Journal of Arrhythmia 28 (2012) 360–363

Contents lists available at SciVerse ScienceDirect

Journal of Arrhythmia

journal homepage: www.elsevier.com/locate/joa

Case Report

Markedly reduced ventricular arrhythmia during the peripartum period in a pregnant woman with Andersen-Tawil syndrome

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ARTICLE INFO

Article history:
Received 29 June 2012
Received in revised form
20 July 2012
Accepted 8 August 2012
Available online 23 October 2012

ABSTRACT

Andersen-Tawil syndrome (ATS), also known as long QT syndrome type 7, is a rare autosomal dominant disease caused by a KCNJ2 mutation. The characteristic triad of ATS is periodic paralysis, dysmorphic features, and ventricular arrhythmia. We describe a case of a woman with Andersen-Tawil syndrome and a history of syncope whose pregnancy was complicated with frequent premature ventricular contractions (PVCs) and nonsustained ventricular tachycardia (NSVT). Her PVCs and NSVT were significantly decreased during the peripartum period, especially during labor. We treated her with beta-blockers throughout her pregnancy, and she experienced no complications. Although the mechanism underlying the decreased PVCs and NSVT in pregnancy has not been elucidated, women with ATS may have less arrhythmic event risk during pregnancy.

1. Introduction

Andersen-Tawil syndrome (ATS) is associated with long QT interval and ventricular arrhythmias (VAs), as well as a distinct potassium-sensitive periodic paralysis and dysmorphic features of low-set ears, micrognathia, and clinodactyly. ATS, also known as long QT syndrome (LQTS) type 7, is an autosomal dominant or sporadic disorder caused by a KCNJ2 mutation [1–3]. The syndrome is mostly benign; however, lethal cases of ventricular tachyarrhythmia have been reported among ATS patients [4,5]. Because ATS is rare and has been diagnosed only recently, there are few reports about pregnancy complicated with ATS. We describe a case of a woman with ATS whose pregnancy was complicated with frequent premature ventricular contractions (PVCs) and nonsustained ventricular tachycardia (NSVT), which were significantly decreased during the peripartum period.

2. Case report

A 26-year-old woman with frequent VA was referred to the National Cerebral and Cardiovascular Center for management of her first pregnancy. Her VA was diagnosed at the age of 4 years. During an athletic meet at the age of 10 years, she experienced a syncopal event, for which she started taking verapamil and atenolol and had no recurrence of syncope since then.

When she first visited our hospital, she was at 13 weeks of gestation. She did not complain of any symptoms, including palpitation, syncope, or weakness. Some minor dysmorphic features such as micrognathia and hand clinodactyly were present. An electrocardiogram showed multifocal polymorphic PVCs (Fig. 1A) and NSVT. QT interval could not be measured because of the frequent PVCs. A 24-hour Holter monitor recording demonstrated multifocal PVCs over 48% of the total heartbeat count and a maximum of 29 continuous events of NSVT (Fig. 1B). The echocardiographic result was normal. With regard to her family medical history, her father was frequently found with asymptomatic PVCs at routine health checkups but underwent no further examination. He also had micrognathia but no periodic paralysis.

We suspected ATS from her physical and physiological examination results and family medical history. A genetic test was performed after obtaining informed consent, and a missense mutation in KCNJ2 (c.899G > T, p.G300V) was identified. We monitored the patient to maintain her potassium level at higher than 4 mmol/L. She continued receiving her medications (120-mg verapamil and 25-mg atenolol daily) throughout her pregnancy. VA was markedly suppressed as her pregnancy progressed (Fig. 2). With maternal beta-blocker use, the fetus grew to an appropriate size according to gestational age. Labor occurred spontaneously at 39 weeks of gestation, and she delivered, under epidural anesthesia, without any complication. The newborn infant weighed 2818 g (within the 10th percentile) and showed

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http://dx.doi.org/10.1016/j.joa.2012.08.002

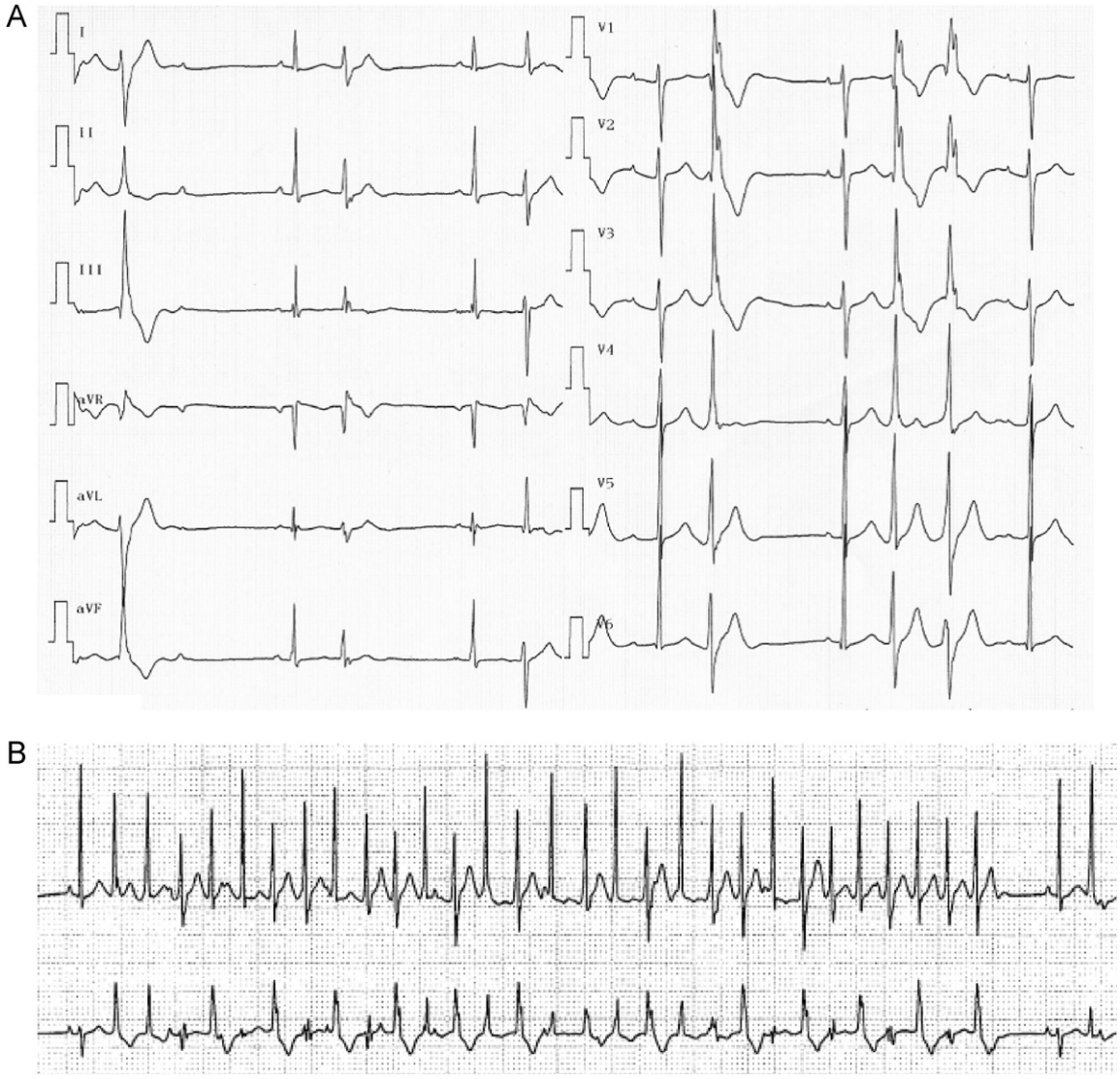


Fig. 1. Electrocardiogram at the first visit (A) and 29 continuous events of nonsustained ventricular tachycardia (13 weeks of gestation) (B).

features of micrognathia and signs of sporadic bigeminy with a QTc of 550 ms. There was scarcely any event of ventricular ectopy during labor (Fig. 3). Her QT and QTc intervals were normal (400 and 496 ms, respectively), and U wave was observed in leads V2–V4. VA gradually increased during the postpartum period, up to the prepregnancy level. However, she had no complications during puerperium.

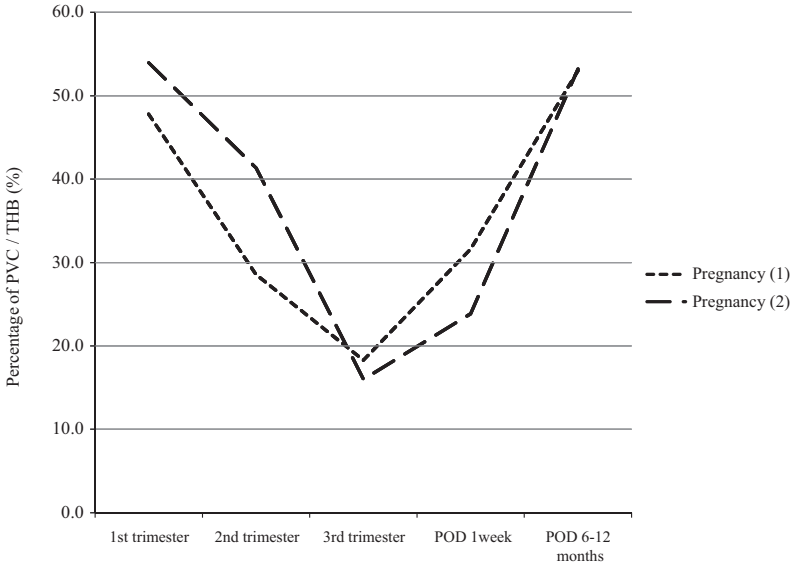
The patient became pregnant again the following year and took only atenolol (25 mg daily) during the pregnancy. VA decreased similarly as in her previous pregnancy, and she also vaginally delivered without any complications at 39 weeks of gestation. The second child had a birth weight of 3056 g (mean birth weight for dates) and QTc of 375 ms. The mother and her children were doing well a year after the second delivery.

3. Discussion

ATS is rare, and there are few reports of pregnant patients with this condition. Subbiah et al. [6] reported a case of pregnancy complicated with ATS in which ventricular ectopy was also decreased during pregnancy. The mechanism underlying the reduction of VA in pregnant patients with ATS remains unclear but may be due to alterations in autonomic balance and significant changes in estrogen and progesterone levels during pregnancy. The same mechanism may explain why patients with LQTS have a reduced risk of cardiac events during pregnancy but an increased risk postpartum, especially patients with LQTS type 2 [7].

Nagase et al. [8] found that epinephrine induced PVC in patients with ATS. However, the epinephrine concentration is maintained at the same level during pregnancy, compared with that in the nonpregnant state, and only elevates markedly during labor [9]. Epidural anesthesia can prevent an increase in epinephrine level during labor but cannot maintain it at a level lower than that in nonpregnant state [10]. Sympathetic nerve activity is increased during pregnancy, with a contrasting decrease in parasympathetic nerve activity [11]. Therefore, catecholamine levels and autonomic nerve activity cannot explain the significantly decreased VA in a patient with ATS.

The production of several sex steroid hormones is increased during pregnancy. Estrogen is generally indicated to prolong QT interval, whereas progesterone and testosterone shorten QT interval. However, Kakusaka et al. [12] found that 17-beta-estradiol (E2) and estrone 3-sulfate (E1) prolong QT interval, whereas estriol (E3) does not. Given that the estrogen hormone E3 is primarily increased during pregnancy, the effects of estrogen on LQTS during pregnancy may be unimportant. Progesterone and testosterone levels are increased



Pregnancy (1) THB (/day)	113,905	113,490	109,851	106,162	136,972
Pregnancy (1) Number of PVC (/day)	54,430	32,407	20,076	33,574	72,628
Pregnancy (1) Number of NSVT (/day)	435	171	36	1.116	3,480
Pregnancy (1) Max NSVT	29	16	15	21	35
Pregnancy (2) THB (/day)	137,813	142,176	136,679	105,314	135,476
Pregnancy (2) Number of PVC (/day)	74,351	58,791	21,894	25,123	72,073
Pregnancy (2) Number of NSVT (/day)	3,098	989	91	27	3,796
Pregnancy (2) Max NSVT	24	32	11	5	24

Fig. 2. Percentage of premature ventricular contraction (PVC)/total heart beat (THB). POD: postdelivery, NSVT: nonsustained ventricular tachycardia, max NSVT: maximum number of continuous events of nonsustained ventricular tachycardia.

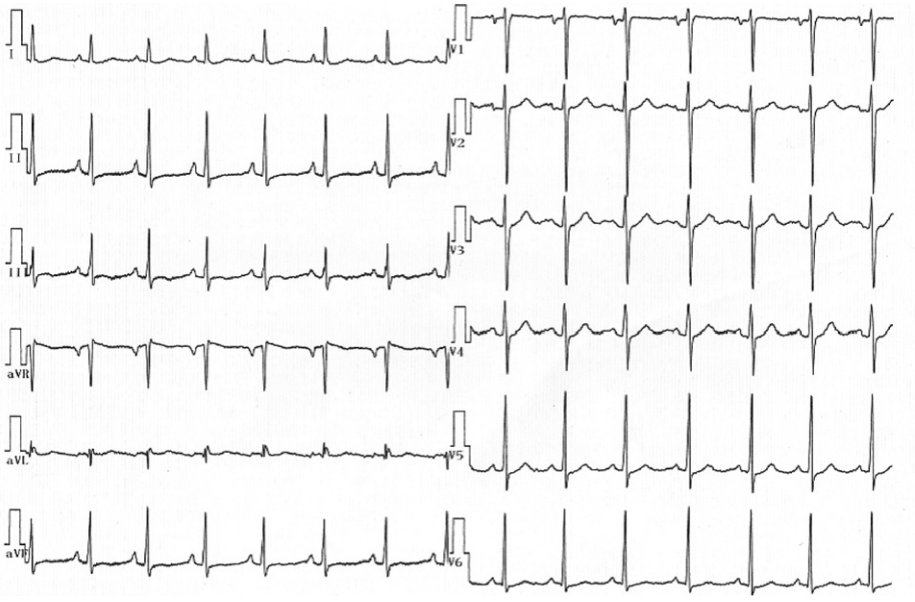


Fig. 3. Electrocardiogram during the second stage of labor.

during pregnancy. The hormones were observed to have protective effects against rhythm disturbances in a congenital LQTS model [13,14] and play an important role in reducing peripartum cardiac events in patients with LQTS, particularly ATS.

Verapamil and flecainide have been reported to be effective in managing ATS cases. However, our patient had a favorable clinical course with beta-blockers after a single syncopal event, suggesting that beta-blockers may also be effective for ATS and other types of LQTS.

Our patient had a C-terminal mutation in KCNJ2 (G300V), which was reported previously. Frequent PVCs, NSVT, and bidirectional VT have been observed also among patients with this mutation [15]. Our patient had a good pregnancy outcome. However, because the clinical characteristics of each genotype of ATS appear to be different to some extent, we need further experience with patients with pregnancy-complicated ATS.

4. Conclusions

In the present case, a woman with ATS and a history of syncope whose pregnancy was complicated with frequent PVCs and NSVT showed a significantly decreased ventricle arrhythmia, especially during labor. She had no complications through her peripartum periods while receiving beta-blockers. Generally, it is well known that arrhythmia worsens during the peripartum period. However, in women with ATS, arrhythmia may be less eventful during pregnancy compared with other types of LQTS. We suggest that beta-blockers may also be effective for ATS.

Financial support

None.

Conflict of interest

All the authors have no conflicts of interest to declare.

Acknowledgments

We thank Dr. Sachie Suga and Dr. Eishu Lin for their clinical assistance.

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