BRUGADA SYNDROME UNMASKED BY DENGUE FEVER

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Abstract

Brugada syndrome is a genetic arrhythmia syndrome characterized by a coved type of ST segment elevation in the ECG.The patients are usually asymptomatic, with unmasking of the disease under certain conditions.We are reporting the case of such a patient who was diagnosed during an attack of dengue fever

INTRODUCTION:

Brugada syndrome, described in 1992 by brothers Josep and Pedro Brugada, is a genetic arrhythmia syndrome caused due to gene defects involving the sodium, calcium, and potassium channels of the cardiac musculature among others. Around 18-30% of defects can be attributed to SCN5A gene mutation affecting the alpha subunit of the cardiac sodium channel(1). The syndrome is characterized by a typical ECG pattern of >0.2 mV of ST-segment elevation with a coved ST segment and negative T-wave in more than one anterior precordial lead (V1-V3) along with Right bundle branch block in a structurally normal heart(2). This is accompanied by a risk of sudden death due to ventricular fibrillation, or syncope resulting from polymorphic ventricular tachycardia.

Most patients with this syndrome are asymptomatic. Nevertheless, diagnosing the syndrome, which is by its specific ECG pattern, is essential, as the first manifestation of the disease may even be sudden cardiac death. An Implantable cardioverter defibrillator (ICD) is indicated for patients who have had unexplained syncope or have been resuscitated from cardiac arrest(3). Anti-arrhythmic drugs like quinidine and catheter ablation of abnormal regions have been beneficial in suppressing VT. This help to reduce the incidence of sudden death to an extent.

The characteristic ST-elevation crucial for diagnosis may not be present always. It fluctuates with time and is precipitated by various factors(3). Most important among them are acute illnesses and fever. The syndrome can unmask itself in the event of a febrile illness and as a result, the disease may present itself for the first time, during such an episode.

In a region where febrile illnesses, such as dengue; and Brugada syndrome are both prevalent, such as Southeast Asia, case reports such as these become relevant. So the factors responsible for precipitating arrhythmias, such as febrile illnesses like dengue need to be analyzed and their relation needs to be understood.

CASE REPORT:

A 56-year-old male presented with a 3 days history of intermittent fever with associated non-productive cough. The fever temporarily subsided on taking medications. The patient also had headaches described as, generalized, pricking, and continuous. He has no history of syncope, palpitations, chest pain, shortness of breath, or any cardio-pulmonary symptoms. The patient is diabetic, hypertensive, and non-compliant with medications. The patient does not have a family history of sudden cardiac death or any cardiac diseases. He has no significant past medical or surgical history. This case has been reported in line with the SCARE criteria (4)..

On physical examination, the patient was febrile (102.7F), and tachycardic, otherwise, the findings were unremarkable. The laboratory findings showed positive for Dengue NS1 antigen and IgM , with a platelet count of 187× 10^3 /µL.

The patient was admitted and managed with intravenous fluids, broad-spectrum antibiotics, and acetaminophen. On the evening of admission, the complete blood count was repeated, showing a platelet count of 29 × 10^3 /µL, hematocrit 45.4%, hemoglobin 15.8g/dL, WBC 8.24 × 10^3 /µL, and lymphocytes 60.2% with suspected thrombocytopenia, large immature cells, and atypical cells. On day 2 of admission complete blood count showed a platelet count of 26 × 10^3 /µL, hematocrit 42.6%, hemoglobin 14.8g/dL, WBC 8.56× 10^3 /µL, and lymphocytes 65.2% with suspected thrombocytopenia, lymphocytosis, and large immature cells. Serum electrolytes, urea, and creatinine were all within the normal range.

	On the day of admission	**Day 2**	**On Discharge**
Temperature	103°F	102°F	100°F
Platelets	29× 10^3 /µL	26 × 10^3 /µL	56 × 10^3 /µL
Trop T	0.01 ng/ml (normal)		
CK-MB	Normal		

The patient had cyclic fevers during his hospital stay which were managed with IV and oral acetaminophen. The sequence of ECG findings was documented showing RBBB with ST-segment elevation. Diagnosed as Brugada syndrome Type 1 unmasked by Dengue fever (Fig. 1 & 2).

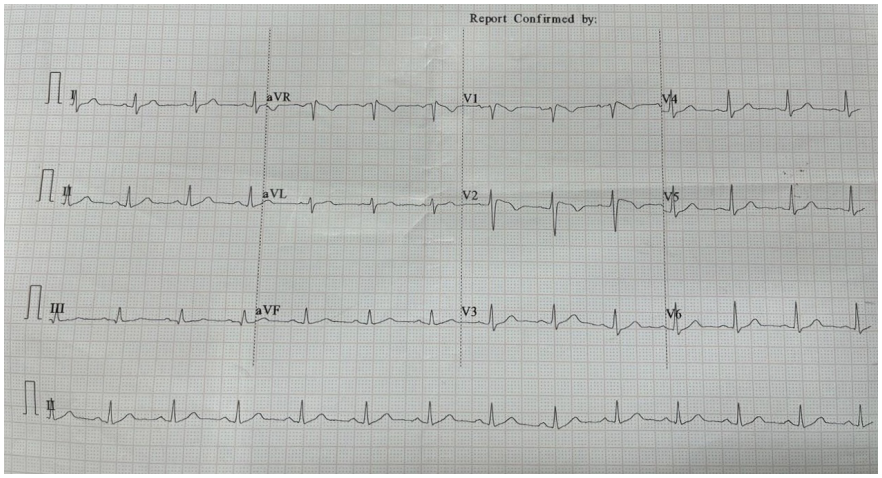

Fig. 1 – ECG taken at the time of Admission [J point elevation of 2mm from PQ with rectilinear ST Depression with T inversion, Satisfying the criteria for Type 1 Brugada Syndrome, Similar Pattern seen in aVR, Sinus rhythm at 78 /minute, QRS axis Normal, QRS Narrow complex, No Atrial or ventricular hypertrophy pattern, QTc interval – 350 ms]

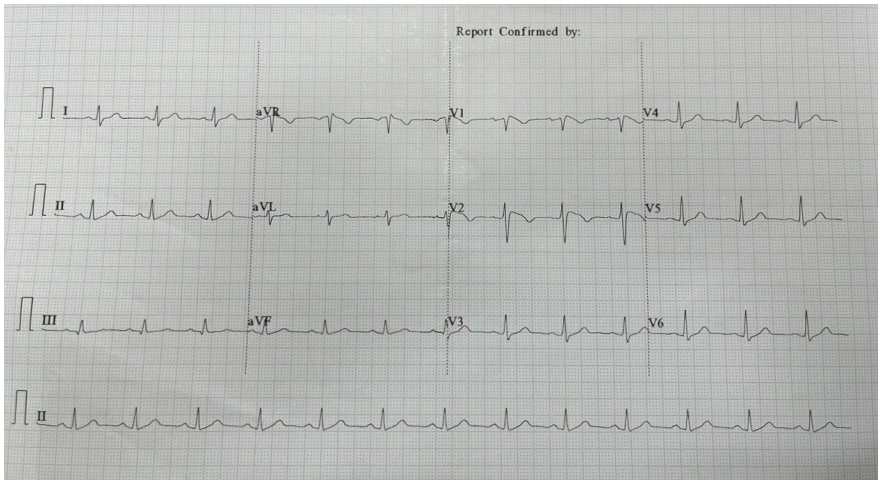

Fig. 2 – ECG taken at the time of Discharge [J point elevation of 2mm from PQ with rectilinear ST Depression with T inversion, Satisfying the criteria for Type 1 Brugada Syndrome, Similar Pattern seen in aVR, Sinus rhythm at 70/minute, QRS axis Normal, QRS Narrow complex, No Atrial or ventricular hypertrophy pattern, QTc interval – 350 ms]

DISCUSSION:

Brugada syndrome is an inherited sodium channel defect that gives rise to fatal ventricular arrhythmia and sudden death(5). Brugada disease is an autosomal dominant inherited disease that runs in families, however, more than 60% of cases are sporadic. The gene involved is SCN5A which encodes the alpha portion of the sodium channels in cardiac muscles. (6) There's not enough evidence to connect this disease with structural changes in the heart (5).

There are 3 types of Brugada Syndrome, which differ in their ECG presentation. Only type 1, when present is considered a diagnostic criterion, whereas the other 2 are suggestive of the disease rather than diagnostic(7). Type 1 is characterized by ST-segment elevation [?]2 mm in more than 1 lead in the pericardial leads (V1, V2, V3) followed with T inversion (8). Type 2 is the same ST elevation criteria but followed by biphasic or normal T wave, and Type 3 where ST elevation is [?]1 mm(9).

Brugada syndrome can be considered as a differential diagnosis when there is a family history, previous cardiac arrhythmia, previous syncope, previous ventricular tachycardia or fibrillation (10).

To diagnose Brugada syndrome a new scoring system was made, namely the Shanghai Score System which was built on the previous clinical research and data available(11). This score takes into consideration the ECG Changes, past medical history, genetics, and family history. If the score is 2-3 , Brugada is a possible diagnosis, if the score is [?]3.5 it's a definite diagnosis(12).

The Proposed Shanghai Score System for diagnosis of Brugada syndrome (12) -

	Points
I. ECG (12-Lead/Ambulatory)	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
Only award points once for highest score within this category. One item from this category must apply.	**Only award point*
II. Clinical History*	
A. Unexplained cardiac arrest or documented VF/ polymorphic VT	3

	Points
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients <30 years without alternative etiology	0.5
Only award points once for highest score within this category.	**Only award point*
III. Family History	
A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD <45 years in first- or second- degree relative with negative autopsy	0.5
Only award points once for highest score within this category.	**Only award point*
IV. Genetic Test Result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5
Score (requires at least 1 ECG finding)	?¿?
3.5 points: Probable/definite BrS	
2–3 points: Possible BrS	
<2 points: Non diagnostic	

BrS = Brugada syndrome; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

Several studies linked the new discovery of Brugada syndrome with fever (13, 14), fever associated with illness such as tonsillitis or pneumonia, unmasking Brugada, and eventually leading to fatal arrhythmias and possible death(15). It has been discovered that the gene SCN5A encodes Thr1620Met which forms the alpha unit of the sodium channel in the heart. This protein is affected by temperature, the higher the temperature, the faster the decay of this protein and that's what reveals the syndrome (16). Another study indicates that Brugada ECG changes are 20 times more obvious when associated with high fever (17).

CONCLUSION: The characteristic ECG findings of Brugada Syndrome are more pronounced in febrile illnesses such as dengue fever. The syndrome can thus be diagnosed by taking ECG during such febrile episodes. Patients presenting with arrhythmias can be managed accordingly, to prevent the progression and complications. In conclusion, Doctors treating patients with febrile illnesses should have high index of suspicion and be ready to manage it. Febrile illnesses need to be taken care of, by quick control of temperature. Further studies on this subject should be done to understand more about the degree of association, other precipitating factors and various treatment modalities.

CONFLICTS OF INTEREST:

None declared.

AUTHOR CONTRIBUTION:

All the authors contributed equally in drafting, editing, revising and finalizing the case report.

ETHICAL APPROVAL:

The ethical approval was not required for the case report as per the country's guidelines.

CONSENT:

Written informed consent was obtained from the patient to publish this report.

DATA AVAILABILITY STATEMENT:

The data that support the findings of this article are available from the corresponding author upon reasonable request.

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