

Original article

The Clinical Significance of Pregnancy in Brugada Syndrome

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ABSTRACT

Introduction and objectives: Little is known about the risks and outcomes of pregnancy in women with Brugada syndrome. We therefore evaluated pregnancy outcomes and the influence of pregnancy in patients with Brugada syndrome.

Methods: A retrospective analysis was performed in all pregnant women with Brugada syndrome. We included 104 women with a total of 219 deliveries.

Results: There were 15 spontaneous abortions. One infant died suddenly during the night 3 months after birth. Six pregnant women reported they had experienced at least 1 syncope during the pregnancy. Of the 3 women who received an implantable cardioverter-defibrillator before the pregnancy, none received arrhythmia episodes. There were no events during the pregnancy in 4 patients with a previously aborted sudden cardiac death. Of 24 patients with syncope when not pregnant, 18 were asymptomatic and 6 experienced a recurrent syncope during the pregnancy. During the follow-up (mean follow-up 298.9 days; 95% confidence interval, 289.6–308.2), 2 women received appropriate shocks.

Conclusions: In this retrospective, single-center study, serious events were not more frequent during pregnancy and the peripartum period in women with Brugada syndrome. The occurrence of syncope during pregnancy was not associated with a worst outcome in the peri- and postpartum periods or during follow-up. The reported rate of miscarriage and sudden infant death will require further studies to confirm or rule out its association with Brugada syndrome.

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Trascendencia clínica del embarazo en el síndrome de Brugada

RESUMEN

Introducción y objetivos: Se sabe poco sobre los riesgos y los resultados del embarazo en mujeres con síndrome de Brugada. Por lo tanto, se evalúa la influencia del embarazo en pacientes con síndrome de Brugada.

Métodos: Se realizó un análisis retrospectivo de todas las embarazadas con síndrome de Brugada. Se incluyó a 104 mujeres con un total de 219 partos.

Resultados: Hubo 15 abortos espontáneos; 1 niño falleció súbitamente durante la noche 3 meses después del nacimiento; 6 embarazadas refirieron haber sufrido al menos un síncope durante el embarazo; en ninguna de las 3 mujeres a las que se implantó un desfibrilador automático implantable antes del embarazo se registraron episodios arrítmicos; 4 pacientes con antecedente de muerte súbita cardíaca recuperada no sufrieron evento alguno durante el embarazo. De las 24 pacientes que habían sufrido síncope cuando no estaban embarazadas, 18 se mantuvieron asintomáticas y 6 sufrieron síncope durante el embarazo. Durante el seguimiento (media, 298,9 días; intervalo de confianza del 95%, 289,6–308,2) 2 mujeres recibieron descargas apropiadas.

Conclusiones: En este estudio unicéntrico y retrospectivo, los eventos graves no fueron más frecuentes durante el embarazo y el periodo periparto en las mujeres con síndrome de Brugada. La aparición de síncope durante el embarazo no se asoció a una peor evolución en los periodos periparto y posparto ni durante el seguimiento. La tasa descrita de abortos espontáneos y muerte súbita infantil deberá investigarse en nuevos estudios para confirmar o descartar su asociación con el síndrome de Brugada.

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Palabras clave:

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Síndrome de muerte súbita infantil

Síndrome de muerte súbita inesperada

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Abbreviations

BS: Brugada syndrome
 ECG: electrocardiogram
 EPS: electrophysiological study
 ICD: implantable cardiac defibrillator
 SCD: sudden cardiac death
 SIDS: sudden infant death syndrome

INTRODUCTION

The sex-related difference in the phenotypic expression of the Brugada syndrome (BS) is more pronounced than in any other autosomally transmitted arrhythmic syndrome.^{1,2} The basis for this intriguing sex-related distinction is not fully understood. Potential explanations are gender-related intrinsic differences in ionic currents and hormonal influences. Due to this hormonal influence, pregnancy represents a particular situation in the life of women with BS. To date, data elucidating the role of hormonal changes secondary to pregnancy in the clinical outcome of this population have been missing. In 1 isolated case report, pregnancy was suggested to be a precipitating factor for triggering electrical storm.³ The aim of our study was to evaluate the frequency of clinical events during pregnancy and the peripartum period.

METHODS

Study Population

Patients were consecutively included in the current study from our database if they met the following inclusion criteria: female sex, age between 18 and 65 years, documented spontaneous or class I antiarrhythmic drug-induced coved type 1 BS electrocardiogram (ECG), and previous deliveries. Those patients who were not followed-up in our institution were contacted through telephone interview. During the interview, several factors were evaluated: the number of deliveries, cesarean or spontaneous delivery, the number of spontaneous abortions, potential arrhythmic events during the pregnancy (syncope, arrhythmias or sudden cardiac death [SCD]), and the status of the newborn (healthy child, sudden infant death).

A proband was defined as the first patient of a family with BS diagnosed with type 1 Brugada ECG pattern. Diagnosis of BS was based on the recommendations of the Brugada consensus reports^{4,5} with recent modifications.^{6,7} Syncope was defined as transient loss of consciousness with abrupt onset and offset.

All included patients gave their informed consent. The Ethics Committee of the UZ Brussels (Brussels, Belgium) approved the study protocol. The database for the purpose of this study was assessed in August 2012.

Statistical Analysis

Continuous variables are expressed as the mean and standard deviation or median. Statistical differences were calculated using the chi-square test for discrete variables and the t-test for continuous variables (expressed as mean values and standard deviation). Cumulative event rates were estimated by Kaplan-Meier estimation. A *P*-value <.05 was considered statistically significant. All statistics were performed with the use of SPSS software (SPSS Inc., Chicago, Illinois, United States).

RESULTS

One hundred and four women (belonging to 79 families) with a total of 219 deliveries were included from a total of 611 individuals in the original database (from 1995 to 2012). Two pregnant women were still pregnant at the time of the interview and were excluded from the analyses. One patient was lost to follow up. Five patients were diagnosed with BS before pregnancy and the remainder of the sample was diagnosed afterward.

The mean age of the sample at diagnosis of BS was 43 (12.9) years. Twenty-nine women were probands. Sixty-six individuals had a positive family history of SCD (Table 1). The mean age at the first symptom was 42 (12.7) years. Fifty-nine patients were classified as asymptomatic, while 24 had had a previous syncope, and 4 had an aborted SCD as the first manifestation of the disease. Baseline ECG showed a spontaneous type 1 BS pattern in 7 patients, a normal pattern in 58 patients, and type 2 and 3 pattern in 39 women. Eighty-six women underwent an electrophysiological study (EPS). A sustained ventricular arrhythmia was induced in 7 study patients. Twenty-seven patients received an implantable cardiac defibrillator (ICD); the reason for the implantation was based on several characteristics but can be summarized as follows: the presence of an aborted SCD (4 women), a history of previous syncope (20 patients, 4 of them with positive EPS), and positive EPS in patients with a positive ajmaline test (3 patients). The mean age was 25 (2.9) years at the first delivery, 27 (3.4) at the second, 31 (3.1) at the third, and 28 (16) at the fourth. There were 5 patients with 4 deliveries, 2 patients with 5, and 1 patient with 6. Thirteen women underwent cesarean section and the remaining newborns were delivered vaginally.

Clinical Events During Pregnancy

During pregnancy, there were 15 spontaneous abortions in 10 patients (5 women with 2 spontaneous abortions and 5 with 1) (Table 2). This subgroup showed no differences in clinical characteristics compared with those in patients without spontaneous abortions (Table 3). Two patients complained of recurrent

Table 1

Baseline Characteristics of the Population Enrolled in the Study

| | |
|----------------------------|------------|
| Patients, n | 104 |
| Age, years | 43.3±12.9 |
| Proband | 29 (27.8) |
| Family history of SCD | 66 (63.4) |
| SCN5A positive | 14 (13.4) |
| Asymptomatic | 59 (56.7) |
| Previous syncope | 24 (23.1) |
| Aborted SCD | 4 |
| Palpitations-presyncope | 17 (16.3) |
| Age first symptom | 42.8±12.8 |
| EPS study | 86 (82.6) |
| VT/VF induction in the EPS | 7 (6.7) |
| ICD implantation | 27 (26) |
| Baseline type I ECG | 7 (6.7) |
| PR interval, ms | 163.4±27.2 |
| QRS interval, ms | 92.1±17.8 |
| cQT V1, ms | 393.7±37.5 |
| cQT lead II, ms | 404.9±27.4 |

ECG, electrocardiogram; EPS, electrophysiological study; ICD, implantable cardiac defibrillator; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

Data are expressed as No. (%) or mean ± standard deviation.

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