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THE OBSTACLES IN REFERRAL, DIAGNOSIS AND MANAGEMENT OF CONGENITAL ATRIOVENTRICULAR BLOCK (CAVB)

KENDALA DALAM RUJUKAN, DIAGNOSIS DAN TATALAKSANA CONGENITAL ATRIOVENTRICULAR BLOCK (CAVB)

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ABSTRACT

Introduction: Congenital atrioventricular block (CAVB) is a rare disease, found in about 1 in 20,000 births, mostly caused by maternal autoantibodies entering the fetal circulation through the placenta. Methods: Case report: A 34-year-old pregnant woman, gravida 3 parity 2 gestational age 31 weeks was referred to Koja Regional Hospital with fetal bradycardia. Ultrasound examination found a grade III CAVB. On ultrasound, the patient had polyhydramnios with an atrial heart rate of 151 bpm and a ventricular heart rate of 67 bpm, planned to be referred to Harapan Kita Hospital for further management. Physical examination showed signs of tachycardia and Swanneck deformity, and rheumatoid arthritis was suspected. Laboratory examination found subclinical hyperthyroidism with gestational diabetes mellitus. The patient was consulted to the internal medicine department, planned for an autoimmune panel examination, but this was hampered by availability at the hospital and patient funding. This patient failed to be referred and decided to go home at his own request. The patient came to Type C Hospital, had an emergency CS with indications of fetal distress, and the baby died on the second day. This cased showed some obstacles in diagnosis in diagnosis and management of CAVB, such as economy, cultural and educational obstacles of the processes. Conclusion: The referral, diagnosis and management of rare disease, such as CAVB has many obstacles which hinders efforts to implement it.

Keywords: *obstacles; congenital atrioventricular block; referral; diagnosis; management*

ABSTRAK

Latarbelakang: *Congenital atrioventricular block* (CAVB) merupakan kondisi langka, ditemukan pada sekitar 1 dari 20.000 kelahiran, sebagian besar disebabkan oleh autoantibodi maternal yang memasuki sirkulasi fetus melalui plasenta. Metode: Laporan kasus: seorang ibu hamil berusia 34 tahun, gravida 3 paritas 2 usia kehamilan 31 minggu dirujuk ke RSUD Koja dengan bradikardia janin. Pada pemeriksaan USG didapatkan CAVB derajat III. Pada USG, pasien mengalami polihidramnion dengan denyut jantung atrium 151 bpm dan denyut jantung ventrikel 67 bpm, direncanakan akan dirujuk ke RS Harapan Kita

untuk penanganan lebih lanjut. Pemeriksaan fisik menunjukkan tanda-tanda takikardia dan deformitas *Swanneck* pada jari tangan, serta diduga rheumatoid artritis. Pada pemeriksaan laboratorium didapatkan hipertiroidisme subklinis dengan diabetes melitus gestasional. Pasien dikonsultasikan ke bagian penyakit dalam, direncanakan untuk pemeriksaan panel autoimun, namun hal ini terkendala oleh ketersediaan rumah sakit dan pendanaan pasien. Pasien ini tidak dapat dirujuk karena memutuskan untuk pulang atas permintaannya sendiri. Pasien datang ke RS Tipe C, dilakukan tindakan SC dengan indikasi fetal distress dan bayi meninggal pada hari kedua. Kasus ini menunjukkan beberapa kendala dalam diagnosis dan penatalaksanaan CAVB, seperti kendala ekonomi, budaya dan pendidikan dalam proses tersebut. Kesimpulan: Terdapat banyak tantangan dalam tatalaksana pasien hamil, termasuk dalam rujukan, diagnosis dan penatalaksanaan penyakit langka seperti CAVB banyak mengalami kendala yang menghambat upaya pelaksanaannya, sehingga perlu upaya bersama untuk memperbaikinya

Kata kunci : Kendala; *congenital atrioventricular block* (CAVB); rujukan; diagnosis; tatalaksana

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INTRODUCTION

Congenital Atrioventricular Block (CAVB) or Congenital Heart Block (CHB) is stated congenital if diagnosed in utero, at birth, or within the first month of life. Complete CAVB is the most severe type of CAVB. The most common pathophysiological process is to be due to injury of the conduction system because of immune-mediated condition, because of transplacental passage of maternal antibodies, such as anti-SSA/anti-Ro and anti-SSB/La.(Baruteau et al. 2016) The condition is rare, but it can lead to neonatal death (81 cases/100.000 live births) with the lethality was about 64.7%. The survival rate at 28 days of life decreased by about 70% in newborns with all type of congenital heart disease. Cardiogenic shock was the main lethal problem for newborn with congenital heart disease.(Lopes et al. 2018) In this article, we present an example of the importance of knowledge about rare cases like this, because if handled in the right place it can improve mother and baby outcomes.

CASE REPORT

A 34-year-old pregnant woman, gravida 3 parity 2 gestational age 31 weeks was referred to Koja Regional Hospital with fetal bradycardia. Patient does not complain of heartburn, or vaginal discharge, with active fetal movement. The patient denies any complaints off fever, cough, cold, or diarrhea. The patient had dental caries, which were never treated. The urination and defecation are within normal limits. The patient admitted that he had difficulties to adapt in cold situation, and often lost weight even though he had a

good appetite from a young age. The patient admitted that she had joints ache in his fingers and knees from 15 years ago when the patient worked in a textile, and the complaints relapse frequently. The patient denies any complaints of palpitations, difficulty in sleeping, anxiety disorders, visual disturbances, eyeball disorders or menstrual disorders.

Marked physical examination at patients arrival includes tachycardia (heart rate 110 bpm), with swanneck deformity, especially in the right hand which correspond to rheumatoid arthritis suspicion. Laboratory examination found normocytic normochromic anemia due to iron deficiency (Hb 7.1 g/dL, Ferritin 11 ng/mL), subclinical hyperthyroidism (FT4/TSH 15.4/0.1) and gestational diabetes mellitus (two-hour postprandial glucose test : 162 mg/dL). The anemia has been corrected with packed red cells transfusion until the Hb levels above 10 g/dL. Ultrasound examination found a grade III CAVB with atrial heart rate of 151 bpm and a ventricular heart rate of 67 bpm. Ultrasound also revealed a polyhydramnios (AFI 39 cm) without any organ abnormalities. Hand X-ray examination showed there is erosion of the small joints of the hand. The patient was planned to be referred to Harapan Kita Hospital for further management.

The patient was consulted to the internal medicine department, planned for an autoimmune panel examination, but this was hampered by availability at the hospital and patient funding. This patient failed to be referred and decided to go home at his own request. The patient came to Type C Hospital, had an emergency CS with indications of fetal distress, and the baby died on the second day. This cased showed some obstacles in diagnosis in diagnosis and management of CAVB, such as economy, cultural and educational obstacles of the processes. Until now, the patient has not been able to be contacted to carry out follow-up regarding possible autoimmunity problems which might become a health problem for the patient or in future pregnancies.

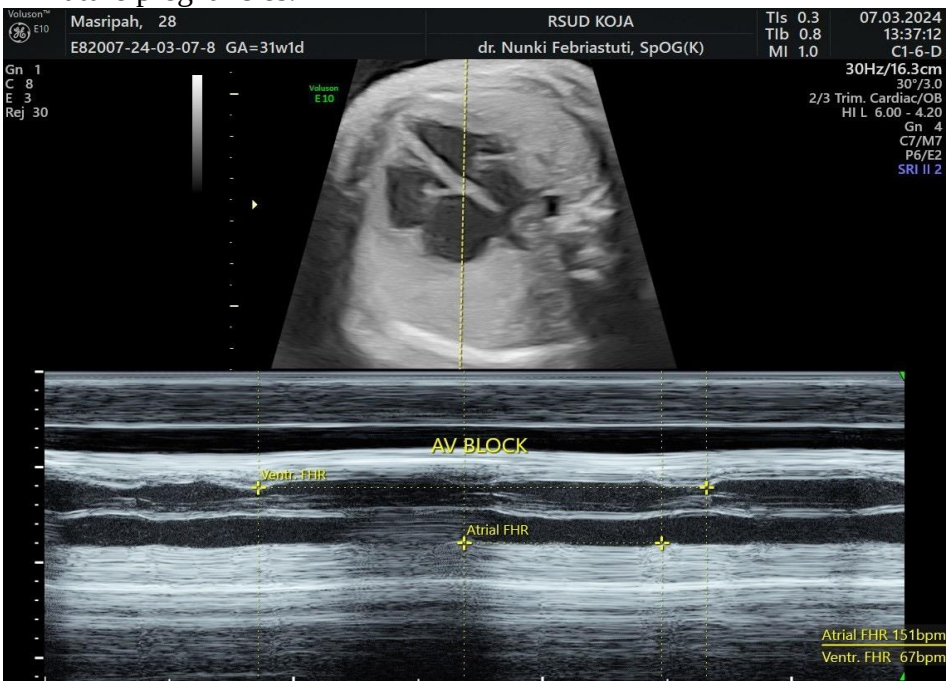

Figure 1. CAVB grade III (atrial HR 151 dpm, ventricular HR 67 dpm)

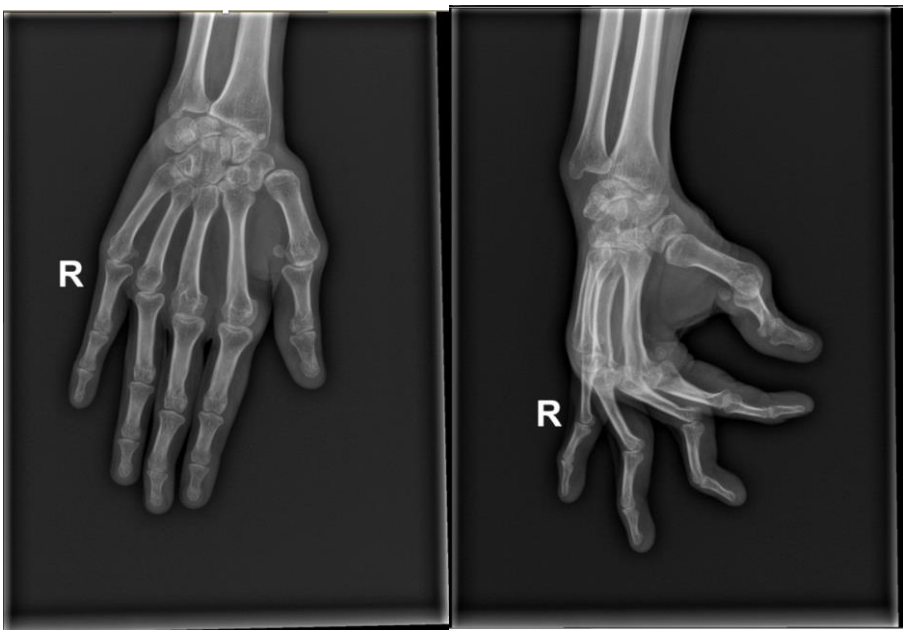

Figure 2. Hand X-Ray showed swanneck deformity and joint erosion with high suspicion of rheumatoid arthritis

DISCUSSION

The prevalence of CAVB was 1 per 15,000 to 20,000 live births. Congenital and childhood AV block may occur not only in structurally abnormal heart but also in a structurally normal heart, or with another concomitant congenital heart disease. The CAVB can occur because of an immune or a non-immune mediated pathologic process. Autoimmune congenital AV block is related to a higher neonatal mortality rate and may develop to dilated cardiomyopathy in up to 30 % case.(Baruteau et al. 2016) The maternal autoantibodies related to CABV was such as anti-Ro/SSA and/or anti-La/SSB, which attached to and damaged the fetal cardiomyocytes and conduction tissue.(Hunter and Simpson 2015).

Immune-mediated AV block is the first type of AV block and leading causes of congenital heart blocks.(Baruteau et al. 2016) About 5 % of fetuses and infants whose mothers has autoimmune disease develop AV block, and the risk to subsequent pregnancies is between 12 and 25 %.(Buyon et al. 2009) In a third of infants with congenital AV block, the mother has an autoimmune disease, such as lupus. However, mostly AV block occurs in fetuses of healthy mothers or mothers with silent anti-Ro/SSA antibodies. (Buyon et al. 2009) CAVB block can be inherited if there is a disease called as progressive cardiac conduction disease (PCCD) in patients less than 50 years old with unexplained progressive heart conduction abnormality but with a structurally normal heart. Inherited PCCD has been linked to genetic variants in the ion channel genes and cardiac connexin proteins genes.(Baruteau et al. 2016) Sometimes, CAVB cannot be explained, mentioned as idiopathic CAVB. It was called idiopathic in the absence of maternal antibodies, structural heart disease, or other overt causes.(Baruteau et al. 2016) The other risk factor for CAVB is metabolic disease such as diabetes mellitus, medication exposures and viral infections. (Pruetz et al. 2019)

Molecular mechanisms of anti-Ro/SSA antibody are not yet fully understood. The maternal anti-Ro/SSA and/or anti-La/SSB autoantibodies can pass the placenta, affecting developing fetal hearth. These autoantibodies directly inhibit calcium channels on fetal

cardiomyocytes. Anti-Ro/SSA antibodies exposure may induce apoptosis and cell death and local inflammation. Finally, fibrosis and calcification can occur, interfering cardiac conduction.(Baruteau et al. 2016, Clancy et al. 2019) The molecular mimicry between the autoantibodies and surface antigen of the calcium channels could cause dysregulation of calcium homeostasis and toxic to cardiomyocytes.(Karnabi et al. 2010)

Mothers with children or fetus with CAVB, the manifestation of SLE had a significantly increased rate of hypothyroidism. Women with hypothyroidism should be tested for anti-Ro antibodies, as they may be at risk to deliver a child with CAVB and being monitored. These association was unclear.(Spence et al. 2006) Maternal hypothyroidism is associated with a wider spectrum of cardiovascular disease other than hypertension in the offspring.(Miao et al. 2021) Thyroid hormone deficiency in utero might predispose adverse cardiovascular development. Thyroid hormones at 14-18 gestational weeks effects important developmental events, including cardiovascular development.(Miao et al. 2021)

Until now there is not much evidence to support that clinical or subclinical hyperthyroidism can cause congenital heart block. Maternal complications include an increased risk of pregnancy loss, gestational hypertension, preeclampsia, placental abruption, and preterm labor.(Franco-Herrera et al. 2023) Thyroid hormones are known to have direct inotropic, chronotropic, and dromotropic effects such as tachycardia and increased cardiac output. Therefore, hyperthyroidism commonly causes tachyarrhythmias such as sinus tachycardia and atrial fibrillation, and bradyarrhythmia occur more commonly in association with hypothyroidism. Complete atrioventricular block can be present in patients with hypothyroidism, which resolves after levothyroxine therapy. In addition, thyrotoxic periodic paralysis rarely causes AV block, which is related with hypokalemia.(Eom and Oh 2020) Maternal subclinical hyperthyroidism may be a coincidence and was unclear. The patients have a gestational diabetes mellitus condition. Diabetic pregnant has an 8-fold higher risk of cardiac malformation compared to non-diabetic pregnant women, such as hypertrophic cardiomyopathy (HCMP), ventricular septal defect (VSD), Tetralogy of Fallot (TOF), truncus arteriosus (TA) etc.(Tabib et al. 2013) These structural cardiac abnormalities are a cause of congenital heart block.(Baruteau et al. 2016).

Main pharmacological management in CAVB is corticosteroids, specially which can cross the placenta, such as dexamethasone or betamethasone. Corticosteroids may reduce immune-mediated damage to the AV conduction tissue and myocardial tissue that leads to myocarditis and cardiomyopathy in CCHB.(Pruetz et al. 2019) Grade III CAVB is irreversible. Thus, pharmacological therapy for CAVB is augmenting cardiac output via beta stimulation of heart rate. Combination of corticosteroids with beta agonist improved 1 year survival and showed that half of beta stimulated fetuses had a small increase in heart rate during treatment.(Pruetz et al. 2019) Plasmapheresis and intravenous gamma globulin (IVIG) aimed to reduce placental transmission, both were safe but expensive, difficult to administer.(Pruetz et al. 2019) Hydroxychloroquine (HCQ) inhibits several TLR pathways suggested to be important in the macrophage induced fibrosis and inflammation in CAVB. A cohort study showed a 70% reduction in CAVB recurrence in pregnant patients with a previous child with CAVB. (Pruetz et al. 2019) The patients in this case report need to be referred to Harapan Kita to seek for potential cardiac pacing treatment when the baby born. A potential therapy for fetal pacing in complete CAVB is self-contained percutaneously

implantable micro pacemaker, with fixed rate at 100–110 bpm. It has recharging capacity allows the pacemaker to be far smaller than other miniaturized pacemakers being developed for adults and large children.(Pruetz et al. 2019)

We present a case that shows the many obstacles encountered when encountering a rare obstetric condition, for example a fetus with congenital AV block. This patient was lucky because he arrived at Koja General Hospital and met a fetomaternal doctor who was able to detect congenital AV block, considering that perhaps many people would have predicted that the fetus in this baby was in a fetal condition that would result in an emergency termination of pregnancy. Because it had been detected, and the Koja General Hospital had not been able to carry out fetal therapy, it was proposed to be referred to Harapan Kita Hospital. The patient had a communication process with the destination hospital until he was informed by the fetomaternal doctor at the destination hospital, however, because the referral procedure was complicated, the patient had been waiting for 2 days for the referral and it had not happened. Finally, the patient wanted to go home at his own request, wanting to go to another hospital closer to home. However, at the hospital because they did not recognize the CAVB condition, the pregnancy was terminated and of course the baby could not be treated for the CAVB condition and ultimately died a few days after birth. It is very unfortunate considering that there are still options for treating the baby.

In the process of managing this patient, it was found that there were various obstacles. The first obstacle arises from the referral system, where the official referral process takes a long time, causing patients who initially wanted to wait to be referred to change their minds. Economic factors are also a barrier because while waiting for an unsuccessful referral process, the patient's husband cannot work. Knowledge factors and level of education also have an influence, where patients and families do not seem to really understand the importance of referral to the destination hospital. Patients who initially wanted to wait finally decided to go home at their own request due to the influence of culture and family. In the end, when the patient went home, he was told to come to the outpatient clinic at Our Hope Hospital, however, due to geographical factors, the patient chose to come to a type D hospital and in the end the patient had the pregnancy terminated and the baby could not be saved.

We tried to point out some processes of the obstacles in this patient as noted : the patient came to the right place, then CAVB is detected by the fetomaternal OBGYN, then referral, diagnosis and treatment were made. The communication to the destination hospital was made, but official referral process takes too long time so patient wants to go home due to various problems. Finally, the patient did not come to the Harapan Kita hospital according fetomaternal OBGYN advice. We present a fishbone analysis to analysis this referral failure in Figure 3.

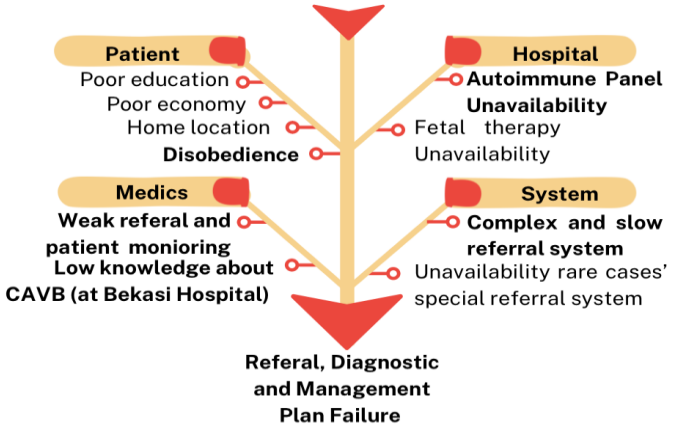

Figure 3. Fishbone Diagram of Referral, Diagnostic and Management Plan Failure

The fishbone diagram above shows that there are several problems in terms of patients, hospital of origin, health workers and the referral system. From the patient's side, there are problems in the form of low education level, low economic condition, poor location and patient non-compliance. On the hospital side, the availability of autoimmune tests and fetal therapy is also very unfortunate. From the perspective of health workers, poor supervision also leads to failure in patient management. Apart from that, the lack of knowledge in hospitals in Bekasi also causes poor management of these patients. Primarily, the referral system also plays a role. A complicated system and too many requirements make the referral process take a very long time. Apart from that, there is no special referral system for rare cases which also has a contribution with the failure. There were some recommendations which we which is abbreviated by the mnemonic 4s: Socialize and build a novel social network for rare fetomaternal case; Specialize referral system for rare fetomaternal case; Simplify existing universal coverage referral system; Spread autoimmune panel laboratory examination facilities and fetal treatment facilities

CONCLUSION

There are challenges in dealing with diseases in pregnancy, especially rare cases. Joint efforts and increased patient awareness are needed to overcome this problem.

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