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RESEARCH ARTICLE

PARAQUAT INTOXICATION: A FATAL POISIONING, CASE REPORT & LITERATURE REVIEW.

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Abstract

Paraquat is among the most dangerous poison in medical field,It causes rapid irreversible damage of lungs and lead to renal failure and liver failure causing to death.It is highly toxic compound for humans with very high mortality due to lack of antidote available. We report a case of a 17 yrs old female, who has ingested a 5ml of paraquat (1, 1′-dimethyl-4, 4′-dipyridylium) which is used as a herbicide and easily available substance in a developing countries like India. Despite it's widely availability in India, its poisoning is uncommon and diagnosis is often difficult in the absence of proper history and lack of definitive laboratory investigations.
Sometimes despite of early diagnosis we may not able to save the victim as in our case because of lack of any effective treatment.

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Introduction:-

Paraquat or N, N′-dimethyl-4, 4′-bipyridinium dichloride is a toxic chemical that is widely used as a herbicide primarily for weed and grass control. It is present in varying concentration and requires to be diluted prior to its use. Paraquat is highly toxic chemical to human beings. The most likely route of exposure that would lead to poisoning is ingestion. Paraquat poisoning is also possible after skin exposure if skin exposure lasts for long time or skin that is not intact(skin that has sores, cuts or a severe rash) .Inhalation exposure to paraquat can irritate the airways and mucus membrane but rarely causes systemic manifestations.[1]

Paraquat causes direct damage when it comes into contact with the lining of the mouth, stomach or intestines; it causes toxic chemical reactions to occur throughout of the body primarily the lungs, liver and kidneys.

The main systemic effects are pulmonary edema, convulsions,cardiac,renal and hepatic failure [2]
We are reporting a case of fatal paraquat poisoning from Eastern Indian state of Odisha. The patient was admitted in our tertiary care hospital. This paper discussed a case of acute paraquat poisoning and detailed review of literature.

Case Presentation:-

A 17 years old female patient from a farmer family background was brought to our Emergency department with history of alleged consumption of approximately 5 ml of paraquat taken 11 hours prior to presentation. she had a dispute with her mother regarding her marriage and she has taken paraquat which was kept in their house for farming purpose. They brought the empty bottle of paraquat by the trade name of "Gramoxone" with them. She doesn't have any past medical or psychiatric illness. she has consumed approximately 5 ml of herbicide as a suicidal

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attempt which is followed by repeated vomiting. Primarily she was taken to Peripheral Health Centre after half an hour of consumption where gastric lavage done and she was referred to higher Centre for further evaluation and management There was no documentation available with patient's attendant, therefore we can't confirmed whether charcoal administration was done at PHC during gastric lavage.

Vitals at the time of presentation in ED are; GCS-15/15, Blood pressure at right arm 100/60mmHg, pulse rate-108/min, Respiratory rate-20/min, Temperature at axillary-98.4 F, Oxygen saturation-97% at room air, Random blood glucose-103mg/dl, bilateral pupils were normal size and reactive to light.

On Primary survey Airway was patent, Lungs were clear to auscultation, there was no respiratory distress, had normal heart sounds, Capillary refill time was < 2 seconds and all peripheral pulses were present.

Secondary survey showed her oral mucosa red and congested and rest of the examination from head to toe were unremarkable.

At Emergency patient has started on maintenance IV fluids, antiemetic and PPI for supportive measures. Foley's catheterization has been done to measure urine output.
All initial investigations (CBC, RFT, LFT, PT/INR/APTT, ECG, X-RAY CHEST, URINE TOX SCREEN), UPT (Negative) were done from Emergency.

Patient then shifted to ICU for continuous monitoring.On the First day in ICU, patient remained asymptomatic. Initial complete blood count, LFT, RFT were within normal limits.ECG revealed sinus Tachycardia with no ST-T changes. Initial chest X-Ray was within normal limits. [Figure 1].

Patient was kept nil orally and on maintenance IV fluids, antiemetics, antacid and triamcinolone acetonide mouth paste to reduce pain and swelling inside the mouth. On the second day she has developed oliguria and increased in urea and creatinine levels for which Nephrology consultation was done and advised to increase the IV fluids and Planned for Hemodialysis if renal function further deteriorates.

On fourth day patient had developed oliguria and further deterioration of her renal function, Hemodialysis was performed and kept on a regular session of hemodialysis .Patient had developed fever (T-101.3*F) for which broad spectrum antibiotic started.Urine routine examination showed 20-25pus cells/HPF, RBC-10-15/HPF and granular cast suggestive of urinary tract infection and acute tubular necrosis. [Figure 2].

On fifth day patient had 2 episodes of hamatemesis for which Pantoprazole infusion and UGI Endoscopy done suggestive of extensive oropharyngeal and esophageal ulcerations with oozing. [Figure 3].

On the following day patient became severely hypoxic, spo2-85% while on 100% FIO2 on Non Invasive Ventilation was used. Heart rate was 124/min, Respiratory rate36/min and blood pressure was 120/66mmHg.ABG showed PaO2 of 45.0mmHg with Respiratory alkalosis[figure4].Chest X-Ray was done showed bilateral alveolar shadows predominately in mid and lower zones suggestive of ARDS. [Figure 5].

Subsequently patient became drowsy, Spo2 was 80% on 100% FIO2 on NIV.In view of persistence hypoxia patient was intubated and kept on mechanical ventilation.
Patient was continued on mechanical ventilation and hemodialysis was performed on daily basis but her condition didn't improved and she expired on 11th day of her admission.

Discussion:-

Paraquat poisoning is a medical challenge for emergency physician because it's rare especially in the northern part of India and patient's vitals remain stable in the initial hours of presentation apart from mouth erosions and it causes mortality in a large number despite treatment in tertiary care setting [3].paraquat poisoning is common in southern part of India, Srilanka and in Africa (Trinidad,, Tobago, South Trinidad) [4][5][6].A lethal oral dose of the 20% concentration solution is about 10 to 20 ml in an adult and 4 to 5 ml in a child[1]. Ingestion of large amounts (>15-20 ml of 20% ion) results in fulminant organ failure resulting in renal and hepatic failure, GI ulceration, pancreatitis.

Toxic myocarditis and death from cardiogenic shock and multi-organ failure within 1-4 days [1].Ingestion of smaller quantities usually leads to toxicity in kidneys and lungs developing over the 2-6 days. Renal failure develops quite rapidly. Paraquat accumulates inside renal tubular cells causing reduction oxidation (redox) cycling and increase reactive oxygen species formation with subsequent proximal tubular injury [7].A decrease in paraquat elimination due to renal failure aggravates systemic toxicity [8].The major effect of paraquat follows its accumulation in the lungs, it accumulates in the alveolar cells of the lungs, where it is transformed into a reactive oxygen species, the superoxide radical [1].The pulmonary lesion has two phases :an acute alveolitis over 1-3 days followed by a secondary fibrosis. The patient develops increasing signs of respiratory involvement over 3-7 days and ultimately dies of severe anoxia due to rapidly progressive fibrosis up to 5 weeks later [9].

Gastrointestinal toxicity is present in majority of the case because most common mode of poisoning is self ingestion or accidental. A burning sensation of the lips and mouth may occur within a few minutes to hours followed by ulceration. Sometimes they may result in perforation, mediastinitis or pneumomediastinum. Direct contact with paraquat solutions may cause skin burns and dermatitis [10].

Some liver toxicity (jaundice, transaminase rise) is also common in these patients.

Early diagnosis are important .we need to obtain details of the exposure, route of exposure, concentration of the product and estimated amount, time of occurrence. Measurement of plasma and urine paraquat concentration is useful both to confirm poisoning and predict prognosis [11][12].Complete blood count,electrolytes,renal and liver function should be done regularly.Serial pulmonary function test,chest radiographs,arterial blood gas determinations may be used to monitor toxicity.

A CT Scan of the chest may be helpful in detecting early lung fibrosis or assessing long term damage in survivors [9].Upper GI endoscopy should be performed to identify the extent and severity of mucosal injury.

Any exposure to paraquat is an Emergency and patient should be admitted even if the patient is asymptomatic. Treatment involves the assessment and management of airway, breathing and circulation as per guidelines. However mild to moderate hypoxia should not be routinely treated with oxygen as it will worsen oxidative stress and it increases mortality in animals models [13][14].Supplemental oxygen should be withheld unless the PaO2 is less than 70mmHg because oxygen may contribute to the pulmonary damage which is mediated through lipid peroxidation[15].Maintain intravascular volume and urine output to prevent prerenal kidney injury.

Immediate GI decontamination with absorbents that bind paraquat is indicated in a patient with protected airways. A single dose of activated charcoal (1 to 2 gm/kg) can be used. Charcoal hemoperfusion can remove paraquat and has been recommended to be started as soon as possible and continued for 6 to 8 hours but there is no evidence to show that prognosis improved [1][16].

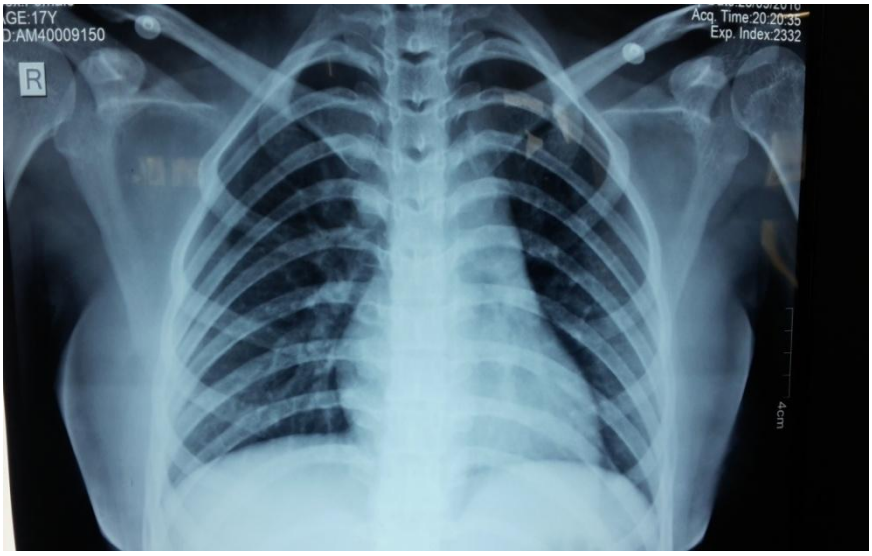
Hemodialysis and hemoperfusion has been tried in many centers to remove paraquat but the benefit of this is very limited because paraquat is rapidly distributed to the lungs and other organs [17][18].

Immunosuppression with combination of cyclophosphamide and methylprednisolone was shown to be beneficial in moderate to severe cases by prevention of ongoing inflammation that lead to lung fibrosis and death [19][20].
Intravenous Methylprednisolone 1gm/day for three consecutive days, Intravenous Cyclophosphamide 15 mg/kg/day for two consecutive days followed by Intravenous Dexamethasone 8mg thrice a day until pao2 is >11.5kpa(80mmHg) and repeated pulse therapy with Methylprednisolone(1gm/day for 3 days) and cyclophosphamide(15mg/kg/day for 1 day) which if pao2 is <8.64kpa(60mmHg)[20].However a 2003 Systemic review of the effectiveness of immunosuppressive therapy in paraquat poisoning found lack of proven efficacy[21].
Several antioxidants like vitamins C and E have been clinically used to protect against free radical toxicity however only animals studies have been done that showed mixed response and human studies are either small or uncontrolled.

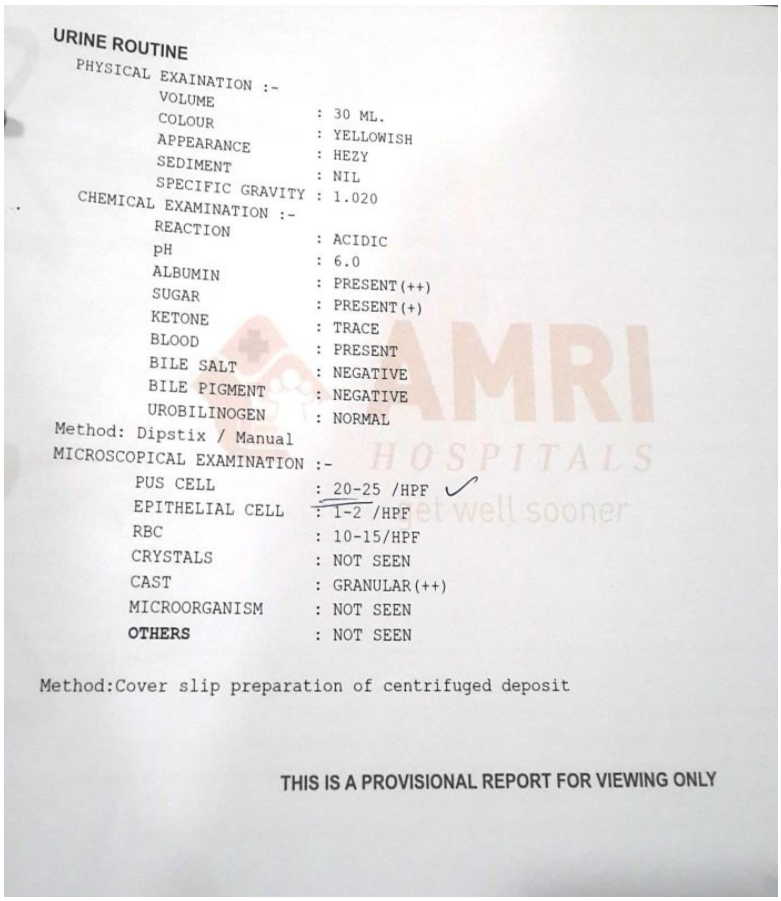
Conclusion:-

Patient presenting to the Emergency department with alleged history of ingestion of paraquat poisoning should be admitted even if they are asymptomatic initially. There is no specific antidote available and prognosis depends upon the amount of paraquat ingestion. Oxygen should be used cautiously in these patients. Early administration of

cyclophosphamide and steroids at Emergency at least 2-3 hours after paraquat exposure is important because it will not be effective once cells have already been infiltrated. However a large randomized controlled trial is required to affirm the role of Immunosuppression in paraquat poisoning.



[fig-1]



URINE ROUTINE

PHYSICAL EXAINATION :-	
VOLUME	: 30 ML.
COLOUR	: YELLOWISH
APPEARANCE	: HEZY
SEDIMENT	: NIL
SPECIFIC GRAVITY	: 1.020
CHEMICAL EXAMINATION :-	
REACTION	: ACIDIC
pH	: 6.0
ALBUMIN	: PRESENT(++)
SUGAR	: PRESENT(+)
KETONE	: TRACE
BLOOD	: PRESENT
BILE SALT	: NEGATIVE
BILE PIGMENT	: NEGATIVE
UROBILINOGEN	: NORMAL

Method: Dipstix / Manual

MICROSCOPICAL EXAMINATION :-	
PUS CELL	: 20-25 /HPF
EPITHELIAL CELL	: 1-2 /HPF
RBC	: 10-15/HPF
CRYSTALS	: NOT SEEN
CAST	: GRANULAR(++)
MICROORGANISM	: NOT SEEN
OTHERS	: NOT SEEN

Method:Cover slip preparation of centrifuged deposit

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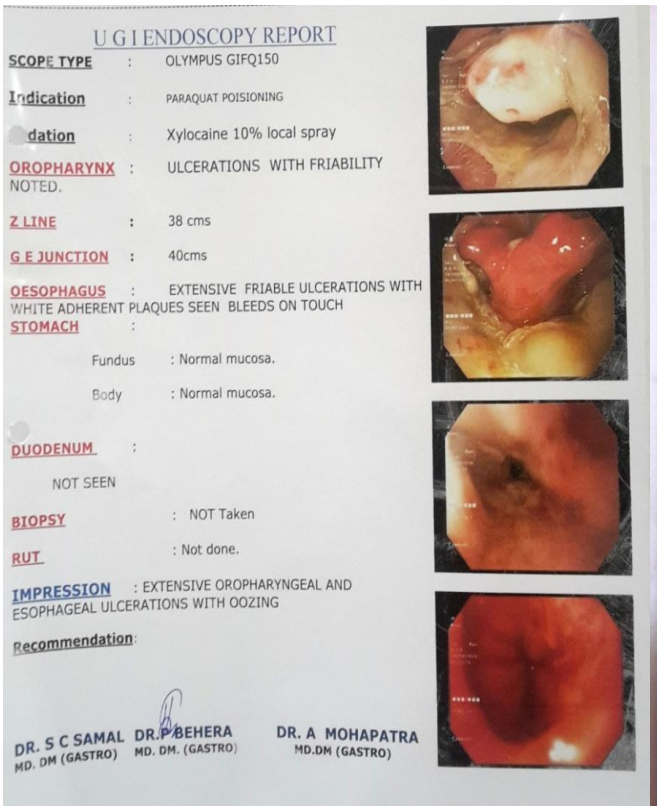
[fig.2]



U G I ENDOSCOPY REPORT

SCOPE TYPE : OLYMPUS GIFQ150

Indication : PARAQUAT POISIONING

dation : Xylocaine 10% local spray

OROPHARYNX : ULCERATIONS WITH FRIABILITY NOTED.

Z LINE : 38 cms

G E JUNCTION : 40cms

OESOPHAGUS : EXTENSIVE FRIABLE ULCERATIONS WITH WHITE ADHERENT PLAQUES SEEN BLEEDS ON TOUCH

STOMACH :

Fundus : Normal mucosa.

Body : Normal mucosa.

DUODENUM :

NOT SEEN

BIOPSY : NOT Taken

RUT : Not done.

IMPRESSION : EXTENSIVE OROPHARYNGEAL AND ESOPHAGEAL ULCERATIONS WITH OOZING

Recommendation:

DR. S C SAMAL MD. DM (GASTRO) DR. P BEHERA MD. DM. (GASTRO) DR. A MOHAPATRA MD.DM (GASTRO)

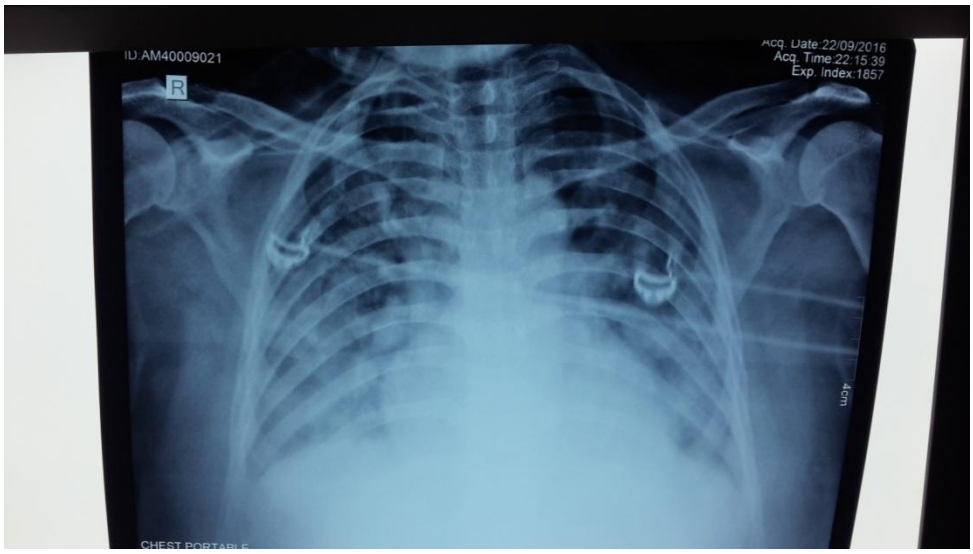
Patient ID: 3013
Date & Time: 29-Sep-16 11:43:30

Results: Gases+			
pH	7.484		High
pCO2	27.9	mmHg	Low
pO2	45.0	mmHg	Low
cHCO3-	20.9	mmol/L	Low
BE(ecf)	-2.5	mmol/L	Low
cSO2	85.0	%	Low
Results: Chem+			
Na+	135	mmol/L	Low
K+	4.7	mmol/L	High
Ca++	0.92	mmol/L	Low
cTCO2	21.8	mmol/L	Low
Hct	Failed iQC		
cHgb	cnc		
BE(b)	-1.2	mmol/L	
Results: Meta+			
Glu	125	mg/dL	High
Lac	1.03	mmol/L	

Reference Ranges

pH	7.350 - 7.450	
pCO2	35.0 - 48.0	mmHg
pO2	83.0 - 108.0	mmHg
cHCO3-	21.0 - 28.0	mmol/L
BE(ecf)	-2.0 - 3.0	mmol/L
cSO2	94.0 - 98.0	%

[fig 3] **[fig 4]**



[fig 5]

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