A case of asymptomatic Brugada syndrome with type 1 ECG pattern and cardiac arrest: an evaluation of the prognostic value of electrophysiology study

Asemptomatik, tip 1 EKG bulguları olan ve ani kalp durması gelişen Brugada sendromlu bir olgu: Elektrofizyolojik çalışmanın prognoz belirleme üzerine etkisinin irdelenmesi

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Brugada syndrome is characterized by ST-segment elevation in the leads V1-3 of electrocardiography (ECG) in the absence of a structural heart disease. A 26-year old male patient was admitted with sudden cardiac arrest. Cardiopulmonary resuscitation was successful and he was referred to the reanimation unit due to unconsciousness. A year before, he was diagnosed as having Brugada syndrome with type 1 ECG pattern at another center, at which time an electrophysiology study (EPS) was not performed due to the lack of symptoms and a family history of sudden cardiac death. In addition, family screening revealed two asymptomatic brothers having Brugada syndrome with type 1 ECG pattern. Medical follow-up was recommended to one of them. The other sibling underwent EPS at a different center where ventricular fibrillation was induced. An implantable cardioverter defibrillator (ICD) was recommended, but the patient refused. A further analysis of the family made at our center showed type 2 ECG changes in the father and in one of the cousins. Due to the development of persistent brain injury and an expected survival of less than a year, an ICD was not considered in the patient. The prognostic value of EPS is still controversial in asymptomatic patients with type 1 Brugada syndrome, without a family history of sudden cardiac death.

Key words: Death, sudden, cardiac; electrocardiography; electrophysiology; heart arrest/etiology; syndrome.

Brugada sendromu, yapısal kalp hastalığı olmadan elektrokardiyografide (EKG) V1-3 derivasyonlarında ST-segment yükselmesinin görüldüğü bir durumdur. Yirmi altı yaşında erkek hasta, kalp durması nedeniyle acil servisimize getirildi. Uygulanan kardiyopulmoner canlandırmaya yanıt veren, ancak bilinci açılmayan hasta reanimasyon ünitesine sevk edildi. Asemptomatik olan hastaya bir yıl önce bir başka merkezde, EKG'de tip 1 özellik görülmesi üzerine Brugada sendromu tanısı konduğu; asemptomatik olması ve ailede ani ölüm öyküsü bulunmaması nedeniyle elektrofizyolojik çalışma (EFS) yapılmadığı öğrenildi. Ayrıca, aile taramasında hastanın asemptomatik olan iki erkek kardeşinde de tip 1 EKG bulguları saptanması üzerine, birine aynı merkezce sadece takip önerilmişti. Diğer kardeşe ise başka bir merkezde yapılan EFS'de ventrikül fibrilasyonu oluşturulması üzerine intrakardiyak defibrilatör (ICD) önerilmiş, ancak hasta bu girişimi kabul etmemişti. Hastanın kurumumuzda yapılan daha ayrıntılı aile taramasında, babasında ve bir erkek kuzeninde tip 2 EKG bulguları görüldü. Kalıcı beyin hasarı gelişen hastanın yaşam beklentisi bir yıldan az olduğundan ICD tedavisi düşünülmedi. Asemptomatik, ailede ani ölüm öyküsü bulunmayan, tip 1 Brugada sendromu olan hastalarda EFS'nin prognozu belirlemede etkisi olup olmadığı konusunda henüz görüş birliği bulunmamaktadır.

Anahtar sözcükler: Ani ölüm; elektrokardiyografi; elektrofizyoloji; kalp durması/etyoloji; sendrom.

Brugada syndrome is characterized by ST-segment elevation in leads V1-3 on electrocardiography (ECG), in the absence of a structural heart disease.[1-3] This syndrome with a familial predisposition was first described in 1992 by the Brugada brothers as a clinical condition with a high risk of sudden death.[1] Mutations on the SCN5A gene which encode the alpha subunit of cardiac sodium channels are thought to be responsible in the pathophysiology of the disease.[4] Identification of this gene mutations in only 20-25% of patients indicated that there may be other genetic defects and suggests that the syndrome may be a genetically heterogeneous disease.[5] The first finding of the disease is mostly sudden death due to fast polymorphic ventricular tachycardia (VT) or ventricular fibrillation (VF). All family members of the patient should undergo thorough investigation due to the familial predisposition of the condition. ECG findings may sometimes be insignificant or

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may completely return to normal due to the dynamic nature of ECG findings in some patients. Sodium channel blockers (ajmaline, flecainide, propafenone, etc.) may be used in these patients to reveal typical ECG findings.[6]

In this article, we present a Brugada syndrome patient with a type 1 ECG pattern together with a family history of the condition, and investigate the effect of electrophysiology study (EPS) on the prognosis.

CASE REPORT

A 26-year old male patient was brought to our emergency unit due to sudden cardiac arrest. The patient responded to the cardiopulmonary resuscitation performed. However, he was referred to the reanimation unit due to failure to regain consciousness. His past medical history revealed that he was diagnosed as having Brugada syndrome with type 1 ECG pattern a year before at another center during routine follow-up, following an asymptomatic period. The patient's ECG was found to be consistent with Brugada syndrome (Figure 1). An EPS was later performed due to the lack of symptoms and a family history of sudden death. A family screening performed around the same period also revealed the presence of Brugada syndrome with a type 1 ECG pattern in two of his brothers (Figure 2). One of these two asymptomatic brothers was recommended follow-up alone at the same center. The other brother underwent EPS at a different center where an implantable cardioverter defibrillator (ICD) was recommended induction of VF; however, the patient was reported to have refused the procedure.

A further detailed screening of the family performed at our center revealed a type 2 ECG pattern of Brugada syndrome in his father and in one of the male cousins (Figure 2). A provocative test with propafenone on these asymptomatic patients was found to be negative. An

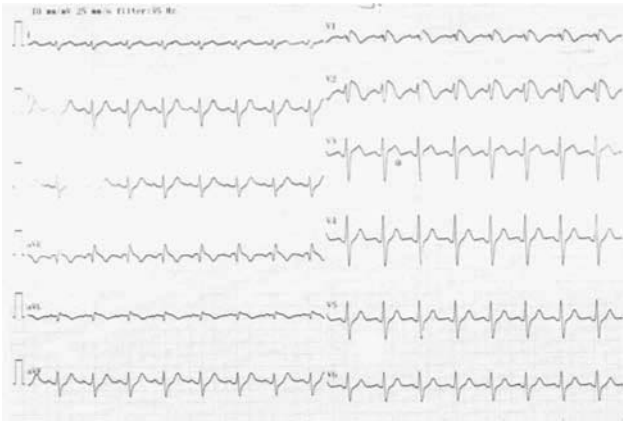

Figure 1. An electrocardiogram obtained one year ago while the patient was asymptomatic

ICD treatment was not considered in the patient who developed hypoxic encephalopathy since his life expectancy was less than one year. ICD treatment was recommended in the type 1 ECG pattern Brugada syndrome sibling with induced VF on a previous EPS, whereas the other patients received EPS.

DISCUSSION

Brugada syndrome is thought to be responsible for 4-12% of sudden death cases.[6] This rate can rise up to 20% in patients with no structural heart disease. ICD in the only treatment modality approved efficacy in the treatment of the syndrome with a high risk of sudden cardiac death.

Identification of the risk of sudden cardiac death is the most important step in the management of Brugada syndrome.[7] In the study by Brugada et al.[7] the risk of sudden death during the 33±39-months follow-up period was found to be 62% in patients with aborted sudden cardiac death, 19% in patients with a history of syncope, and 8% in asymptomatic patients. VT/VF was indu-

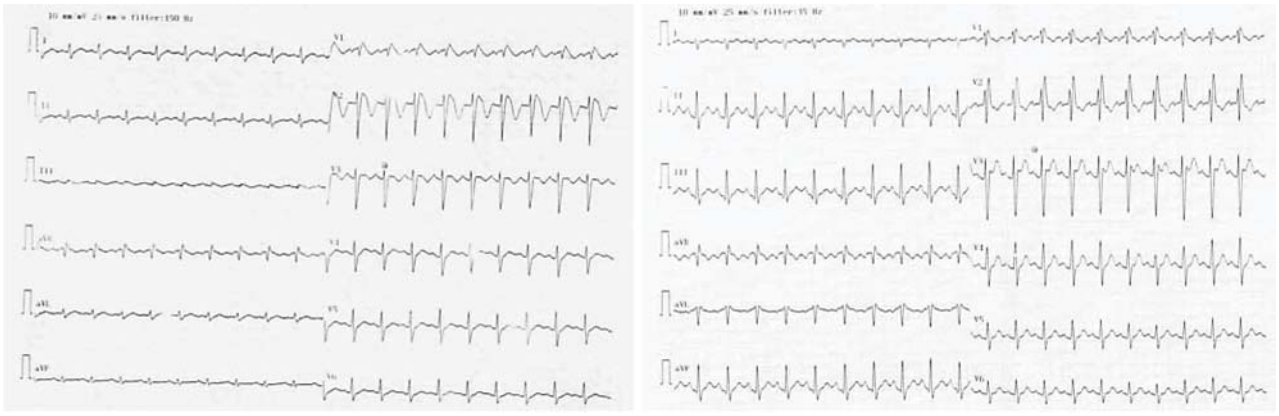

Figure 2. (A, B) Electrocardiograms of the patient's two brothers

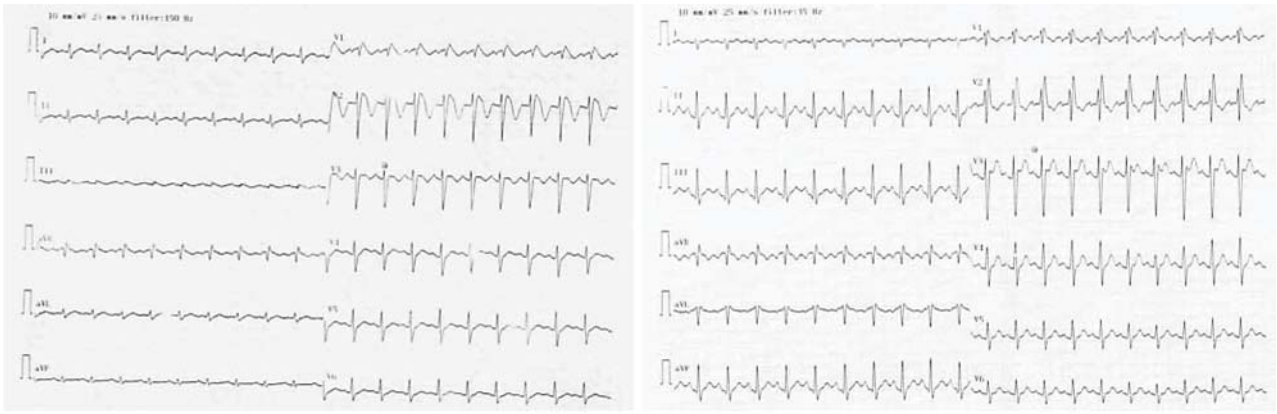

Figure 3. Electrocardiogram of the patient's **(A)** father and **(B)** cousin

ced during EPS in 83% of patients with aborted sudden cardiac death, 68% in patients with a history of syncope, and 33% in asymptomatic patients. In the same study, the predictor of the high risk of sudden death was reported as the induction of VT/VF during EPS in aborted sudden cardiac death and in those with a history of syncope, whereas male gender, ST-segment elevation or induction of VT/VF during EPS were predictors of high risk of sudden death in asymptomatic patients. In another study conducted by Brugada et al.[8] the incidence of cardiac events during the 24±32-month follow-up period in Brugada syndrome patients with no history of cardiac arrest was reported as 8.2%. Induction of VT/VF during EPS and a history of syncope were referred to as very important risk factors for the development cardiac events. The incidence of cardiac events was found to be 6-fold in induction of VT/VF during EPS compared to those with induction, whereas it was 2.5-fold higher in patients with a history of syncope than in those without. The studies by Brugada et al.[7,8] have demonstrated that induction of VT/VF during EPS is an important predictor of prognosis.

On the other hand, Priori et al.[9] did not find any relationship between prognosis and the induction of VT/VF during EPS. Cardiac arrest was reported in patients who developed VT/VF during EPS and in those without at a rate of 8% and 7%, respectively during the 34±44-month follow-up of asymptomatic patients with a history of sudden death. Similarly, Kanda et al.[10] also demonstrated that there was no relationship between VF during EPS and prognosis. No difference was found between patients with and those without VF during EPS with regards to the incidence of recurrent cardiac events during the 38-month follow-up period in patients with a history of sudden cardiac arrest or syncope. Eckardt at el.[11] also found the development rate of VT/VF during EPS to be similar in patients with a history of sudden or syncope and asymptomatic patients.

In a meta-analysis of 15 studies involving 1217 patients VT/VF was induced in 53% of the 1036 patients who underwent EPS.[12] The induction of VT/VF during EPS and the incidence of ventricular tachycardia during follow-up was found to be higher in patients with a history of sudden cardiac arrest or syncope, compared to asymptomatic patients. However, no significant relationship was found between the incidence of ventricular tachycardia and induction of VT/VF during EPS within the 34±40-month follow-up period of the patients.

In the latest consensus report on Brugada syndrome, it was recommended that family members (with a history of sudden death) of asymptomatic patients with Brugada syndrome type 1 ECG findings should undergo EPS, and that an ICD should be implanted in the event of VT/VF induction during EPS. No consensus was reached concerning family members with no history of sudden death.[13] EPS was also recommended to our patent at the presenting center in accordance with the consensus report, due to the asymptomatic nature and the presence of a family history of sudden death.

Sudden death was reported to develop after a one-year follow-up period without EPS in our patient who was asymptomatic at diagnosis and who had no family history of sudden death. This supports the suggestion by Brugada et al. that risk identification by EPS should be performed on these patients although it is difficult to detailed assessment since EPS was not performed on the patient. On the other hand, the fact that the brother who developed VF during EPS lived for at least one year without ICD protection and no cardiac event seems to support those who suggest that EPS results have no effect on prognosis in these group of patients. However, a follow-up period of only one year on a family with Brugada syndrome is not sufficient to make detailed assessments.

In this report we tried to discuss the role of EPS in predicting the risk of asymptomatic Brugada patients with a type 1 ECG pattern who had no family history of sudden death. However, our patients were unable to provide us with sufficient information. We could not identify any risk determination tool due to the dynamic nature of the condition, variation with age, and due to the presence of different arrhythmic risks despite similar clinical findings. The role of electrophysiology on risk determination is also a matter of controversy.

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