Received: 03 March 2024 | Revised: 28 April 2024 | Accepted: 05 May 2024
DOI: 10.48309/JMPCR.2024.450945.1179
Journal of Medicinal and Pharmaceutical Chemistry Research
SAMI

FULL PAPER

# A challenge in managing fetal congenital total avb with negative anti-ro and anti-la and positive anti nuclear antibody pregnant woman: A case report

**Dahlia Ningrum*** |**Manggala Pasca Wardhana** |**Nareswari Imanadha Cininta Marcianora** | **Aditiawarman Aditiawarman**

*Department of Obstetrics and Gynaecology, Faculty of Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia*

Atrioventricular block (AVB) occurs in approximately one in 15,000 to 20,000 live births. Congenital complete AV block (AVB) may arise from various mechanisms, whether immune-mediated or otherwise. In the context of immune-mediated AV block, a variety of factors contribute to its development, often including the passage of maternal autoantibodies (anti-Ro/SSA and/or anti-La/SSB) across the placenta. Of all AVBs, 40% are predominantly linked to maternal antibodies positive for SSA/Ro or SSB/La. Through placental circulation, these antibodies may cause immune-mediated inflammation or fibrosis in fetal cardiac tissues, which is crucial for conduction. Presented here is a case of complete congenital atrioventricular block in the fetus, characterized by negative maternal Ro/SSA and La/SSB but positive in the Anti Nuclear Antibody test. The baby was delivered by cesarean section at term with Apgar scores of 7 and 8, and a temporary pacemaker was installed at one day old, leading to a favorable outcome.

***Corresponding Author:**
Dahlia Ningrum
Email: dahlianingrum1606@gmail.com
Tel.: +81245838493

**KEYWORDS**

Autoimmune; congenital; fetal AV block.

## Introduction

Characterized by the interruption of electrical impulses from the atria to the ventricles, congenital atrioventricular block (CAVB) presents itself in diverse clinical manifestations. The occurrence of CAVB is estimated to be around one in 15,000-20,000 live births. Complete CAVB can result from processes mediated by the immune system or those unrelated to immune responses. In the case of immune-mediated CAVB, the disease complexity arises due to the trans-placental transmission of maternal autoantibodies. Maternal antibodies, particularly SSA/Ro or SSB/La-positive, are primarily associated with 40% of CAVBs. The antibodies, upon crossing the placental circulation, could trigger inflammation or fibrosis in the fetal cardiac tissue through immune-mediated mechanisms [1-5].

This results in a notable decrease in ventricular rate, potentially leading to fetal cardiac failure, including fetal hydrops. The presence of a complete AV block poses a risk of intrauterine or postnatal demise, and determining the optimal prenatal therapy for affected fetuses remains a subject of debate [2,6]. There are three types of CAVB. First-degree CAVB, found in 3% of cases, is identified by a prolonged AV interval. Second-degree AVB, affecting 10% of cases, exhibits a pattern where some beats are conducted while others are blocked. In third-degree AVB, observed in over 80% of cases, AV conduction is entirely interrupted [7,8]. Maternal autoantibodies to Ro/SSA and La/SSB are often found in cases of CAVB where the heart displays no structural abnormalities [9]. Affected neonates often have mothers diagnosed with systemic lupus erythematosus, Sjögren syndrome, or other rheumatic conditions [10].

*Case Study*

The patient is a 26-year-old female, gravida 2, para 0, abortus 1, at 32 weeks gestational age, with a history of hyperthyroidism controlled with 100 mg/day of PTU for the past two years. She was referred at 31 weeks gestational age with a history of fetal bradycardia, which had been identified since 26 weeks gestational age. Physical examination revealed slight exophthalmos, a mass in the anterior cervical region, obesity (BMI 30.06), and a uterine fundal height of 35 cm with irregular fetal heart rate ranging from 100 to 110 beats/minute. An anatomy ultrasound revealed a single live fetus with an EFW of 1,856 g, an anterior placenta (Grade II-III), and an amniotic fluid index of 35.6 cm. No major or minor structural anomalies were found, and Doppler velocimetry was normal. Fetal echocardiography revealed complete atrium and ventricular FHR dissociation, and she was diagnosed with a third-degree congenital atrioventricular block (CAVB) (Figure 1). Laboratory test results indicated a positive anti-nuclear antibody (ANA) test with negative anti-Ro/SSA and anti-La/SSB, and other ANA profile examinations indicated normal serum electrolytes. Specific thyroid examinations revealed a normal free thyroxine (FT4) level of 1.42 and a low thyroid-stimulating hormone (TSH) level of 0.01, with a positive Thyroid Receptor Antibodies (TRAb) test. The patient was administered Dexamethasone orally twice daily at a dosage of 2.5 mg, along with oral PTU at a dose of 100 mg once daily. The baby, delivered by cesarean section at term, was female, weighing 2,700 g, measuring 50 cm, with Apgar scores of 7 and 8, clear amniotic fluid, and a heart rate of 45 bpm (Figure 2). Umbilical cord TRAb results were negative (1.3 IU/L). A temporary pacemaker was installed one day after birth, resulting in a heart rate of 120 bpm (Figure 3).

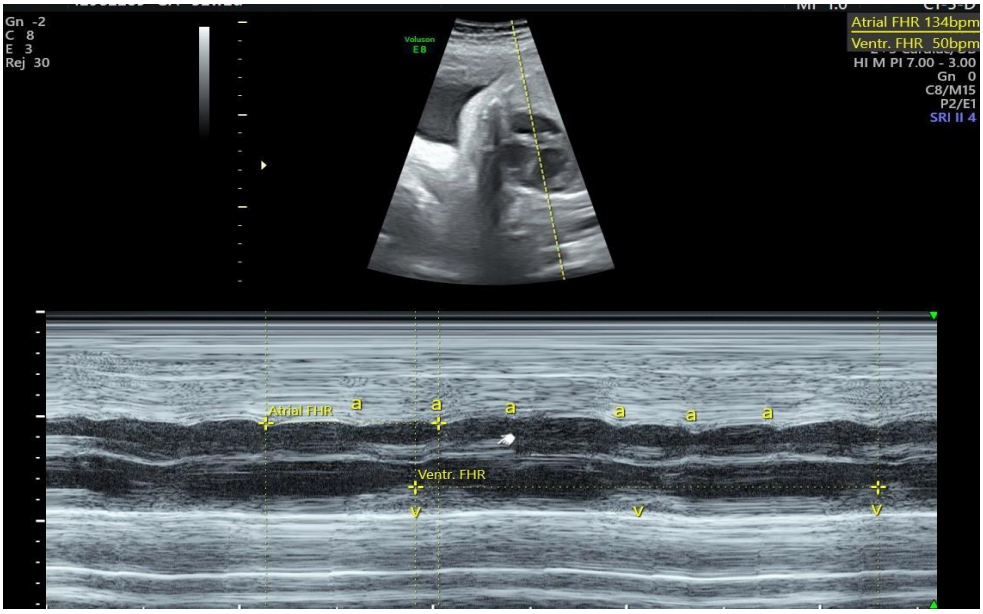


**FIGURE 1** Fetal heart rate with M-mode ultrasound examination at 32 weeks and two days

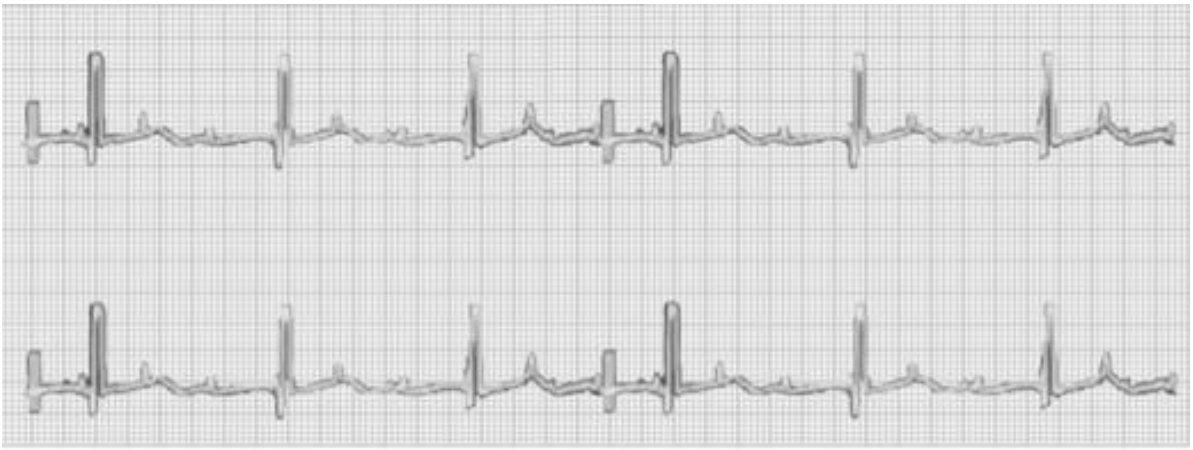

**FIGURE 2** An electrocardiogram before the pacemaker was installed

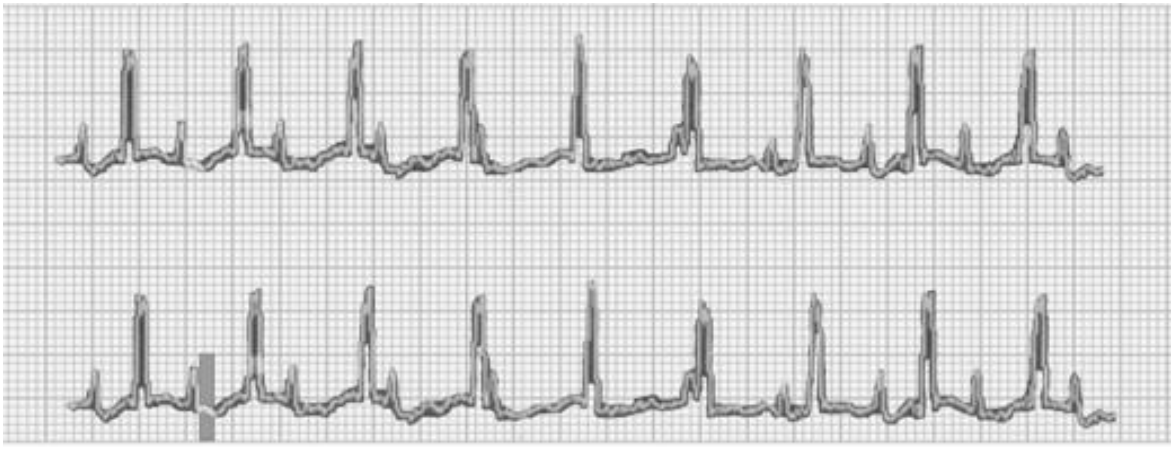

**FIGURE 3** An electrocardiogram after the pacemaker was installed

## Discussion

AVB occurs in approximately one in 20,000 live births. CAVB may result from either non-immune or immune-mediated mechanisms. Diagnosis of CAVB typically involves fetal echocardiography and postnatal electrocardiography [11]. CAVB cases are predominantly driven by autoantibodies,

posing a significant and life-threatening condition. Moreover, third-degree CAVB accounts for over 80% of these cases. The non-immune cause of third-degree CAVB is structural heart disease, such as left atrial appendage isomerism and atrioventricular junction discordance. No structural fetal heart abnormalities were found in this case [2,12-13].

We conducted several immunological tests, revealing a positive ANA test, negative anti-Ro/SSA and anti-La/SSB tests, and other ANA profile examinations [14]. Given the patient's history of hyperthyroidism, a serum TRAb test was performed, yielding a positive result.

In 2002, Julkunen *et al*. conducted a retrospective study of children born in Finnish hospitals between 1950 and 2000 who had been diagnosed with CAVB. There were 67 mothers, but only two were asymptomatic and negative in all autoantibody tests. Five seronegative mothers became positive after being retested by ELISA, immunoblot, and immunofluorescence [15].

In our case, the negative results for SSA and SSB may either truly indicate negativity or potentially turn positive with additional testing, as observed in the study by Julkunen *et al.*, which we did not conduct due to limited facilities.

In the literature, Dexamethasone has been administered in cases of autoimmune-mediated CAVB. In this case, after having multidisciplinary discussions, we decided to administer Dexamethasone as a therapy to the patient with a positive ANA test result despite negative SSA and SSB results. During the weekly evaluation of fetal echocardiography throughout pregnancy, no improvement was observed in the fetal heart rate or rhythm. In 2012, a case study by Hoxha et al. detailed a scenario where complete atrioventricular block (CAVB) was associated with positive anti-Ro/SSA antibodies and concurrent negative anti-La/SSB antibodies, where treatment with Dexamethasone did not lead to any improvement [10]. Similarly, Carrilho *et al.* also reported a similar case in 2020 [1]. Ciardulli *et al.* conducted a systematic review and meta-analysis examining the effects of administering maternal steroids to fetuses diagnosed with second-degree CAVB. The study showed that out of 71 fetuses, the rate of progression to CAVB at birth was 52% in fetuses treated with steroids and 73% in fetuses not receiving steroid treatment [7].

Saito *et al.* conducted a study on 59 fetuses with CAVB. The study compared the effectiveness of Dexamethasone administration at different gestational ages. It was found that administering Dexamethasone at a gestational age of less than 24 weeks led to improvement in 17% of cases. However, no improvement was observed when administering the drug at a higher gestational age. In contrast, certain studies demonstrated no significant enhancement associated with steroid use [16,17].

## Conclusion

Dexamethasone, a fluorinated steroid, can reduce levels of autoantibodies in the mother, yet it does not offer direct shielding to the fetal myocardium and conduction tissue from autoantibody-induced damage [2]. The baby was delivered by cesarean section at term with Apgar scores of 7 and 8 at 1 and 5 minutes, respectively, without any sign of hydrops or cardiac heart failure, and a temporary pacemaker was installed at one day old, leading to a favorable outcome. However, most surviving affected infants require pacing before adulthood [18,19]. Early diagnosis of intrauterine CAVB and good teamwork in pregnancy management and preparation for delivery are essential to prevent morbidity and mortality in cases of CAVB.

## Acknowledgments

I would like to express my gratitude to Manggala Pasca Wardhana, Nareswari Imanadha Cininta Marcianora and

Aditiawarman of the Maternal Fetal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, for their invaluable contributions in preparing this article based on the report "A Challenge in Managing Fetal Congenital Complete AVB with Negative Anti-Ro and Anti-La and Positive Anti-Nuclear Antibody Pregnant Woman: A Case Report."

**Funding**

This study did not receive funding from governmental, commercial, or non-profit sources.

**Authors' Contribution**

Each author contributed to both the preparation and revision of the article, sharing collective responsibility for all aspects of this study.

**Conflict of Interest**

The authors have stated their absence of any conflicts of interest regarding this study.

**Data Availability**

The study incorporates data within the article itself and/or supplementary materials.

**Disclosure**

The authors have confirmed that they have no conflicts of interest related to this study.

**Limitation of The Study**

This is a single case report, and long-term evaluation of infant outcome and effectiveness of management is not presented.

**Ethics**

Ethical approval was not required for this case report. We have obtained written approval from the patient to publish the report while maintaining confidentiality.

***Orcid:***

*Dahlia Ningrum*:*
*https://orcid.org/0009-0007-5883-9959*
*Manggala Pasca Wardhana:*
*https://orcid.org/0000-0001-8013-4639*
*Nareswari Imanadha Cininta Marcianora:*
*https://orcid.org/0000-0003-2599-7786*
*Aditiawarman Aditiawarman:*
*https://orcid.org/0000-0003-0680-5136*

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**How to cite this article:** Dahlia Ningrum, Manggala Pasca Wardhana, Nareswari Imanadha Cininta Marcianora, Aditiawarman, A challenge in managing fetal congenital total avb with negative anti-ro and anti-la and positive anti nuclear antibody pregnant woman: A case report. *Journal of Medicinal and Pharmaceutical Chemistry Research*, 2024, 6(10), 1637-1642. **Link:** https://jmpcr.samipubco.com/article_196002.html