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Research Paper

Drug-induced Brugada Syndrome A Need for Psychosocial Intervention

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ABSTRACT
Brugada syndrome is a rare cardiovascular disorder characterized by disturbances affecting the electrical system of the heart. The Brugada syndrome describes a subgroup of patients at risk for the occurrence of ventricular fibrillation who have no definable structural heart disease associated with a right bundle branch block conduction pattern and ST-segment elevation in the right precordial leads. This defect causes a reduction in the sodium channel current, which accentuates the epicardia action potential notch leading to ST-segment elevation. The clinical phenotype manifests in adulthood, and it is more frequent in males. Frequently, sudden death can be the first manifestation of the disease. Brugada syndrome is a genetic disease and follows autosomal dominant inheritance. Currently, the prevalence of Brugada syndrome is estimated at 5 in 10,000 people. This case report provides a concise review of the clinical manifestations, pathophysiology, and therapeutic options for the patient having Brugada syndrome induced by drug abuse.
***KEYWORDS**: Drug-induced, Brugada syndrome, sudden cardiac death*

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I. INTRODUCTION

Brugada Syndrome is an ECG abnormality with a high incidence of sudden death in patients with structurally normal hearts. First described in 1992 by the Brugada brothers, the disease has since had an exponential rise in the numbers of cases reported. The mean age of sudden death is 41, with the age at diagnosis ranging from 2 days to 84 years. Brugada syndrome is associated with one of several electrocardiographic (ECG) patterns characterized by incomplete right bundle-branch block and ST elevations in the anterior precordial leads. As shown in the image below. Three types of ST-segment elevation in Brugada syndrome, as shown in the precordial leads on ECG in the same patient at different times. In the initial description of Brugada syndrome, the heart was reported to be structurally normal, but this concept has been challenged. Subtle structural abnormalities in the right ventricular outflow tract have been reported. Brugada syndrome is genetically determined and has an autosomal dominant pattern of transmission in about 50% of familial cases. Patients with Brugada syndrome are prone to develop ventricular tachyarrhythmia's that may lead to syncope, cardiac arrest, or sudden cardiac death (Martini B, Nava A, Thiene G, et al, 1989). Conduction delay and atrial fibrillation may also be manifestations of the syndrome (Vorobiof G, Kroening D, Hall B, Brugada R, Huang D,2008). About 5% of survivors of cardiac arrest have no clinically identified cardiac abnormality. About half of these cases are thought to be due to Brugada syndrome (Alings M, Wilde A.,1999). At present, implantation of an automatic implantable cardiac defibrillator (ICD) is the only treatment proven effective in treating ventricular tachycardia and fibrillation and preventing sudden death in patients with Brugada syndrome.

Pathophysiology

Brugada syndrome is an example of a channelpathy, a disease caused by an alteration in the transmembrane ion currents that together constitute the cardiac action potential. Specifically, in 10-30% of cases, mutations in the SCN5A gene, which encodes the cardiac voltage-gated sodium channel Nav 1.5, have been found. These loss-of-function mutations reduce the sodium current (INa) available during the phases 0 (upstroke) and 1 (early repolarization) of the cardiac action potential. This decrease in INa is thought to affect the right ventricular endocardium differently from the epicardium. Thus, it underlies both the Brugada ECG pattern and the clinical

manifestations of the Brugada syndrome. The exact mechanisms underlying the ECG alterations and arrhythmogenesis in Brugada syndrome are disputed (Meregalli PG, Wilde AA, Tan HL., 2005). The repolarization-defect theory is based on the fact that right ventricular epicardial cells display a more prominent notch in the action potential than endocardial cells. This is thought to be due to an increased contribution of the transient outward current (Ito) to the action potential waveform in that tissue. A decrease in INa accentuates this difference, causing a voltage gradient during repolarization and the characteristic ST elevations on ECG. Research has provided human evidence for a repolarization gradient in patients with Brugada syndrome using simultaneous endocardial and epicardial unipolar ecordings(Nagase S, Kusano KF, Morita H, etal.,2008). As shown in the image below. Different alterations of the epicardial action potential that produce the ECG changes observed in patients with Brugada syndrome. Adapted from Antzelevitch, 2005. When the usual relative durations of repolarization are not altered, the T wave remains upright, causing a saddleback ECG pattern (type 2 or 3). When the alteration in repolarization is sufficient to cause a reversal of the normal gradient of repolarization, the T wave inverts, and the coved (type 1) ECG pattern is seen. In a similar way, a heterogeneous alteration in cardiac repolarization may predispose to the development of reentrant arrhythmias, termed phase 2 reentry, that can clinically cause ventricular tachycardia and ventricular fibrillation (Antzelevitch C, Brugada P, Brugada J,2005). An alternative hypothesis, the depolarization/conduction disorder model, proposes that the typical Brugada ECG findings can be explained by slow conduction and activation delays in the right ventricle (in particular in the right ventricular outflow tract). One study used ajmaline provocation to elicit a type 1 Brugada ECG pattern in 91 patients, and found that the repolarization abnormalities were concordant with the depolarization abnormalities and appeared to be secondary to the depolarization changes (Postema PG, van Dessel PF, Kors JA, et al.2010). Using vectorcardiograms and body surface potential maps, investigators were able to show that depolarization abnormalities and conduction delay mapped to the right ventricle.

Etiology

The prototypical case of Brugada syndrome has been associated with alterations in the SCN5A gene, of which nearly 300 mutations have been described (Kapplinger JD, Tester DJ, Alders M, et al.2007). which are thought to cause a syndrome of precordial ST elevation, sudden death, and short QT interval. Many clinical situations have been reported to unmask or exacerbate the ECG pattern of Brugada syndrome. Examples are a febrile state, hyperkalemia, hypokalemia, hypercalcemia, alcohol or cocaine intoxication, and the use of certain medications, including sodium channel blockers, vagotonic agents, alpha-adrenergic agonists, beta-adrenergic blockers, heterocyclic antidepressants recreational drugs , and a combination of glucose and insulin (Antzelevitch C, Brugada P, Brugada J, Brugada R.2005)

Epidemiology (prevalence)

Because of its recent identification, the prevalence of Brugada syndrome is not well established. In a large university hospital on the West Coast of the United States, the prevalence of a Brugada ECG pattern among unselected, mainly white and Hispanic adults was 2 of 1348 patients (0.14%); in both cases, the ECG patterns were type 2 (Donohue D, Tehrani F, Jamehdor R, Lam C, Movahed MR.2008).The prevalence in Asian and other ethnic populations may be higher.

The highest prevalence of Brugada syndrome is in Southeast Asia; the lowest is in North Africa(Vutthikraivit W, Rattanawong P, Putthapiban P, et al.2018). In parts of Asia (eg, the Philippines, Thailand, Japan), Brugada syndrome seems to be the most common cause of natural death in men Northeast Thailand, the mortality rate from Lai Tai is approximately 30 cases per 100,000 population per year (Nademanee K, Veerakul G, Nimmannit S, et al.1997) .

Race-, sex-, and age-related demographic

Brugada syndrome is most common in people from Asia. The reason for
this observation is not yet fully understood but may be due to an Asianspecific sequence in the promoter region of SCN5A (Bezzina CR, Shimizu
W, Yang P, et al.2006)
Brugada syndrome is 8-10 times more prevalent in men than in women,
although the probability of having a mutated gene does not differ by sex.
The penetrance of the mutation therefore appears to be much higher in men
than in women. The mean age of patients who die suddenly is 41 years (Antzelevitch C, Brugada P, Brugada J, Brugada R.2005)

Prognosis

Implantable cardioverters-defibrillators (ICDs) are often used to treat patients with Brugada syndrome, exposing them to complications related to device implantation and the potential for inappropriate shocks.

During a mean follow-up of 24 months, sudden cardiac death or ventricular fibrillation occurred in 8.2% of patients with Brugada syndrome. A history of syncope, a spontaneously abnormal ECG, and inducibility during programmed electrical stimulation (by one study) significantly increased this risk (Brugada J, Brugada R, Brugada P.2003).
Brugada syndrome may be a significant cause of death, aside from accidents, in men under 40.

Signs and symptoms: may include:
- Syncope and cardiac arrest: Most common clinical manifestations; in many cases, cardiac arrest occurs during sleep or rest
- Nightmares or thrashing at night
- Asymptomatic, but routine ECG shows ST-segment elevation in leads V1-V3
- Associated atrial fibrillation (20%) (Bordachar P, Reuter S, Garrigue S, et al, 2004)
- Fever: Often reported to trigger or exacerbate clinical manifestations

The lack of a prodrome has been reported to be more common in patients with ventricular fibrillation documented as the cause of syncope in patients with Brugada syndrome (Take Y, Morita H, Toh N, et al,2012).

Physical examination:
- Nevertheless, physical examination is required to rule out other possible cardiac causes of syncope or cardiac arrest in an otherwise healthy patient e.g., heart murmurs from hypertrophic cardiomyopathy or from a valvar or septal defect).

Diagnostic Considerations
The differential diagnosis of cardiac arrest in an otherwise presumably healthy subject is varied, but it includes such entities as acute cardiac ischemia due to atherosclerosis or coronary anomaly, hypertrophic cardiomyopathy, catecholaminergic polymorphic ventricular tachycardia, long QT syndrome, and arrhythmogenic right ventricular cardiomyopathy (ARVC). Many of these entities can be differentiated on the basis of history and physical examination. Occasionally, however, there is overlap that requires special consideration.

Differential Diagnoses
- Acute Pericarditis
- Hypothermia
- Pulmonary Embolism (PE)

Approach Considerations
Many patients with Brugada syndrome are young and otherwise healthy and may present with syncope. Patients with syncope should not be assumed to have a benign condition, and a 12-lead ECG should be performed. A drug challenge with a sodium channel blocker should be considered in patients with syncope in whom no obvious cause is found.
Further testing may be indicated to exclude other diagnostic possibilities.

Laboratory Studies
1. Check serum potassium and calcium levels in patients presenting with ST-segment elevation in the right precordial leads. Both hypercalcemia and hyperkalemia may generate an ECG pattern similar to that of Brugada syndrome.
2. Creatine kinase-MB (CK-MB) and troponin, is Laboratory markers, should be checked in patients who have symptoms compatible with an acute coronary syndrome. Elevations indicate cardiac injury.
3. Genetic Testing
Patients with high likelihood of Brugada syndrome may be genetically tested for a mutation in SCN5A, which codes for the alpha subunit Nav 1.5

of the cardiac sodium channel.
4. Echocardiography and MRI: should be performed, mainly to exclude arrhythmogenic right ventricular cardiomyopathy.
5. Electrocardiography
Three ECG patterns have been described in Brugada syndrome . Exercise stress testing may suppress ECG changes and arrhythmias.

Challenges with sodium channel blockers
In some patients, the intravenous administration of drugs that block sodium channels may unmask or modify the ECG pattern, aiding in diagnosis and/or risk stratification in some individuals. Infuse flecainide 2 mg/kg (maximum 150 mg) over 10 minutes, procainamide 10 mg/kg over 10 minutes, ajmaline 1 mg/kg over 5 minutes, or pilsicainide 1 mg/kg over 10 minutes. This challenge should be performed with continuous cardiac monitoring and in a setting equipped for resuscitation.
In patients with a normal baseline ECG, the results are positive when the drug generates a J wave with an absolute amplitude of 2 mm or more in leads V1, V2, and/or V3 with or without an RBBB.
Administration of the drug should be stopped when the result is positive, Isoproterenol and sodium lactate may be effective as antidotes if the sodium channel blocker induces an arrhythmia, and the isoproterenol response may also have diagnostic use.

Electrophysiological Study:
Some investigators use an electrophysiologic study (EPS) to determine the inducibility of arrhythmias, in an effort to risk-stratify patients with Brugada syndrome.
Treatment
1. Placement of Implantable Cardioverter-Defibrillator
At present, implantation of an automatic implantable cardioverterdefibrillator (ICD) is the only treatment proved effective in treating
ventricular tachycardia and fibrillation and preventing sudden death in patients with Brugada syndrome.
2. Radiofrequency catheter ablation
has been recently reported as an effective new treatment
3. No pharmacologic therapy has been proved to reduce the occurrence of ventricular arrhythmias or sudden death Treatments include preventive measures such as avoiding aggravating medications and reducing fever
- **Treat a fever aggressively.** Fever is a known trigger of abnormal heartbeats in people with Brugada syndrome, so use feverreducing medications at the first sign of a fever
- **Avoiding drugs that may trigger an abnormal heart rhythm.** Many drugs can increase the risk of an irregular heartbeat, including certain heart medications and antidepressants. Too much alcohol can also increase your risk. Always tell your doctor about the medications you take, including drugs and supplements bought without a prescription.
- **Avoiding playing competitive sports.** If you're at high risk of a serious irregular heart rhythm, your doctor may tell you not to play competitive sports.

4. Consultations:
A board-certified cardiologist who specializes in cardiac arrhythmic disorders (ie, a clinical electrophysiologist) should evaluate patients with suspected Brugada syndrome. Consultation with a genetic counselor is indicated for genetic screening and counseling of patients and their relatives.
5. Long-Term Monitoring
A board-certified electrophysiologist should closely follow patients with

Brugada syndrome. Taking a careful history is important, as not all syncope is necessarily arrhythmic in Brugada syndrome. For example, a clear prodrome suggesting vasovagal syncope does not suggest an adverse prognosis in an otherwise asymptomatic patient with a Brugada ECG pattern

Case Presentation

A 45-year-old male patient, married and has 4 children(3 daughter and 1 son) he is work as a driver with his brothers.4 days before his arrival to hospital the patient was suffering from severe diarrhea, fever, sever influenza and general fatigue, despite taking treatment and medication the patient condition did not improved. At 24/3/2019 was brought to emergency department in a state of sever hypoxia and cardiac arrest. Glasgow Coma Scale of 3/15, Blood pressure (BP), pulse and oxygen saturation were unrecordable at the time of admission. The patient was unconscious and cyanosed at the time of reaching emergency department. History was derived from the relatives, he was a history of diabetes mellitus type 2 since 3 years ago after his mother died of cancer (treated for it with glucagon 5 mg), chronic bronchial asthma since 10 year ago(treated with Ventolin nebulizer 2.5 mg).There was history of drug abuse (tramadol and lovenox)since 3 year ago after death of his mother. There was history of hospitalization 3 times during the period 2011-2019 for treatment bronchial asthma. Immediately were as patient putted on monitor Blood pressure (BP) 0 mmhg , pulse 0 b/m and No respiratory breathing and oxygen saturation were 0 , ECG on monitor reveal no sinus rhythm, Immediately a large bore intravenous (IV) cannula was secured, and CPR were started. The simultaneously patient intubated with endotracheal tube and tube secured. Rescue breaths were given with AMBU at 12/min. Injection adrenaline 1 mg i.v was given twice and all others resuscitative measures were taken. The patient was revived within 7 min of CPR, Inotropes were started to maintain BP with dopamine at 10 µg/kg and noradrenaline infusion 10-20mic/min. after 7 minutes of CPR on monitor ECG pulseless ventricular tachycardia appear so synchronized DC shock with 300 j was given then CPR continue till sinus rhythm appear and Restoration of spontaneous circulation (ROSC) was achieved with a HR of 48 bpm) and a BP of 50/32 mmHg , pulse rate 50 bpm, 12. Then the patient was shifted to ICU and put on synchronized intermittent mandatory ventilation volume control (SIMV-VC) mode of ventilator with following settings RR 12-14 FiO2: 100%, tidal volume (TV): 500 ml, positive end expiratory pressure (PEEP): 5, central line RT subclavian inserted and ABGs withdrawn the result was (PH 7.33 PCO2 43 PO2 44 HCO3 20 BE 3 SO2 82%) then after 5 days putted on CPAP.Patient's vitals on ICU admission were as follows: BP 80/50 mmHg on the right side of the arm, pulse rate (PR): 90 bpm, SPO2: 95%. The patient was managed in ICU with vasopressor drug (norepinephren),infusion 10- 20mic/min,sedation (propofol infusion 1-3mg/kg/hr , fentanyl infusion 0.5-1 mic/kg/hr),prophylactic antibiotic (Rocephen 1 gm/12 hr), for diabetes (regular insulin according to our sliding scale(NPH 7U/12hr together with regular insulin subcutaneous) , antacids (Ranitidine 50mg /8hr),for bronchial asthma (ventolin nebulizer 1 ml+ 3 ml NS /6hr and hydrocortisone 100mg/6hr)for thromboembolic prophylaxis (heparin 5000u/8hr)antiarrhythmic(amiodarone) his electrocardiogram (ECG) showed a ventricular tachycardia and ST elevations in the anterior precordial leads which diagnosed as type 1 brugada syndrome, intravenous fluid were given G5% NS 0.09%(Normal Saline 500 ml given I.V every 8 hrs. and Dextrose Saline 500 ml given I.V every 8 hrs). After 2 hour, the patient vitals BP 100/64 on norepinephren infusion 10-20mic/min PR 90 bpm. Patient experienced several episodes of generalized seizures rising the dose of sedation performed as doctor prescribed . new blood samples were taken and sent for laboratory examination again, The lab test result as following CBC (WBC 8.4k/ul, HGB 13.2g/dl.PLT 56 k/ul) blood chemistry (Blood Sugar 450mg% , Na 139 meq/l, K 3.1 meq/l Creatinine 5.51 mg/dl, Urea 276 mg/dl reveal malfunctioning of the kidney which treated with Lasix 10mg/12 h and acidisis with sodium bicarbonate and monitoring intake and output and dopamine (0.5-3.0 mcg/kg/min) . During the following days, potassium supplementation was continued to achieve normal plasma potassium level as a sustainable dose,ECG show Brugada syndrome characteristic (st elevation for V1 nad V3 ,long QTc, Physical assessment, skin moist, pale, integrity healthy nails color bluish, texture smooth, head and face symmetrical, eye symmetrical, white sclera. Ears symmetrical auricles, nose and, nasal sinuses, patent nostrils, mouth throat and tongue moist, pink, teeth regular spaced, tongue pink, throat enlarged tonsils, neck full range of motion, carotid pulsation 90 beat/minute symmetrical, thorax and lung on mechanical ventilation (SIMV-VC) mode of ventilator with following settings RR 12-14 FiO2: 100%, tidal volume (TV): 500 ml, positive end expiratory pressure (PEEP): 5), on inspection symmetrical chest, cough use accessory muscles, on percussion resonance, on auscultation abnormal breath sounds rhonchi, wheezes, crepitation, heart and blood vessels, apical pulse 80beat/minute irregular, weak, BP90/50mmhg, peripheral pulses palpable , central line RT subclavian, a abdomen soft and relaxed, patient unconscious not oriented . Abdomen Inspection Palpation -smooth to touch -no lesion –no swelling -warm to touch -round and symmetrical -abdomen rises with inspiration in synchrony with chest. Lower Extremities Inspection - bilaterally symmetrical and equal -right foot has complete fingers – skin color is as same as the other parts of the Posterior Lower Inspection and normal skin color, After 2 days the

patient condition deteriorated and he develop mechanical ventilation pneumonia (MVP) with sever cough and dyspnea, fever 39 c, with a greenish sputum on auscultation crepitation, and wheezy sound heard and the patient become irritable and try to do accidental extubation. Chest x-ray show Lt lower lobe pneumonia, CBC show ((WBC 17k/ul,HGB 11.6g/dl.PLT 37 k/ul), ascetic fluid C/S done the result was negative then Sputum culture done and the result show Escherichia coli which more sensitive to (cefuroxime, cefotaxime, amikacin, gentamicin, meropenem, and colistin)then the choice was to treat with meropenem 1gm /8hr according to the culture. After 4 days blood sample for CBC result show (WBC 12.3k/ul, HGB 12.1g/dl.PLT 70 k/ul) and other test result show negative for (hepatitis B,hepatitis C and HIV). On 29/3/2019 blood sample for CBC result show ((WBC 9.3k/ul, HGB 10.5g/dl. PLT 92 k/ul) On 31/3/2019 blood sample for CBC result show ((wbc 6.5k/ul, HGB 9.2g/dl.PLT 206 k/ul) then the patient temperature were normal with mild crepitation and dyspnea and the general condition of the patient is very good and stable. The patient was intensively monitored in ICU. Inotropes were tapered off in next 4 days. The patient regained consciousness, responded to verbal commands, and was weaned off from the ventilator on 7th day. He was discharged with intact neurological functions with flaccid and general weakness overall the body and the family advised to do for the patient placement of an implantable cardioverter defibrillator (ICD) and the patient was transferred to rehabilitation hospital and stay in it for 5 days without any progress for the condition of the patient and negligence was happened for the patient as relative told me . then his family discharge him from the hospital to home of his sister husband who work as a doctor in primary health care in Ministry of health , a comprehensive treatment and rehabilitative plan were prepared by his sister husband Dr,the plan included psychological,nutritional and rehabitation treatment ,as the family played a major role in the treatment.since his bad friend were prevented from visiting him , so as not to have an effect on him to return to drug abuse.

Medication

- dopamine 10 µg/kg
- noradrenaline infusion 10-20mic/min.
- norepinephren),infusion 10-20mic/min,
- propofol infusion 1-3mg/kg/hr
- fentanyl infusion 0.5-1 mic/kg/hr
- Rocephen 1 gm/12 hr
- regular insulin according to our sliding scale(NPH 7U/12hr together with regular insulin subcutaneous)
- Ranitidine 50mg /8hr
- ventolin nebulizer 1 ml+ 3 ml NS /6hr
- hydrocortisone 100mg/6hr
- heparin 5000u/8hr
- amiodarone
- G5% NS 0.09%(Normal Saline 500 ml given I.V every 8 hrs. and Dextrose Saline 500 ml given I.V every 8 hrs)
- meropenem 1gm /8hr
- Lasix 10mg/12 h
- Potassium chloride supplement 1meq/kg/day
- Sodium bicarbonate 2 meq/kg/day

II. DISCUSSION

In approximately one fourth of Brugada patients, a mutation has been reported in the cardiac sodium-channel gene (SCN5A) on chromosome 3, which encodes for the a-subunit of the cardiac sodium channel (Keller DI, Rougier JS, Kucera JP, Benammar N, Fressart V, Guicheney P, et al,2005). The mode of inheritance is autosomal dominant, and the mutated gene is seen more often in familial than in sporadic cases. More than 60 different mutations of this gene have been reported to produce BrS, and some may cause overlapping conditions, since this is the same gene in which different mutations can lead to a congenital form of long QT syndrome and Lenegre's disease (Antzelevitch C, Brugada P.2005). The transient outward current at the end of phase 1 is more prominent in men than in women. This explains why, despite an autosomal transmission, the symptomatic phenotype is about 10 times more common in men (Antzelevitch C, Brugada P.2005). Any condition or medication that increases outward currents or decreases inward currents may precipitate or unmask BrS (Grant AO.2005) Therefore, sodium-channel blockers such as procainamide or flecainide can unmask the syndrome by decreasing the inward current, as can calcium-channel blockers, β-blockers, cocaine, and antidepressants. Vagotonic agents and hypokalemia have the same effect, but they work by enhancing the outward current. A normal sodium channel may be inactivated prematurely by above-normal body temperatures,

and it has been observed that this inactivation is exaggerated in BrS. This may explain the frequency with which BrS and polymorphic VT have been unmasked in febrile patients (Antzelevitch C, Brugada P.2005). .this is what happened with this case presented in this report; as the patient before entering the hospital suffering from severe diarrhea and high fever in addition to his addiction (drug abuse) to lovenox and tramadol drug, During the last few years, other class drugs have been reported to induce Brugada ECG pattern, and an increasing number of reports of drug-induced Brugada have been published(Hermida JS, Jandaud S, Lemoine JL, Rodriguez-Lafrasse C, Delonca J, Bertrand C, et al.2004). A possible mechanism could be a latent dysfunction of the membrane channels due to an individual susceptibility similar to that in drug-induced long QT syndrome(Yap YG, Behr ER, Camm AJ.2009). However, further studies are needed to support this hypothesis. It is always important to pay attention to the administration of these agents in psychiatric patients. Physicians need to have a thorough understanding of the clinical history, and an ECG has to be performed at baseline and after drug administration. Commonly administered antipsychotic and antidepressant drugs should be used at the lowest possible dose, and with great care in BS cases or when combined with agents known to prolong QT intervals or predispose to acquired forms of BS. Patients should be screened for relevant clinical risk factors to minimize the cardiac risk. Major risk factors include structural heart disease, congenital BS, family history of sudden death, and previous episode of drug-induced ECG alterations. Secondary risk factors include old age, kidney and renal failures, dyselectrolytaemia, or concomitant use of other drugs inducing the Brugada phenotype. SCD in patients with normal heart structure and is responsible for an The most common clinical presentation of BrS is syncope (Brugada J, Brugada R, Antzelevitch C, Towbin J, Nademanee K, Brugada P.2002). Three types of changes may appear on 12-lead ECG. In type-1 Brugada pattern, ECG shows J-point elevation ≥2 mm with a down-sloping coved ST segment and usually a negative T wave. Types 2 and 3 show the same J-point elevation, but the positive T wave gives a saddleback appearance to the ST-T segment. In type-2 BrS, the terminal portion of the ST segment is elevated 1 mm or more and the T wave may be positive or biphasic, whereas the terminal ST elevation in type 3 is less than 1 mm and the T wave is not biphasic, but only positive (Wilde AA, Antzelevitch C, Borggrefe M, Brugada J, Brugada R, Brugada P, et al. 2002). Brugada and Brugada1 initially described a right bundle branch block (RBBB) pattern among their 8 cases of BrS. Thereafter, it was shown that, whereas the presence of the RBBB pattern is not necessary in reaching a diagnosis of BrSit is supportive (Wilde AA, Antzelevitch C, Borggrefe M, Brugada J, Brugada R, Brugada P, et al. 2002). Because the Brugada ECG pattern is dynamic, all of the above changes may be seen in the same patient at different times. Placing the right precordial ECG leads at an upper position, such as the 2nd intercostal space, increases the sensitivity of ECG to detect all types of the syndrome; however, it decreases specificity (Antzelevitch C, Brugada P.2005). The diagnosis of BrS is considered deinite when 1 of the ECG criteria and 1 of the clinical criteria are present. The ECG criteria are type-1 ECG changes or the conversion of type 2 or 3 to type 1 after administration of a sodium-channel blocker. Type-2 and -3 changes are considered nonspecific and nondiagnostic for BrS (Antzelevitch C, Brugada P, Borggrefe M, Brugada J, Brugada R, Corrado D, et al.2005). unless they convert to a type-1 pattern after the sodium-blocker challenge test. Even after conversion to type 1 upon challenge, types 2 and 3 remain less specific for diagnostic purposes than a type-1 ECG pattern. One of the following clinical criteria must be present to confirm the diagnosis: syncope, history of VT or ventricular fibrillation, family history of SCD or type-1 ECG changes, or inducibility of VT via electrophysiologic . Because ST elevation can accompany many underlying conditions, it is good practice to exclude other causes of ST elevation by considering clinical and laboratory information. The most common and important causes of ST elevation on ECG in the differential diagnosis of BrS are acute myocardial infarction, atypical RBBB, Prinzmetal's angina, hyperkalemia, early repolarization, and acute pericarditis. Some rarer conditions have also been reported to mimic the Brugada ECG changes, such as hypothermia(Fish JM, Antzelevitch C.2004) and a mediastinal tumor with mechanical compression on the right ventricle (Tarin N, Farre J, Rubio JM, Tunon J, Castro-Dorticos J.1998). Now, the only treatment proven effective for BrS is placement of an implantable cardioverter defibrillator (ICD) (Antzelevitch C, Brugada P). Brugada J, Brugada R.2005). A large multicenter trial (Brugada J, Brugada R,Brugada P.1998) showed that ICD placement was 100% effective in preventing SCD after 5 years of follow-up of 690 Brugada patients. In that study, appropriate shocks were delivered in 51% of the patients who initially presented with syncope and in 37% of the patients who were initially asymptomatic. In a recent clinical trial, it was shown that ICD therapy provided full protection from SCD in Asian male patients who had survived an episode of Sudden Unexplained Death Syndrome (Nademanee K, Veerakul G, Mower M, Likittanasombat K, Krittayapong R, Bhuripanyo K, et al2003).So that The ICD is recommended for this case to treat brugada syndrome and preventing sudden cardiac death so the patient and his family were adviced to do this procedure. Alternative treatments are pacemaker placement, radiofrequency ablation, and some antiarrhythmic medications. Experimental models have shown that quinidine decreases ST elevation and prevents phase 2 reentry and associated T(Belhassen B, Viskin S, Fish R, Glick A, Setbon I, Eldar M1999).Isoproterenol, which is a β-agonist, and cilostazol(Tsuchiya T, Ashikaga K, Honda T, Arita M.2002), a phosphodiesterase inhibitor, also may be helpful. Ablation of the premature ventricular beats that trigger VT and

ventricular fibrillation may be a treatment option as well(Haissaguerre M, Extramiana F, Hocini M, Cauchemez B, Jais P, Cabrera JA, et al.2005). Because SCDs that occur during sleep or rest are usually associated with a slow heart rate, a pacemaker is a possible treatment. None of the above-mentioned treatment options are as effective as ICD therapy to prevent SCD. Management this patient having severs pneumonia due nosocomial infection related to mechanical ventilation which known as Mechanical Ventilated pneumonia (MVP) and associated with chronic bronchial asthma with brugada syndrome is mostly challenge issue facing healthcare worker which happened in this case the patient deterioration in his health condition. Management of pneumonia, maintain airway and O2saturation above 93%, promote nutrition and hydration, provide small, frequent, highcarb, high protein meals and administer antibiotics. Although our patient's chest pain and ST elevation prompted us to send her to the catheterization laboratory for investigation of a possible STelevation myocardial infarction, her chest pain was pleuritic. Unmasked by the fever associated with pneumonia, the ST elevation met the criteria for type-1 Brugada pattern. However, our patient had no family history of BrS, VT, or SCD. Although EPS is recommended in type-1 ECG patients(Grant AO.2005). the value of EPS in induced cases is still unknown. Our patient had experienced no cardiac event in her 45 years; therefore, because of the normalization apparent on the electrocardiogram, she was discharged from the hospital on antibiotic therapy for pneumonia. Because regular physical activity may increase vagal tone, sport ma eventually enhance the propensity of athletes with Brugada syndrome to have ventricular fibrillation and sudden cardiac death at rest or during recovery after exercise. Accordingly, Pelliccia et al recommended that patients with a definite diagnosis of Brugada syndrome be restricted from participation competitive sports(Pelliccia A, Fagard R, Bjornstad HH, etal.2005) this is actually happened to our case when plan putted to treat flaccidity and improve health status of the patient which contribute to enhance the health condition without vigorous activity that later before disease practicing it so he stop these heavy exercise after recovering from the disease. In discussing the abnormal lab result for this case especially ABG result and kidney function test we firstly should understand the causes of abnormal lab test and its relation to cardiac arrest. Cardiac arrest and resuscitation causes multiple organ dysfunctions due to ischemia and reperfusion injury. Post-cardiac arrest syndrome comprises manifestations of various disease problem such as acute renal ailure{Neumar RW, Nolan JP, Adrie C, Aibiki M, Berg RA, Böttiger BW, Callaway C, Clark RS, Geocadin RG, Jauch EC, et al.2008) After return of spontaneous circulation (ROSC), the systemic inflammatory response triggered by ischemia and reperfusion produces a post-arrest 'sepsis-like syndrome', where the release of cytokines, adhesion molecules, and plasma endotoxins can cause multi-organ failure and influence clinical outcome after cardiac arrest (Adrie C, Adib-Conquy M, Laurent I, Monchi M, Vinsonneau C, Fitting C, Fraisse F, Dinh-Xuan AT, Carli P, Spaulding C, et al.2002) The kidney is one of the organs susceptible to injuries from ischemia and reperfusion. Ischemia-reperfusion acute kidney injury (AKI) results from endothelial and vascular injuries from activation of various inflammatory cytokines, inflammation involving tubular epithelium and immune cell subgroups, and abnormal repair processes including incomplete repair of tubular cell and fibrosis formation Really this was happened to our case after successful CPR the pt. enter acute renal failure as lab test show in the table of laboratory test good effort done from the health team to treat acute renal failure by continuous monitoring and administering therapeutic measures, treating metabolic acidosis and hypokalemia as shown in case presentation till the lab test of kidney return to normal rang and the health status of the patient become stable. On the other hand, hypokalemia that may be caused due to diarrhea which lead to decreases level of potassium in the blood so the maintenance dose given to the patient to normalize potassium level in the blood. Hypokalemia is defined by potassium serum levels below 3.5mEq/L. Patients commonly diagnosed with this electrolyte imbalance include individuals who are on diuretics such as Lasix or laxatives. Other common causes may include chronic diarrhea, vomiting, malnourishment, alcoholism, burns, gastric suction-NG.(Lonnemann, E. (2015)).

Psychosocial issues:

Although initially there may be many psychosocial aspects to Brugada syndrome and drug abuse, it is susceptible to fatigue which can be physically and mentally exhausting. This can lead to depression, emotional stress, Emotional and behavioral problems, anxiety and depression, Eating disorders; Cognitive disorders Behavioral and conduct disorders, Nonadherence, Psychological interventions by emotional support. **In** this case facing Psychosocial issues when his mother died with a cancer so that the patient manifest anxiety, depression, fatigue and withdrawal from family and social life, individual, can require extensive psychosocial support to deal with this issue, where he was supposed to receive psychosocial treatment, but unfortunately the patient did not receive any of that support, which forced him to resort to drug addiction, especially tramadol and lovenox, which affected him negatively as the patient seemed to live in isolation from his family and joined bad friend, so it is considered that psychological and social support is very important to avoid many psychological and social problem of the individual in his society Whatever the group, BrS patients have a good quality of life

with no difference between implanted and non-implanted patients. However, ICD implantation is accompanied by difficulties in their social and professional life.

This work emphasizes the need to propose specific recommendations applicable to insurance to reduce the complications experienced by these patients.

Ethical and legal malpractice

Related to the case Maintaining safe care is the first ethical and legal duty of any hospital, and all health professionals. Setting and meeting its staffing standards is a hospital's regulatory and moral duty. Indeed, the patient when discharged form ICU to rehabilitative hospital negligence were occur as the patient did not benefit from the rehabilitation program and his mental and health status worsened, and this may due to medical negligence form some of healthcare provider in the rehabilitation hospital due social stigma toward addicted patient. So the family of the patient discharged him from hospital to home and preparing a plane to rehabilitate the patient with assistance of his sister husband who work as a doctor then after 2 month the patient health status become well and the flaccidity disappear and the nutritional status was good and the patient return to his normal life with attention to healthy diet helps maintain the patient's health.

III. CONCLUSION:

Brugada syndrome is a rare cardiovascular disorder characterized by disturbances affecting the electrical system of the heart. The main symptom is irregular heartbeats and, without treatment, may potentially result in sudden death. The Brugada syndrome describes a subgroup of patients at risk for the occurrence of ventricular fibrillation who have no definable structural heart disease associated with a right bundle branch block conduction pattern and ST-segment elevation in the right precordial leads. Majority of BrS patients afterwards SCD come from "low risk" population (according to current standards), who had no previous history of arrhythmia-related syndromes prior to their fatal event and therefore were not protected with an ICD. Nowadays there are no reliable methods for identification of these patients and there is an urgent need to develop new, sufficiently sensitive and specific methods for RS in the BrS.Novel ECGbased strategies based on computerized methods for depolarization and repolarization analysis seem to be most suitable for better identification of BrS patients at higher risk of malignant arrhythmias

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