular muscle involvement.

Kanamycin toxicity presenting with Gitelman like Syndrome has only been reported ONCE in Indian Literature.



BMC Nephrology

BioMed Central

Case report

Open Access

Gitelman-like syndrome after cisplatin therapy: a case report and literature review

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Abstract

Background: Cisplatin is a well-known nephrotoxic antineoplastic drug. Chronic hypokalemic metabolic alkalosis with hypomagnesemia and hypocalciuria is one of the rare complications associated with its use.

Case presentation: A 42- year-old woman presented with a 20 year-history of hypokalemic metabolic alkalosis with hypomagnesemia and hypocalciuria after cisplatin-based chemotherapy for

Case report from USA described a patient on CISPLATIN who developed GS-like Syndrome.

(Cisplatin: focal tubular necrosis in DCT, direct DNA damage of NCCT gene)

DISCUSSION...contd.

AMINOGLYCOSIDE INDUCED NEPHROTOXICITY (AIN)	GITELMAN-LIKE SYNDROME
Hypercalciuria Urinary casts/sediments seen	Hypocalciuria No casts/sediments
Metabolic Acidosis	Metabolic Alkalosis
Damage to PROXIMAL tubular cells	Damage to DISTAL tubular cells

MANAGEMENT OF MDR TUBERCULOSIS

01/10/18

- Sputum ZN: 1+
- Sputum Genexpert: Rifampicin Resistant

↓ DOTS CAT IV

05/01/2019

- Sputum LiPA (sent on 01/10/18): FQ Resistant/2nd Line Inj. Sensitive
- Sputum MGIT c/s (sent on 01/10/18): NO GROWTH !!??

05/01/2019

- Sputum ZN: Negative
- Sputum Genexpert: Rifampicin Resistant

07/02/2019

- Sputum solid c/s(sent on 10/01/19): No Growth till 07/02/2019

TAKE HOME MESSAGE

Hence, clinical, radiological and microbiological evidence should be taken into consideration while managing a case of Drug Resistant Tuberculosis.

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THANK YOU