Clinical presentation and electrocardiographic features of Brugada syndrome in Iraq

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Abstract

Background: Brugada syndrome is a clinical entity composed of twelve leads electrocardiographic changes of coved or saddle shaped ST-segment elevation in V1 and V2 with serious ventricular arrhythmias which may cause sudden cardiac death.

Objectives: The objectives of this study is to highlight the clinical presentation and the types of ECG changes of Brugada syndrome cases seen in Iraq and to orient physicians about this fatal condition.

Patients and Methods: Patients presented with symptoms of palpitation, dizzy attacks or syncope and diagnosed as Brugada syndrome were included in this case series study. The diagnosis of Brugada syndrome based mainly on the typical coved or saddle shaped or variant ST-segment elevation in electrocardiographic leads V1, V2.

Results: Eighteen patients were included in this case series study. All are males. Age ranged from 15-45 Y. The presenting symptoms were palpitation in 12 patients, syncope in 8, dizzy spells and pre syncope in 14 and chest pain seen in 2. The arrhythmic events were clinically documented in 10. Monomorphic VT seen in 4, VF in 2, atrial fibrillation in 2 and atrial flutter in 2. Induced VF by EP study seen in 2. Type I Brugada ECG pattern was seen in 6 patients, type II in 4 and three of type III. Five showed a variant type of the syndrome. Family history of sudden cardiac death was seen in 8 patients while in 10 it was negative. ICD was implanted in 6 patients. In 12 patients (67%) the diagnosis of Brugada syndrome was missed during the provisional medical contacts.

Conclusion: Brugada syndrome is not uncommon in Iraq but needs a high diagnostic suspicion through appreciating the symptomologies and electrocardiographic features of this fatal syndrome to plan management to prevent sudden cardiac death.

Keywords: Brugada syndrome, Electrocardiographic, Iraq

Introduction

Brugada syndrome (BrS) is an inherited clinical entity characterized by serious ventricular arrhythmias including ventricular fibrillation (VF) and sudden cardiac death (SCD) in structurally normal heart patients. It shows a specific 12 leads electrocardiographic (ECG) changes of right bundle branch block (RBBB), characteristic type of persistent coved-shaped or saddle-shaped ST segment elevation (STE) and T wave inversion (TWI) at the anterior pre cordial leads specifically in leads V1 and V2. The syndrome was first described by the Brugada brothers in 1991-1992. Before that report a similar condition has been reported by Martini B, Antoni Nava and colleagues in 1989. Later more detailed description of the condition was reported by the Brugada brothers. Since the report of this condition a large number of patients with BrS has been reported in many parts of the world. The
worldwide prevalence of this syndrome is around 0.01%. 5,6,7,8. The prevalence varies among regions and ethnicities. Male is predominantly affected. It is more common at certain localities than others, the highest prevalence was found in Southeast Asia, Thailand has highest prevalence 9. Low prevalence has been reported in the Arab countries like Egypt. 10 Few case reports were from Saudi Arabia.11,12 Since its first description in 1992, continuous achievements have expanded our understanding of the genetic basis and electrophysiological mechanisms underlying the disease. Currently, despite several genes identified, SCN5A has attracted most attention, and in approximately 30% of patients, a genetic variant may be implicated in the causation after a comprehensive analysis. In BrS the genetic background is the main determinant for the extent of the electrophysiological abnormalities.8

In Iraq the first case of BrS has been reported in 2007 by Mohamaad Hashim et al .13 After that reported case many other patients have been diagnosed. The ECG changes of BrS is not always constant, minor changes may be aggravated by a challenge test with flecanide or ajmaline.14-17 The ST segment elevation may vary in shape and extent, accordingly three types of BrS ECG changes has been described: type I shows coved –shaped STE more than 2mm and TWI with or without drug challenge, Type II shows saddle-back STE morphology defined as J wave amplitude more than 2mm, while Type III shows STE not more than 1mm with either coved or saddle-back morphology of STE and this can be converted to Type I by challenge test.10 See Figure 7. Changing pattern from type I in to type II has been reported .15 ECG changes of BrS may be seen in asymptomatic individuals without clinical signs or symptoms.16 Many random public survey for the BrS ECG changes has been conducted in asymptomatic individuals which showed variable prevalence and prognostic value.17,18,19 The clinical findings in BrS are: the most severe form is SCD due to VF which can be the first manifestation, other symptoms include: agonal respiration during sleep, history of palpitation, syncope, pre syncope , dizzy spells or inducible VT/VF by electrophysiological study (EPS) in patients with unexplained palpitation or syncope.20,22

Missing the diagnosis of BrS have a serious consequence because it is a marker of SCD. The ECG changes of BrS should always be evaluated in correlation to the symptoms and risk stratification which should include: family history (FH) of SCD or BrS, inducibilty of VF/VT by EPS in symptomatic or asymptomatic patients with Brugada ECG changes and the results of drug challenge test in borderline cases.20 At least 12 features of standard ECG are associated with a higher risk of sudden death in BrS. A multipara metric risk assessment approach based on ECG parameters associated with clinical and genetic findings could help improve current risk stratification scores of patients with BrS and warrants further investigation.21,22

Early repolarization syndrome is a term used to describe an ECG changes of prominent or elevated J-point with notching or slurring of the distal part of R wave.22, 23 This syndrome is a synonymous to BrS and the two conditions are called J-wave syndrome. 24 Both are associated with high risk of VT/VF and SCD. A group of heterogeneous conditions induce a Brugada ECG
pattern, including metabolic conditions, mechanical compression, myocardial ischemia, pulmonary embolism, myocarditis and pericardial diseases and post DC-shock within few hours.22,25 These situations must be distinguished from true BrS as these are potential reversible causes and do not need invasive treatment and ICD implantation. There is an overlap between BrS and sick sinus syndrome and cardiac conduction defects. BrS share many similarities to LQTS 3.26 Therapeutic approach of BrS continues to be challenging. Although there were limited therapeutic measures, essentially ICD implantation and quinidine.27 ICD is indicated in symptomatic BrS including: a, resuscitated cardiac arrest. b, syncope with FH of SCD or BrS .c, BrS ECG with induced VF by EPS. ICD carries many complications over the patient’s lifetime.28 Catheter ablation in BrS has developed remarkably over the last few years. Epicardial 3D mapping has helped to discover well defined potentially reversible substrate where RF ablation proved to be effective in controlling VT/VF 29. Successful Catheter ablation may well eliminate the BrS ECG changes. Ablation therapy can pave the way to cure BrS and potentially removes the need for ICD implantation or chronic quinidine therapy 30 . Further advances in this aspect of management of BrS may well revolutionize management of this fatal condition. There has been a remarkable progress in the effectiveness of catheter ablation since epicardial substrate ablation was first applied in 2011 and such approach is now widely applicable.30 Endocardial mapping followed by endocardial substrate modification has an excellent long term outcome.31,32 The aim of this case series study is to highlight the clinical presentation of BrS in Iraq to orient general practitioners, general physicians and cardiologists to the clinical symptoms and ECG features of this syndrome to help minimizing miss-diagnosis.

Methods

Over a period of 11 years’ patients with symptomatic BrS has been identified and included in this case series study. The reported cases were diagnosed by a single author at private clinic and Alhassani heart center in Sulaimanya during the period from 2009 up till 2020. The patients are both Arabs from the middle or south of Iraq or Kurds from Kurdistan region. All the patients were presented with symptoms and BrS ECG changes. The diagnostic criterion to diagnose BrS was as follows: a, symptoms of palpitation, dizzy spells or syncope with documented tachyarrhythmias and ECG pattern of coved-shaped or saddle-back shaped ST segment elevation at V1-V2 or V3 with TWI. b, resuscitated patient from VT/VF and findings of coved or saddle - shaped ST segment elevation in V1, V2 or V3 in the ECG of sinus rhythm. c, findings of BrS type ST elevation in patients assessed for unexplained palpitation, dizzy spells or syncope. The type of BrS was assessed according to the following criteria: a, type I if the STE of coved–shaped more than 2 mm with TWI. b, type II diagnosed if the STE is of saddle-back shape of more than 2mm. c, type III if the STE is of 1mm size of saddle- back shape. Those who was not classically fitting any of the three types was labelled as variant type of BrS. Family history of sudden death was asked for in all patients. All patients had 12 leads ECG, CXR,
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echocardiogram and Holter recording for 24 or 48 hours. Arrhythmic events were looked for and classified accordingly. EPS done if felt necessary in unexplained palpitation or dizzy spells and syncope. The miss-diagnosis of BrS was defined as the patient presented to the medical care and miss-diagnosed as other medical problems and later diagnosed as BrS according to the diagnostic criteria. The number of medical contacts before reaching to BrS diagnosis was identified.

Unfortunately, genetic testing was not available in Iraq up till the time of writing this paper. Coronary angiogram was done for chest pain presentation. Full biochemical and hematological testing including electrolyte was done in all patients. Thyroid hormones were measured in all patients.

ICD implantation was done in patients with resuscitated VT/VF and those with positive FH of SCD and ECG changes of BrS and symptoms of palpitation or syncope. No quinidine therapy given to our patients because it is not widely available in Iraq.

Results

A total of 18 patients were included in this case series study. All are males. Age ranged from 15-45 Y. The symptoms they presented with were as follows: sudden palpitation was seen in 12 patients, syncope in 8, dizzy spells and pre syncope in 14. Chest pain seen in 2 p. The arrhythmic events were clinically documented in 10. Monomorphic VT of LBBB pattern seen in 4, VF in 2, atrial fib in 2 and atrial flutter in 2. Induced VF by EPS seen in 2. The pattern of ECG changes suggesting BrS was as follows: The type I Brugada ECG pattern was seen in 6 patients, and in 4 type II was seen, three showed type III. Five showed a variant type of BrS. TWI seen in all type I, II and III. FH of SCD was seen in 8 patients while in 10 the FH was negative for SCD. ICD was implanted in 6 patients according to the indication mentioned in patients and methods.

In 12 patients (67%) there was provisional one or two medical contacts where the diagnosis of BrS was missed. The over diagnosis was IHD in 7 and variable unrelated diagnosis in the other 5. The figures 1 to 6 are showing different types of BrS and VA.

<table>
<thead>
<tr>
<th>TABLE 1. THE DEMOGRAPHIC CHARACTERISTICS.</th>
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<tr>
<td>Number</td>
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<td>Age (yrs.)</td>
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<tr>
<td>Gender</td>
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<td>Symptoms</td>
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<td>palpitation</td>
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<td>syncope</td>
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<td>dizziness</td>
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<td>chest pain</td>
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<td>Arrhythmias</td>
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<td>monomorphic ventricular tachycardia (MVT)</td>
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<td>ventricular fibrillation (VF)</td>
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<td>atrial fibrillation (AF)</td>
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<td>atrial flutter (AFL)</td>
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<tr>
<td>Electrophysiology study induced VF (EPS VF)</td>
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<td>Family history</td>
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<td>Sudden Cardiac Death</td>
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<td>No Family History</td>
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<tr>
<td>Misdiagnosed</td>
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<tr>
<td>IHD</td>
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<td>Others</td>
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<th>TABLE 2. THE TYPES OF BRUGADA SYNDROME ECG CHANGES.</th>
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<td>Type I Brugada Syndrome</td>
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<td>Type 2 Brugada Syndrome</td>
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<td>Type III Brugada Syndrome</td>
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<td>Variant Brugada Syndrome</td>
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<td>Total</td>
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Fig 1, Twelve leads ECG of a patient presented with palpitation and syncope. Note the coved-shaped ST segment elevation at V1-V3 and TWI (arrows), suggesting type I Brugada syndrome.

Fig 2, Monomorphic VT of LBBB pattern in a patient presented with recurrent palpitation and pre syncope. In the 12 leads SR ECG (left) notice the saddle-back STE of type III Brugada in leads V1&V3 (circles).

Fig 3, a 32-y male patient presented with syncope and found in VF at the ED (top ECG strip), the first ECG (right) done few hours after resuscitation with DC shock showed extensive, extreme coved-shaped ST segment elevation in leads I, aVL, V1-V4., the second ECG (left) one day later showed ST segment saddle in V1 suggesting type II BrS. FH: His father died suddenly at the age of 35Y. Bottom EGM from his ICD showed VF successfully defibrillated 8 months after implantation.

Fig 4, 42 Y Male patient with unexplained syncope, Right, the 12 leads ECG showed RBBB and minor coved ST segment elevation in aVF (arrow). During EP study VF induced by ventricular programmed stimulation. Left, the 12 leads SR ECG showing an IRBBB and atypical (variant) ST segment elevation in V1, V2, V4 and V5. (arrows).

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Fig 5, the ECG of a 43 Y old male patient presented with palpitation and pre syncope. The rhythm is Atrial Flutter. Note the coved ST segment elevation in V1-V3. Findings suggesting type I BrS.

Fig 6, the twelve leads Holter ECG of a 45 Y male with syncope and chest pain. CTA: normal. FH: two male brothers SCD at 25, 30Y. Note the coved-shaped ST segment elevation in V2, aVL and lead I (arrows) suggesting type I BrS.

Fig 7, the three classical types of BrS ECG changes, observe the ST segment elevation character in each type. In type I a coved - shaped STSE, in type II a saddle-back STSE of more than 1mv, Type III shows an STSE saddle-back shaped of less than 1mv. Wilde AAM et al, Circulation. 2002; 106:2514–2519

Discussion
The BrS is worldwide reported disease causing SCD due to VF/VT. The prevalence of the syndrome varies in between different global localities. In the middle east and the Arab countries few series have been reported. In Iraq the first case was reported in 2007 in a boy of 16 y old with FH of SCD. The character of the ST segment elevation noticed in five of our patients is rather of a variant type than the three classical types in literature, this has been observed by others at different regions in the world as in the report of Ari, Martini and Matsuo. It seems that there are world wide variations of the pattern of ST elevation in BrS which need a much wider international observational studies. Random ECG survey in healthy population for BrS ECG changes as in Furuhashi and Sakabe reports is rather a different matter than ECG changes in symptomatic patients presented with syncope and have a VF/VT documented.
clinically or induced by EPS$^{15,16}$. The cases involved in our series are all symptomatic with documented ventricular arrhythmias.

As far as the clinical presentation and diagnosis of BrS, achieving a high diagnostic suspicion index is highly required in medical practice to minimize missing the diagnosis of BrS and offer a therapeutic measure to prevent SCD. The suspicion of the diagnosis of BrS starts with the clinical presentation of patients with palpitation, dizzy spells or syncope and the ECG changes of coved or saddle shaped ST-segment elevation in the anterior chest leads. Challenge test in borderline ECG changes can help to establish the diagnosis. There is a clear need to organize a national Iraqi registry for the cases with BrS and introduce a detailed genetic studies to understand the pattern of inheritance and look for the correlation of consanguinity to the incidence and prevalence of this condition in Iraq and other regional countries. Cooperation with the international registry for BrS can help to further understand the pattern of this disease and improve the process of management in different countries. Improving the therapeutic procedures level specifically catheter ablation therapy is heavily required to minimize the need for ICD implantation and quinidine drug therapy.

Limitation of the study: small number of the cases because it is a single author observation.

Conflict of interest: The authors declare no conflict of interest.

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References

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