MALIGNANT HYPERTHERMIA – THE ULTIMATE CATASTROPHE

Presenter : Dr. Jekha Mary Babu (JR2)

Department of Anaesthesiology

CHIEF COMPLAINTS

19 year old female came to our hospital with chief complaints of :

Deformity of spine since childhood, which aggravated since 4 years

HISTORY OF PRESENTING ILLNESS

- Patient was apparently alright till 4 years of age after which her parents noticed the deformity of back, which gradually progressed and increased over the subsequent years

- It was associated with change in gait, which was more noticeable as the deformity increased with age, not associated with pain or discomfort

PRESENT MEDICAL HISTORY

- Patient had history of **dyspnea on exertion since 1 month , (she had breathlessness after climbing 1-2 flight of stairs), MMRC grade II**

  METS : 3

- No history of cough/cold/fever/ covid exposure
- No history of muscle weakness/ muscle atrophy or hyperthrophy/ neurofibromatosis over skin
- No history of palpitations/ chest pain
- No history of tuberculosis/ seizure/ asthma/ thyroid disorders/ hypertension/ diabetes mellitus
- No history of previous surgeries/ ICU stay/ Blood transfusion

Personal history :

- Diet – mixed
- Appetite – normal
- Sleep – disturbed
- Bowel and bladder – normal
- Denies addictions

Family history :

- No significant family history present
- **No history of anaesthesia related complications**

GENERAL EXAMINATION

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

Weight: 43Kg	Height: 144 cms	BMI: 20.73 kg/m^2

- No pallor, icterus, cyanosis, clubbing, lymphadenopathy or oedema

- Pulse : 92 bpm, right radial artery, regular in rate and rhythm, all peripheral pulses palpable
- BP : 120/80 mmHg recorded over the right brachial artery in supine position
- RR : 18 breaths/min

- **Spine** : Skin normal, **kyphoscoliosis present, double major curve seen in thoracic and lumbar spines, curvature to the right and left respectively**

➢ Airway Examination:

- Teeth : mal-aligned teeth, No missing teeth, no loose teeth
- Mouth opening : adequate
- Mallampati Score : II
- Temporomandibular joint mobility : Normal
- Thyromental distance : > 6.5 cm
- Neck Movement : Normal

- **Cardiovascular System:**

- S1S2 normally heard, no murmur present

- **Central Nervous System :**

- Power, tone and reflexes were normal, no focal neurological deficit

- **Respiratory System :**

- RR – 18/min, Thoracoabdominal breathing pattern
- Air entry bilaterally equal, no adventitious sounds

- **Per abdomen:**

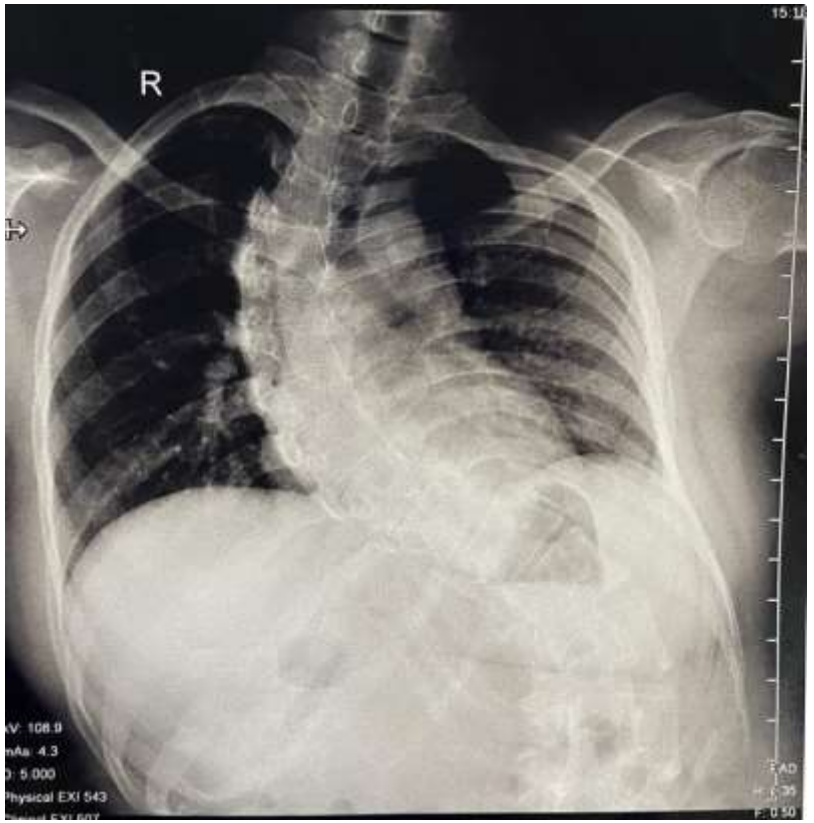
- Soft, non tender, bowel sounds present, no organomegaly

INVESTIGATIONS:

Hemoglobin	13.3g/dl
TLC	6700 /µL
Platelet count	2.53/µL
PT/INR	11.9 sec /0.99
Blood group	A positive

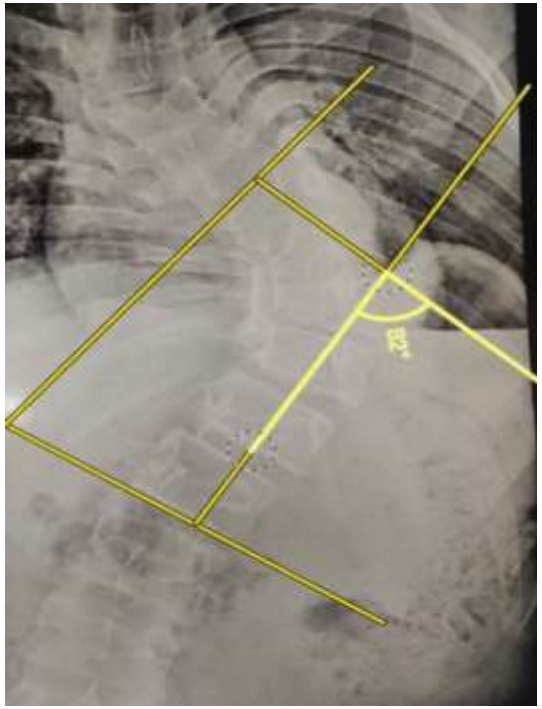
Urea Creatinine	22 mg/dl 0.54 mg/dl
S. Na+ S.K+	135 mmol/L 4.19 mmol/L
T. Bilirubin	0.39 mg/dl
SGOT SGPT	23 U/L 20 U/L
ALP	61 U/L

- **<u>Chest Xray</u>** showed increased broncho-vascular markings and **kypho-scoliosis over thoracic and lumbar spines**

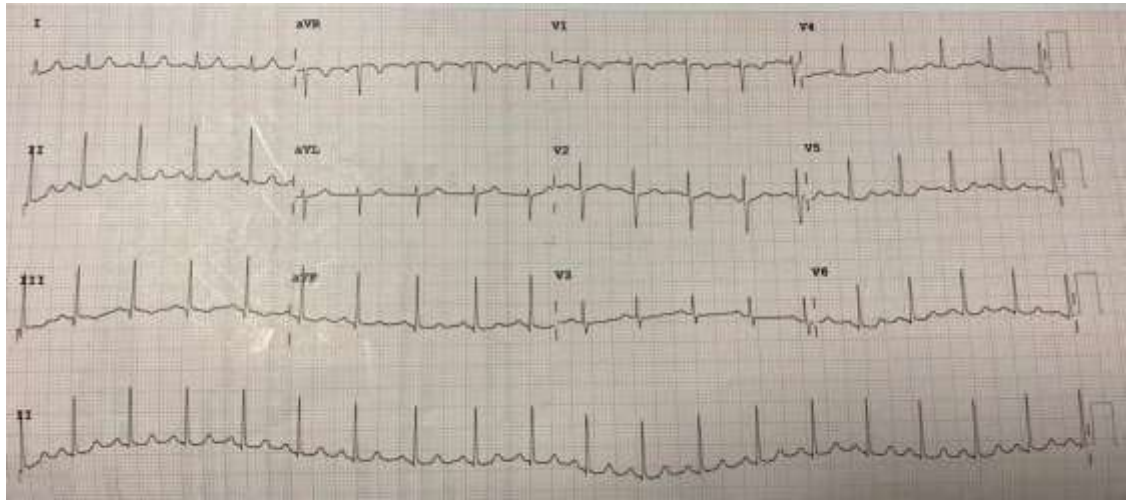


- Crowding of ribs on left side

- **Cobbs angle : 82 degrees**



- **<u>ECG</u>** showed normal sinus rhythm, sinus tachycardia (HR~120bpm)



- **<u>2D Echo</u>** revealed EF 65%, normal study

- **<u>Spirometry</u>:**

- Manoeuvre accepted
- No obstruction
- **Mild restriction present**
- Flow volume loop normal
- Volume time curve normal

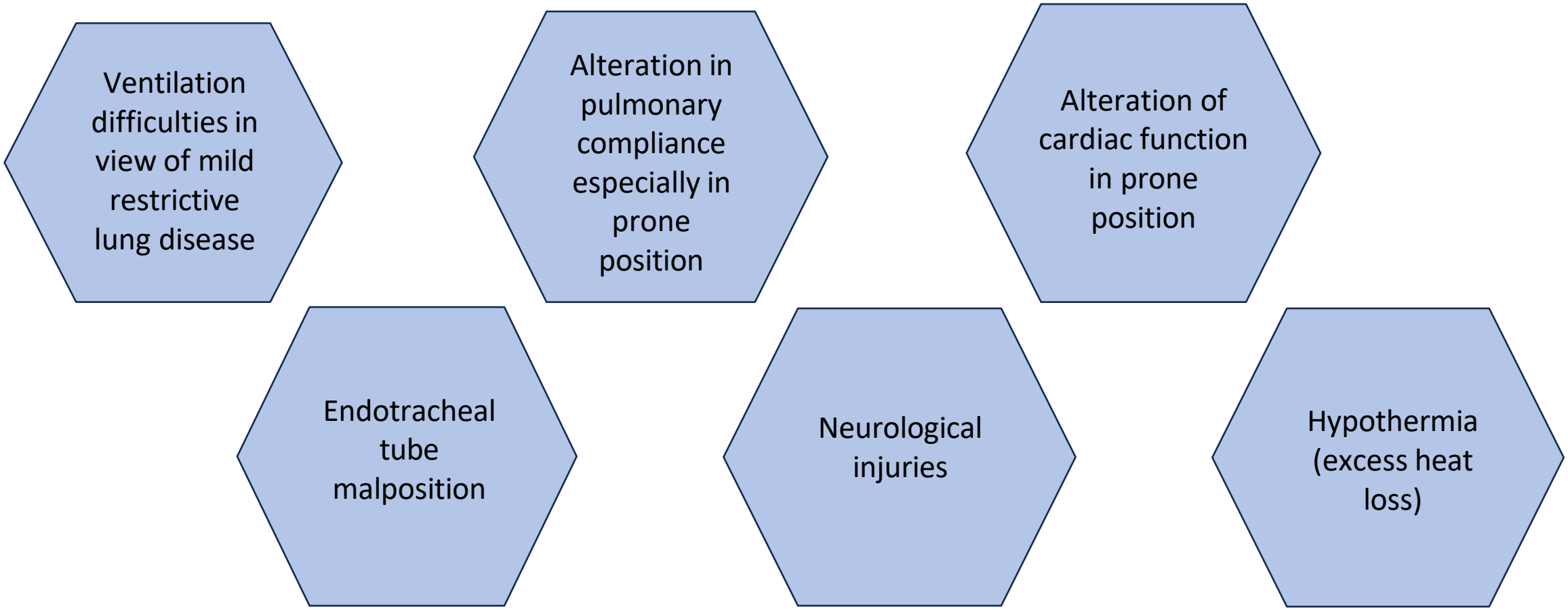
PROVISIONAL DIAGNOSIS

19 year old female, with thoraco-lumbar kyphoscoliosis and mild restrictive lung disease, was posted for pedicle screw fixation of T2-L4 levels.

PRE-OPERATIVE PREPARATION

- The risks and potential outcomes related to the surgery and anaesthesia was explained to the patient and relatives
- Written and informed consents taken
- Patient was advised to continue incentive spirometry till prior to surgery, every 2 hourly
- Patient was nebulized with Duolin (Ipratropium bromide + Levosalbutamol) and Budesonide twice daily and on the morning of surgery
- Patient was given fitness under ASA II with high risk

ANAESTHETIC CHALLENGES FOR KYPHOSCOLIOSIS SURGERY



ANAESTHESIA MANAGEMENT

Choice of anaesthesia :

General anaesthesia with Total Intravenous Anaesthesia (TIVA) with minimal inhalational agents (MAC less than 0.5)

PRE OPERATIVELY

- Patient was nil by mouth for more than 6 hours, confirmed
- Preop Vitals : Pulse – 94 bpm Blood Pressure : 110/74 mmHg SPO_2: 99%
- Fasting BSL : 108 mg/dL
- One 20 G and one 18 G IV canula were secured
- Adequate blood and blood products were reserved and confirmed after cross matching
- IV Inj. Ceftriaxone 1 g was given 30 minutes prior to surgery

- Baseline ABG –

pH - 7.46
pCO2 - 32 mmHg
pO2 - 255 mmHg
Na - 134 mmol/L
K - 3.9 mmol/L
Lactate - 1.0 mmol/L
HCO3 - 22.8 mmol/L
Hb - 11.8 g/dl

- All standard ASA monitors (ECG, Pulse oximetry and NIBP) were attached and warm IV fluids were started

- Preoxygenated with 100% oxygen using 3 size face mask

- Premedication : Inj. Glycopyrrolate 0.004mg/kg, Inj. Midazolam 0.02mg/kg given and
- Inj. Fentanyl 2mcg/kg (for analgesia) were given intravenously

- Induction : Inj Propofol 2 mg/Kg given slowly

- Muscle relaxant: Inj Atracurium 0.7mg/Kg IV

- Intubation : 7.0 size oral, cuffed, flexometallic tube and was secured, patient was put on volume control mode after confirming bilateral air entry and tracing of end tidal CO2

- Nasogastric tube inserted (14 Fr), and throat packing was done

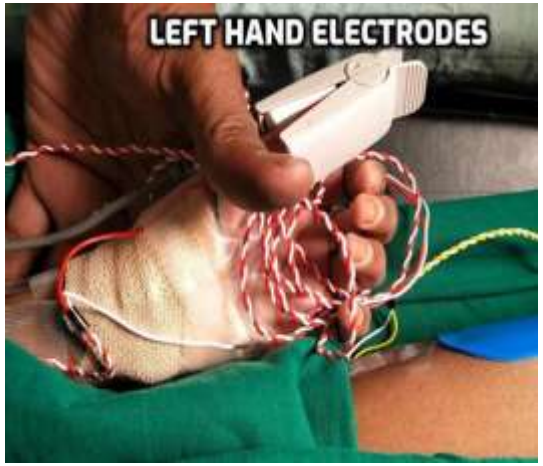
- Anaesthesia was maintained with oxygen: air (50:50), sevoflurane at 0.2% (MAC less than 0.5) and on Total Intravenous Anaesthesia (TIVA)
- Right radial invasive arterial line (20 gauge intracath) and right internal jugular central line (7 French triple lumen) were secured
- Temperature probe was attached
- Patient was shifted to prone position with due precautions to prevent IVC compression.

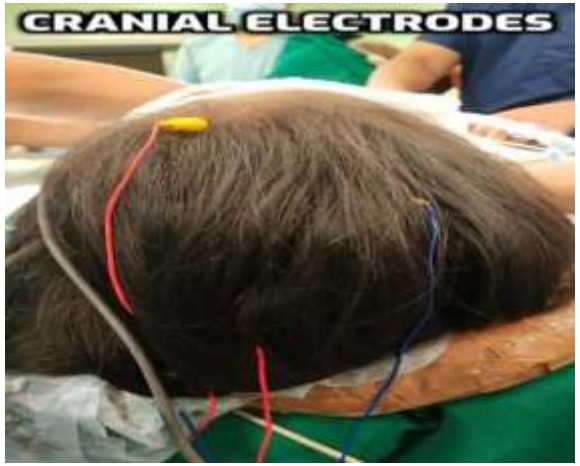
- **In our case, muscle relaxant was not used after the first dose.**

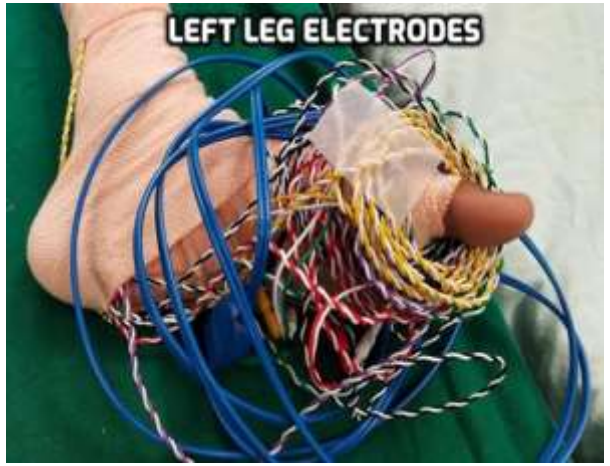
- In scoliosis correction surgery, baseline Somatosensory Evoked Potential (SSEP) and Motor Evoked Potential (MEP) are measured at regular intervals during correction and rod placement.

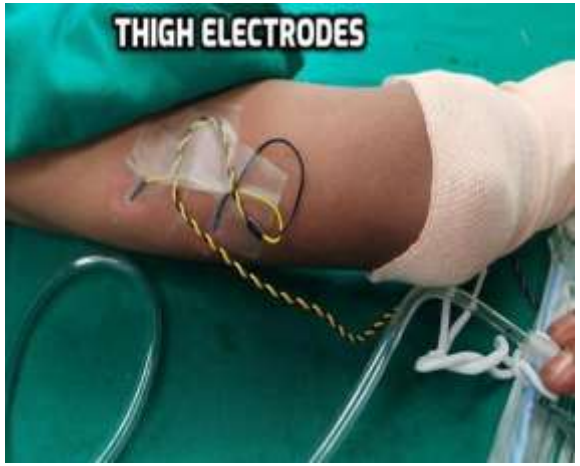
- Muscle relaxant if used, will mask the evoked potentials, hence was avoided.

Attachment of electrodes at different locations:









○ Anaesthesia management under Total Intravenous Anaesthesia :

➢ IV anaesthetic infusions used for TIVA were :

- **Inj. Propofol : started at 50-100 mcg/kg/min**
- **Inj. Fentanyl : 1-2 mcg/kg/hour**
- **Inj. Dexmedetomidine : 0.3-0.7 mcg/kg/hour**

- BIS monitor (Bispectral index) was attached simultaneously targeting a BIS of 40-60 by titrating the infusion doses

- After the confirmation of BIS, TOF, baseline SSEP and MEP readings, the surgery was started.

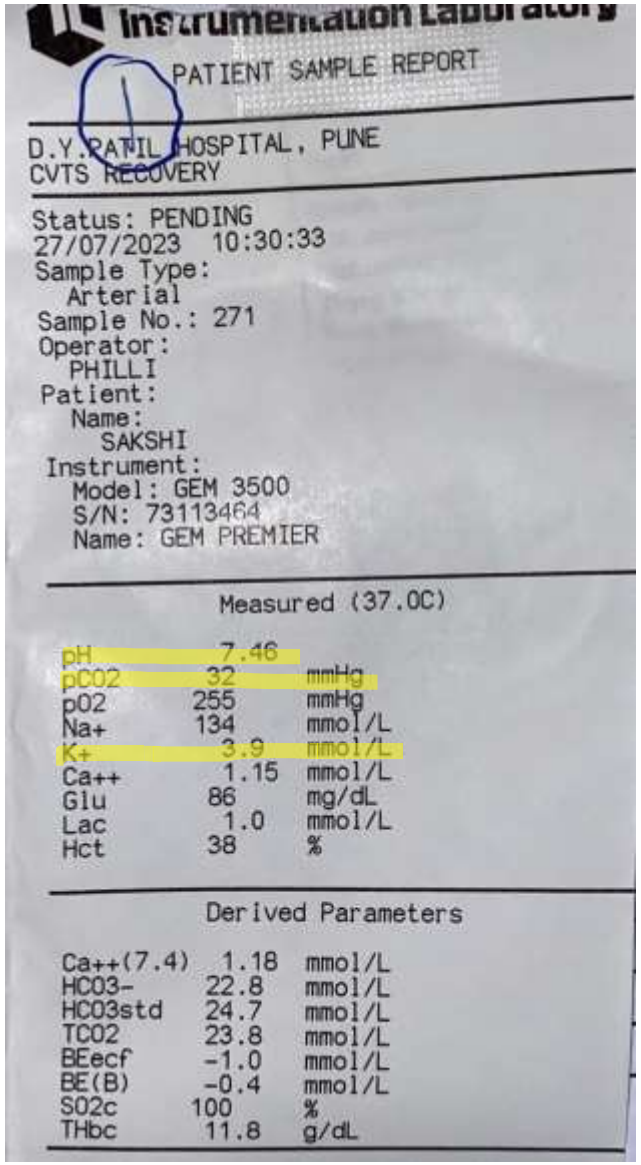
- **After 4.5 – 5 hours from induction, EtCO2 (48-60 mmHg), core temperature (39-41 deg Celsius) and peak airway pressures started rising.**

- Ventilatory parameters were adjusted, and changed from controlled ventilation to manual ventilation **to manage EtCO2, however it remained high.**

- After 20 minutes, EtCO2 and peak airway pressure continued to rise, **temperature recorded was 39.4 deg C, with tachycardia (106 bpm) and hypotension (70/48 mmHg), so vasopressor was started**

- **ABG sample was taken for analysis and it showed fall in pH, rise in pCO2 and serum potassium** (4.9 mmol/L intraoperatively)

TIME	EtCO2(mmHg)	TEMPERATURE (deg Celcius)	pH	S. POTTASIUM (mmol/L)	HEART RATE (bpm)	BLOOD PRESSURE (mmHg)
9:30 AM	30	36.8	7.46	3.9	92	116/74
10:30 AM	32	36.4	7.42	3.8	84	110/70
11:30 AM	32	38.2	7.35	4.1	82	104/66
12:30 PM	35	38.5	7.32	4.2	90	90/62
1:30 PM	***48***	***39.4***	***7.28***	***4.4***	***106***	***70/48****
2:30 PM	***65***	***42***	***7.24***	***4.8***	***128***	***92/54***
3:30 PM	***95***	***42.2***	***7.23***	***5.3***	***145***	***90/52***
4:30 PM	***139***	***43.2***	***7.21***	***5.4***	***169***	***97/51***



Instrumentation Laboratory

PATIENT SAMPLE REPORT

1

D.Y.PATIL HOSPITAL, PUNE
CVTS RECOVERY

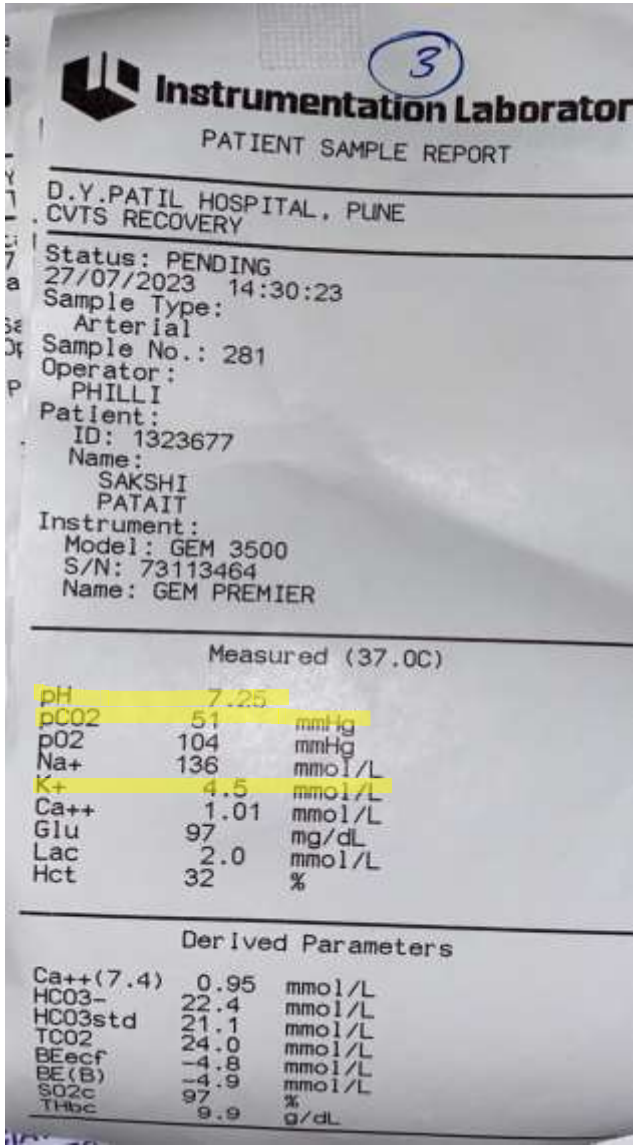
Status: PENDING
27/07/2023 10:30:33
Sample Type:
Arterial
Sample No.: 271
Operator:
PHILLI
Patient:
Name:
SAKSHI
Instrument:
Model: GEM 3500
S/N: 73113464
Name: GEM PREMIER

Measured (37.0C)

pH	7.46	
pCO2	32	mmHg
pO2	255	mmHg
Na+	134	mmol/L
K+	3.9	mmol/L
Ca++	1.15	mmol/L
Glu	86	mg/dL
Lac	1.0	mmol/L
Hct	38	%

Derived Parameters

Ca++(7.4)	1.18	mmol/L
HCO3-	22.8	mmol/L
HCO3std	24.7	mmol/L
TCO2	23.8	mmol/L
BEecf	-1.0	mmol/L
BE(B)	-0.4	mmol/L
SO2c	100	%
THbc	11.8	g/dL



Instrumentation Laboratory

3

PATIENT SAMPLE REPORT

D.Y.PATIL HOSPITAL, PUNE
CVTS RECOVERY

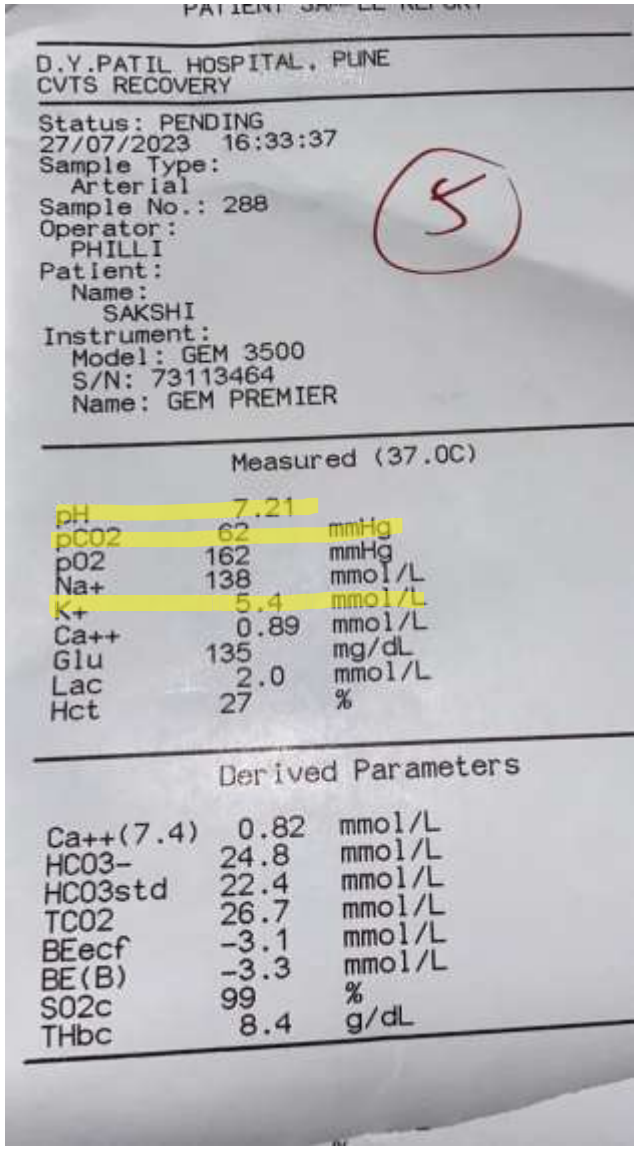
Status: PENDING
27/07/2023 14:30:23
Sample Type:
Arterial
Sample No.: 281
Operator:
PHILLI
Patient:
ID: 1323677
Name:
SAKSHI
PATAIT
Instrument:
Model: GEM 3500
S/N: 73113464
Name: GEM PREMIER

Measured (37.0C)

pH	7.25	
pCO2	51	mmHg
pO2	104	mmHg
Na+	136	mmol/L
K+	4.5	mmol/L
Ca++	1.01	mmol/L
Glu	97	mg/dL
Lac	2.0	mmol/L
Hct	32	%

Derived Parameters

Ca++(7.4)	0.95	mmol/L
HCO3-	22.4	mmol/L
HCO3std	21.1	mmol/L
TCO2	24.0	mmol/L
BEecf	-4.8	mmol/L
BE(B)	-4.9	mmol/L
SO2c	97	%
THbc	9.9	g/dL



D.Y.PATIL HOSPITAL, PUNE
CVTS RECOVERY

Status: PENDING
27/07/2023 16:33:37
Sample Type:
Arterial
Sample No.: 288
Operator:
PHILLI
Patient:
Name:
SAKSHI
Instrument:
Model: GEM 3500
S/N: 73113464
Name: GEM PREMIER

5

Measured (37.0C)

pH	7.21	
pCO2	62	mmHg
pO2	162	mmHg
Na+	138	mmol/L
K+	5.4	mmol/L
Ca++	0.89	mmol/L
Glu	135	mg/dL
Lac	2.0	mmol/L
Hct	27	%

Derived Parameters

Ca++(7.4)	0.82	mmol/L
HCO3-	24.8	mmol/L
HCO3std	22.4	mmol/L
TCO2	26.7	mmol/L
BEecf	-3.1	mmol/L
BE(B)	-3.3	mmol/L
SO2c	99	%
THbc	8.4	g/dL

- **30 minutes later $EtCO_2$ had risen to 50mmHg, body temperature rose to 41 degree C and SSEP, MEP signals disappeared**

- Plane of anaesthesia was deepened by giving additional dose of inj. Propofol and inj. Atracurium

- As the patient deteriorated, surgery was temporarily stopped to stabilize the patient and **sevoflurane was completely stopped**.

- **Suspicion of malignant hyperthermia (MH) was raised**, after ruling out other causes for patient instability like bronchospasm, thyroid storm, neuroleptic malignant syndrome.

- The critical condition of the patient was discussed with the surgeon, who decided to **abort the procedure.**

- **Active cooling measures** like cold IV saline and irrigation through RT and bladder wash was started and forced air warmers were removed

- **We changed the anaesthesia machine and circuit, and used 100% oxygen using an open circuit (Bains circuit).**

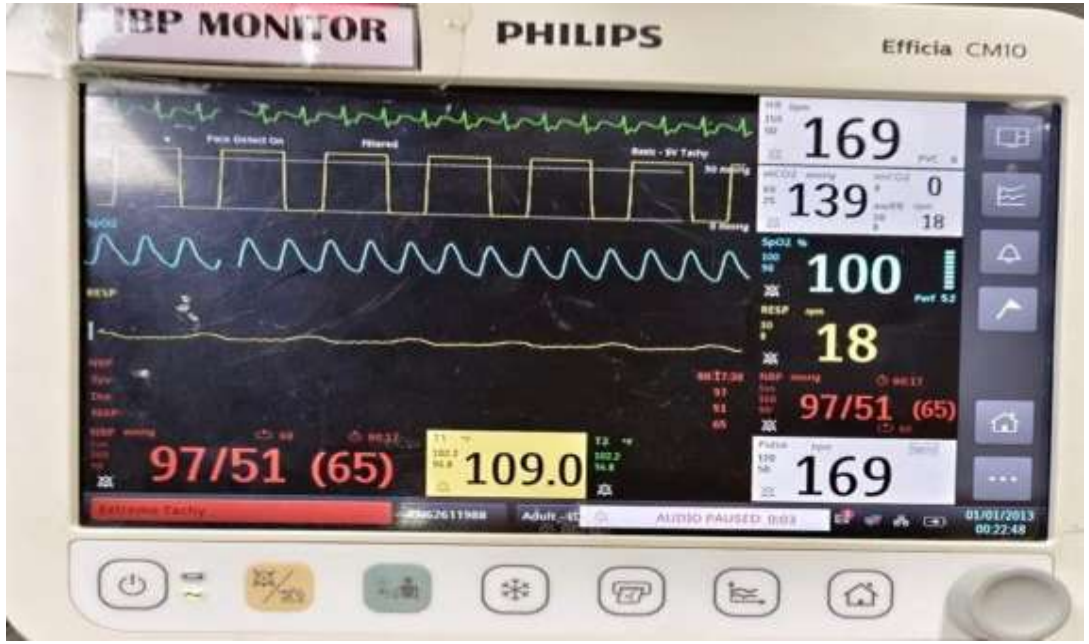
- In view of hemodynamic instability, rising EtCO2 and increased core body temperature (? malignant hyperthermia) **patient was shifted to SICU for further management**

- **In the SICU, EtCO2 was 139 mmHg, temperature was 43 deg C (109 deg F), with blood pressure of 97/51 mmHg on support and heart rate of 169 bpm**

- **Inj Dantrolene Sodium, which is the only 'DRUG OF CHOICE FOR MALIGNANT HYPERTHERMIA'** was not available at our institute, nor in the state.

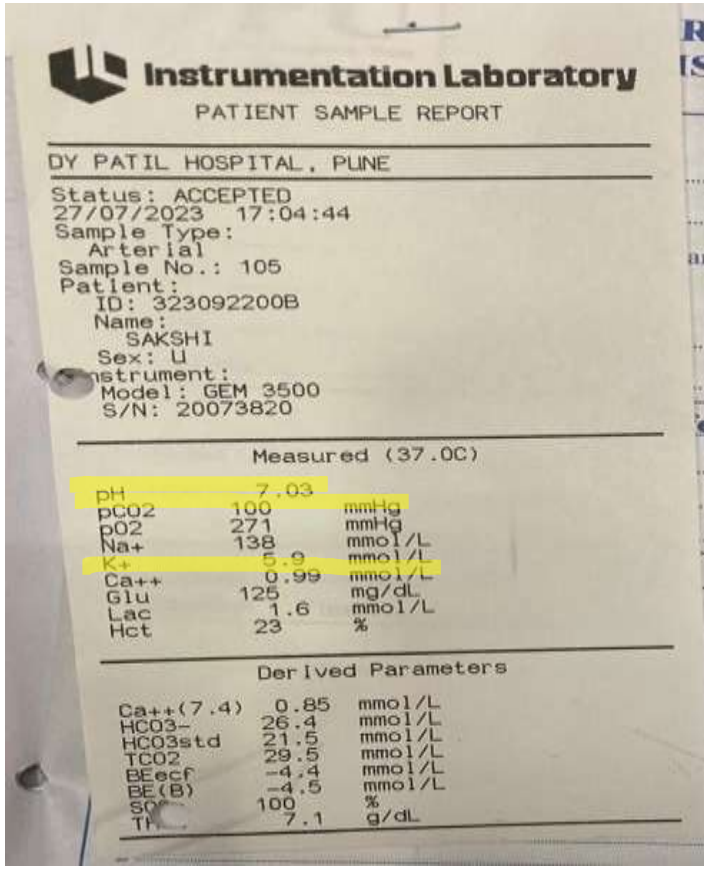
- So the unavailability of Inj. Dantrolene and poor prognosis of patient was explained to the relatives.

- In SICU, investigations were sent for further evaluation



Vitals in SICU

- **After 1 hour, the patient went into cardiac arrest and could not be revived inspite of all resuscitative measures**



Instrumentation Laboratory

PATIENT SAMPLE REPORT

DY PATIL HOSPITAL, PUNE

Status: ACCEPTED
27/07/2023 17:04:44
Sample Type:
Arterial
Sample No.: 105
Patient:
ID: 323092200B
Name:
SAKSHI
Sex: U
Instrument:
Model: GEM 3500
S/N: 20073820

Measured (37.0C)

pH	7.03	
pCO2	100	mmHg
pO2	271	mmHg
Na+	138	mmol/L
K+	5.9	mmol/L
Ca++	0.99	mmol/L
Glu	125	mg/dL
Lac	1.6	mmol/L
Hct	23	%

Derived Parameters

Ca++(7.4)	0.85	mmol/L
HCO3-	26.4	mmol/L
HCO3std	21.5	mmol/L
TCO2	29.5	mmol/L
BEecf	-4.4	mmol/L
BE(B)	-4.5	mmol/L
SO	100	%
TH	7.1	g/dL

ABG after shifting to SICU

Muscle rigidity

Serum CPK Mb (creatine phosphokinase-Mb) – 691U/L (normal 26-192 U/L)

MALIGNANT HYPERTHERMIA

- Life threatening emergency characterized by **elevated core temperature, tachycardia, tachypnoea, hypercarbia, muscle rigidity and rhabdomyolysis, acidosis and hyperkalaemia** triggered by :

a. Inhalational anaesthetic agents

b. Depolarising muscle relaxant

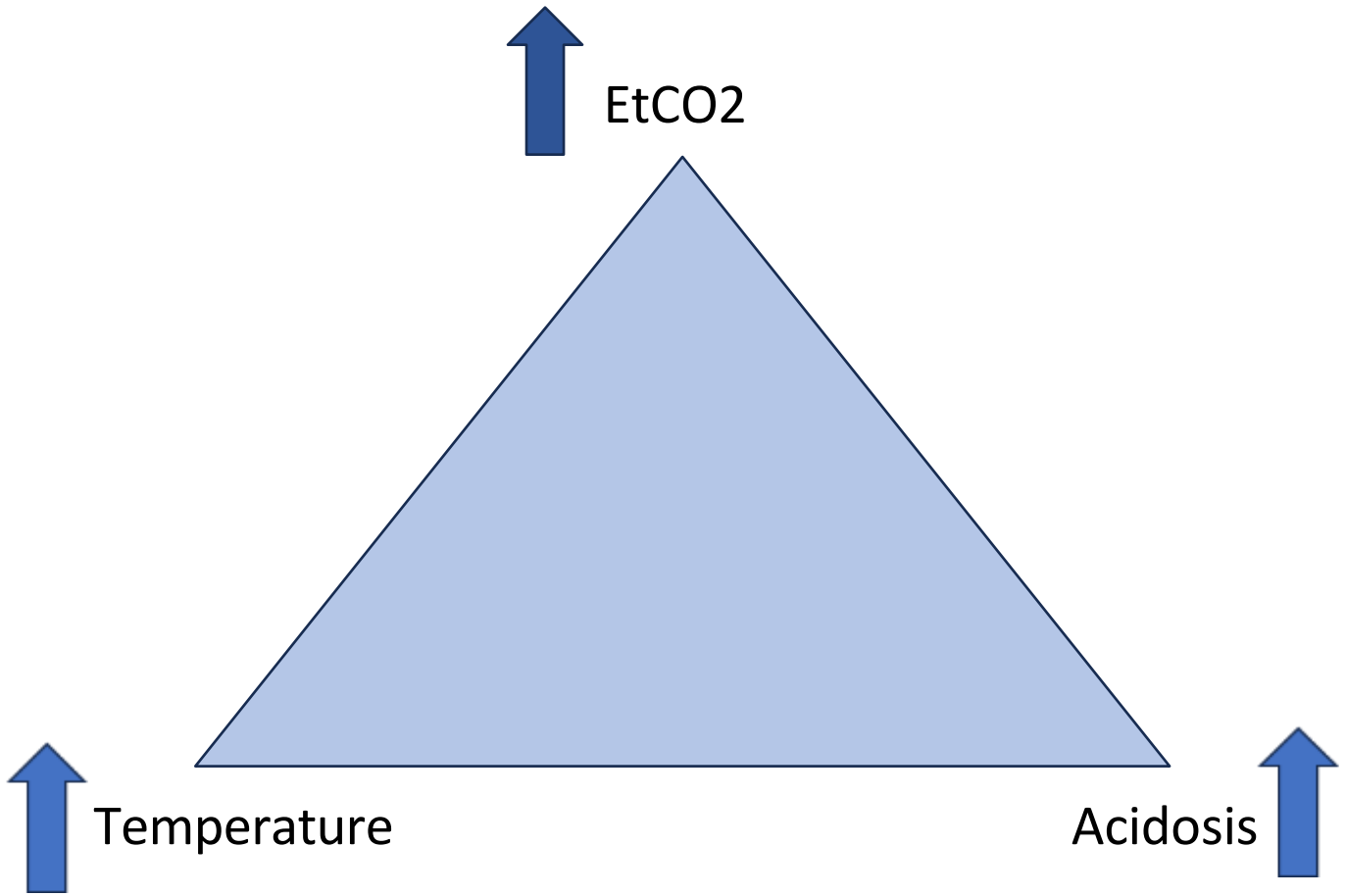
- Pharmacogenetic clinical syndrome that occur with **uncontrolled elevation of intracellular calcium in skeletal muscle cells,** leading to activation of muscle contractile elements and hypermetabolism.

- **Incidence : 1/10,000 – 2,50,000 patients receiving general anaesthesia**

- Males > Females
- Family history (first degree relative)
- Associated with comorbidities such as scoliosis and muscle disorders
- Mortality 60% (**if Dantrolene used <1.4%)**

- **Inheritance** : rare **genetic autosomal dominant** disorder
- Linked to the **Ryanodine R1 receptor (RYR1)** located on chromosome 19
- Mutation in gene coding for **dihydropyridine receptor (DHPR)** known as CACNA-1

TRIAD OF MALIGNANT HYPERTHERMIA



LARACH'S CLINICAL GRADING SCALE

Muscle rigidity :

- Generalized rigidity 15
- Masseteric rigidity 15

Myonecrosis :

- CK > 20000 (with succinylcholine) 15
- CK > 10000 (without succinylcholine) 15
- Cola colored urine 10
- Myoglobin is urine > 60 µg/l 5
- Serum K+ > 6 mEq/L 3

Respiratory Acidosis :

- ETCO2 > 55 with controlled ventilation 15
- PaCO2 > 60 with controlled ventilation 15
- ETCO2 > 60 with spontaneous ventilation 15
- Inappropriate hypercarbia 15
- Inappropriate tachypnea 10

Temperature :

- Rapid increase in temperature 15
- Inappropriate temperature > 38.8 ºC 10

Cardiac Involvement :

- Inappropriate tachycardia 3
- VT or VF 3

Sum of > 50 implies - almost certainly Malignant Hyperthermia.

In our case, the Larach score was 66

- Diagnosis was made clinically, as definitive diagnosis requires genetic sequencing.

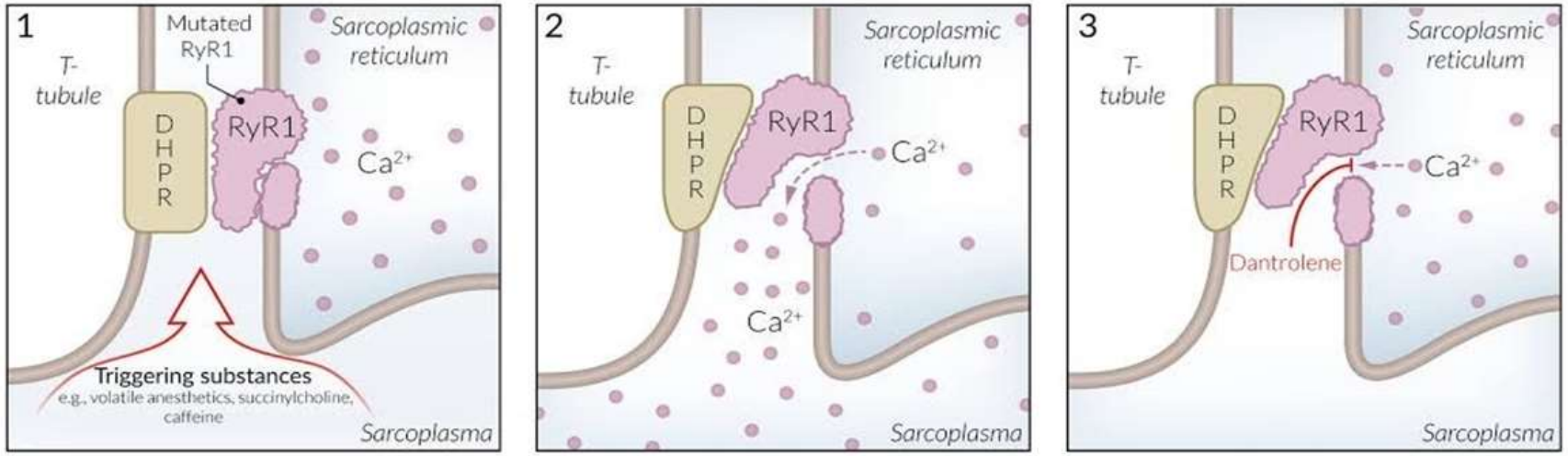
- The **genetic sequencing was done for our patient later, which came positive for RYR1 receptors, thus confirming our diagnosis of malignant hyperthermia**

Gene[4] (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification[5]
***RYR1* (+)** (ENST00000359596.8)	Exon 39	c.6521A>T **(p.Glu2174Val)**	Heterozygous	Congenital myopathy-1A with susceptibility to malignant hyperthermia (OMIM#117000)	Autosomal dominant	Uncertain Significance **(PM2, PP3)**

DNA testing result of the patient showing heterozygous variant of the RYR1 gene

TREATMENT

1. Stop Inhaled anaesthetic immediately (Add activated charcoal filters if available)
2. Notify the surgeon immediately
3. Call for help
4. **Inj. DANTROLENE SODIUM Initial bolus - 2.5 mg/kg , repeat dose every 5– 10 minutes until symptoms are controlled.**



5. To prevent recrudescence - inj. Dantrolene - 1 mg/kg IV every 6 hours till 72 hours

- **Supportive treatment for MH** : cold sponging, cold gastric and bladder wash, cold IV fluids, correction of ABG with sodium bicarbonate

TAKE HOME MESSAGE :

- Malignant hyperthermia is a rare condition that occurs in a susceptible patient when a triggering anaesthetic agent is administered
- It can be reversed with the administration of inj. Dantrolene
- But making inj. Dantrolene available in emergency is difficult.
- Timely intervention with inj. Dantrolene could have saved the life of our patient.
- **So we urge to make Inj. DANTROLENE available at least at district level to save the patients from becoming unfortunate victims of malignant hyperthermia.**

REFERENCES

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- We also thank Dr Tushar Pisal sir, from the department of Orthopaedics for his help in sending the samples for genetic testing and helping us arrive at a final diagnosis

Thank You