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RESEARCH ARTICLE

AN UNCOMMON STEMI MASQUERADER: A CASE OF IMIPRAMINE INDUCED BRUGADA PHENOCOPY (BRP)

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Abstract

Brugada syndrome(BrS) is an arrhythmogenic disorder characterized by a bulging ST-segment elevation and a J-point elevation of at least 2 mm in at least two of the right precordial electrocardiogram (ECG) leads (V1-3). It has an incidence of 4 to 12% in sudden cardiac death (SCD) patients due to ventricular tachycardia (VT) or ventricular fibrillation (VF). The Brugada type 1 ECG pattern may occur in various conditions independent of the actual syndrome, and this clinical phenomenon is often referred to as Brugada phenocopy (BrP). A wide variety of other drugs have been reported to unmask or induce Brugada phenotype which may otherwise be concealed, including antianginals, antidepressants, antipsychotics, and antihistamines. In this article, we present a case of Drug-induced BrP due to Imipramine. A 60-year-old hypertensive female patientwith 3 days of chest pain, who was referred to us as possible Acute Coronary Syndrome (ACS) by a general practitioner. She had a history of psychiatric illness and her ECG showed type 1 Brugada pattern with elevation of the J point with an elevation of the curved ST segment in leads V1 to V3. We found that the patient had been taking imipramine for 8 years due to her psychiatric disorder. Psychiatric opinion was sought and drug induced Brugada was suspected following which Imipramine was discontinued. After 2 weeks of follow-up there was resolution of the ST-T changes on the ECG, supporting the diagnosis of drug-induced BrP.

Introduction:-

Brugada syndrome (BrS) is an inherited cardiac arrhythmic disorder, characterized on electrocardiography (ECG) by J point elevation and coved type ST-segment elevation (≥2 mm) and subsequent inverted T wave in a minimum of two right precordial leads (V1-V3) or "saddle back" morphology consistent with Brugada type 1 and type 2 patterns, respectively. It is associated with malignant ventricular arrhythmias leading to syncope or sudden cardiac death (SCD) in individuals with structurally normal hearts. It is associated majorly with SCN5A gene mutations and is transmitted as autosomal dominant mode. It can often be concealed and unmasking of the ECG can be accomplished by drugs such as sodium channel blockers(class 1A and 1C antiarrhythmic drugs) and in febrile states. In addition to antiarrhythmic drugs, a wide variety of other drugs have been reported to unmask or induce the ECG and arrhythmic manifestations of BrS, including antianginals, antidepressants, antipsychotics, and antihistamines.The Brugada type 1 ECG pattern may occur in various conditions independent of the actual syndrome, and this clinical phenomenon is often referred to as Brugada phenocopy (BrP). These patients normally do not have any symptoms or history of

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ventricular arrhythmias.We report a case of drug induced Type 1 Brugada pattern due to imipramine in an elderly female with psychiatric illness, referred to us as Acute coronary syndrome.

Case Report:

A 60 year old female patient known case of hypertension referred by a general physician as possible Acute coronary syndrome (ACS) , came with complaints of chest pain since 3 days. She had history of similar complaints in December,2019 for which she was managed conservatively at a local hospital. On examination, her vitals and systemic examination were normal. Her ECG showed PR segment prolongation and J point elevation with coved ST segment elevation in V1 to V3 leads which was suggestive Type 1 Brugada pattern (Fig1). On targeted interrogation, she was on treatment for Psychiatric disorder- possibly Generalized Anxiety Disorder since 8 years on Imipramine,Escitalopram and Clonazepam. Patient had no history of syncope and palpitations nor family history of SCD. Her routine blood investigations were normal. Her Echocardiography showed a structurally normal heart with normal biventricular function and absence of Regional wall motion abnormality. She was evaluated for associated coronary artery disease in view of angina. Coronary angiogram done showed mild Coronary Artery Disease (CAD). Psychiatrist opinion was taken for possible Drug induced Brugada phenotype. Her psychiatric medications were readjusted, Imipramine was suspected as possible etiology and was stopped. She was managed conservatively with the probable offending agent stopped. Repeat ECG done after 2 weeks resolution of ST-T changes and normalization of the PR interval (Fig2). Provocation test was not attempted as patient was not willing and also was asymptomatic.

Discussion:-

There are various ST elevation MI masqueraders. It is prudent to keep the clinical presentation before interpretingthe ECG findings. Various commonly seen ST Elevation Myocardial Infarction (STEMI) masqueraders are enumerated in Table 1, of which the most common causes include Right Ventricular Myocardial Infarction, Acute pericarditis,myocarditis , Left Ventricular aneurysm , Early repolarization changes and Coronary vasospasm. Rarely, Type 1 Brugada pattern mimics STEMI.

Table 1:- Frequent causes of ST segment elevation in right precordial leads other than brugada [18].

Right Ventricular Myocardial Infarction
Left Ventricular Hypertrophy
Right or Left bundle branch block
Myocarditis
Pulmonary embolism
Hyperkalemia
Hypercalcemia
Tricyclic Antidepressants overdose
Cocaine intoxication
Arrhythmogenic Right Ventricular Dysplasia
Early repolarization

In our case, as patient had a history of treatment for Psychiatric Illness with Tricyclic Antidepressants (TCAs) and ECG showed type 1 Brugada pattern, hence Drug induced BrP was considered.

BrS is an an inherited cardiac disorderwithincomplete penetration in families. Carriers of known or suspected mutations may have a normal ECG or a nondiagnostic partial Brugada pattern of a saddle-shaped ST segment with or without elevation: the ECG patterns of type 2 and 3, respectively. Asymptomatic patients represent the majority of patients. In these cases, a diagnostic challenge with a sodium channel blocker, such as ajmaline or flecainideinduce the complete type 1 ECG pattern and aid the diagnosis. [1]

On the other hand, the Brugada sign has been described in asymptomatic patients after exposure to various drugs.[2] These patients generally do not have symptoms or a history of ventricular arrhythmias. In these asymptomatic patients, the abnormal ECG can often be reproduced with class 1A and 1C antiarrhythmics such as flecainide, procainamide, or ajmaline, which block the sodium channel. The prevalence of drug-induced Brugada syndrome was reported to be 5 in 1000. [3]

Postema et al. recently created a website that tracks drugs that are capable of causing Brugada phenotype. Drugs were classified based on their arrhythmogenic potential into four classes with Type 1 being the most potential.[4]Some of the most potent drugs are discussed below.

Lithium which is the drug used in treatment of bipolar disorder reported to unmask Type 1 Brugada patterns, due to potent cardiac sodium channel blockade in a concentration dependant manner at levels below the therapeutic range.[5]Cocaine has a powerful sodium channel blocking effect similar to flecainide. The sodium channel blocking property of cocaine following overdose is believed to be an important mechanism behind cocaine-induced SCD[6].Propofol the common anaesthetic used with fewer side effects, at higher doses reported to has SCD at higher doses due to its arrythmogenic potential.[7]

TCAs have been reported to unmask concealed BrS and also cause Brugadaecgpatterns. Clinical presentation in published case reports has ranged from asymptomatic[8]to ventricular fibrillation (VF), cardiac arrests.[9,10,11]Various tricyclic antidepressant agents (TCAs)including nortriptyline,[10,11] amitriptyline,[12,13] and desipramine[13,14] have been implicated. The Brugada sign has been observed in cases of TCAs overdose[11,15] as well as during routinely used dosages of TCAs. [9,13]

TCAs are known to block Fast sodium channels in the His-purkinje system and also atrial and ventricular myocardials cells thus similar to the effects of class I antiarrhythmic agents, by decreasing the maximum rate of rise of phase 0 depolarization and causing early action potential repolarization.The major hypothesis for Brugadaecg pattern in right precordial leads due to a reduction in the inward sodium current and a prominent outward current (I_{to}), which leads to shortened action potential duration in right ventricular epicardial tissue.[16]

The significance of drug-induced Brugada sign depends upon the clinical scenario. In asymptomatic patients without a family history of sudden death, drug-induced Brugada sign is likely self-limited once the offending agent is discontinued, and benign.[4] This is further supported by reports of drug-induced Brugadasign from TCAs, fluoxetine, trifluoperazine, diphenhydramine, and cocaine demonstrating the disappearance of ST-segment elevation in the right precordial leads despite flecainide or procainamide challenge once the offending drug was withdrawn.[12,14,17]

In contrast, patients with drug- induced Brugada sign who have a family history of sudden death should undergo electrophysiologic study for further evaluation, while those who present with syncope or ventricular arrhythmias should receive an implantable cardiac defibrillator[1]

The relationship between drug-induced Brugada sign and the genetically determined BrS has not yet been systematically investigated.

Several cases have been reported showing that TCAs overdose may elicit a Brugada ECG in otherwise healthy subjects.[8,12] Inaddition, in a systematic review of 98 consecutive cases of TCAs overdose in 95 patients, Goldgran-Toledano and co-workers reported that a Brugada ECG was present in as many as 15 cases. [15]

Conclusion:-

Drug induced Brugada is not an uncommon cause of STEMI masquerader in patients with genetic predisposition. In patients on psychiatric medication, TCAs like Imipramine have been reported to unmask concealed BrS and also cause Brugada ecg patterns. Thorough history to be taken in patients presenting with STEMI.In asymptomatic drug induced Brugada patients with negative family history, drug discontinuation would be adequate, with reversal of ECG changes that can be expected with few weeks of follow-up.

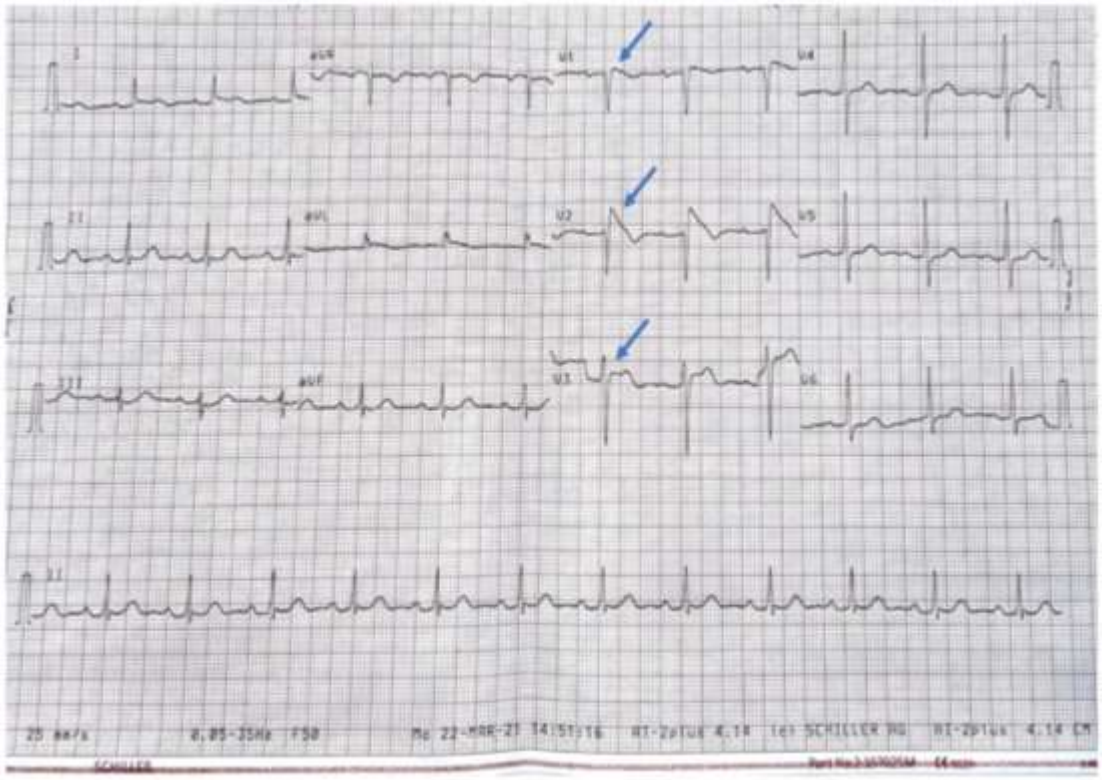

Fig1:- PR segment prolongation and J point elevation with coved ST segment elevation in V1 to V3 leads which was suggestive Type 1 Brugada pattern.

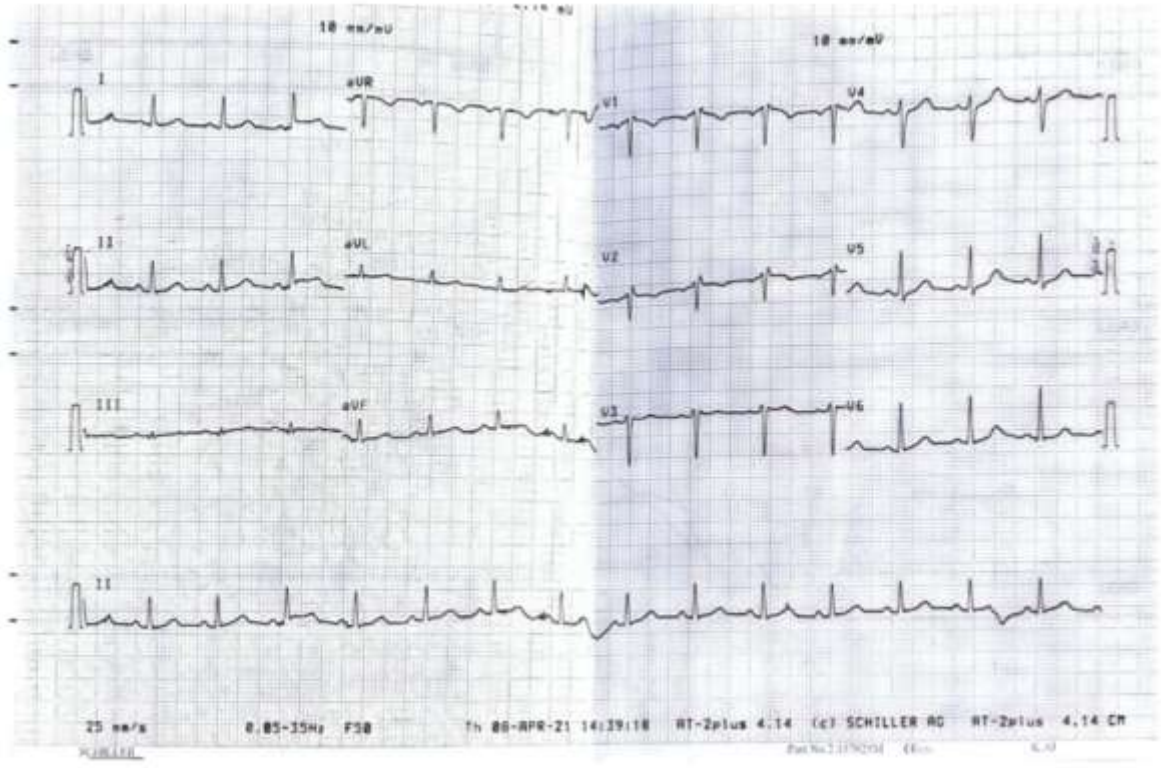

Fig2:- Resolution of ST-T changes and normalization of the PR interval after drug discontinuation.

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