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Case Report

PERIOPERATIVE MANAGEMENT OF MARFAN SYNDROME IN PREGNANCY AND CONGESTIVE HEART FAILURE

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ABSTRACT

Introduction: A mutation in fibrillin-1 (FBN1) leads to the autosomal dominant condition known as Marfan Syndrome (MFS). The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. Due to a greater frequency of maternal problems and fetal involvement, pregnancy with Marfan syndrome (MFS) provides challenges to healthcare professionals and patients and requires special treatment. **Objective:** This study aimed to analyze the perioperative management of Marfan syndrome in pregnancy and congestive heart failure (CHF). **Case report:** A 27-year-old primigravida with 38-39 weeks gestation presented with a referral letter with a diagnosis of G1P0A0 with scoliosis and peripartum cardiomyopathy. The patient complained of shortness of breath accompanied by cold sweat since the second trimester of gestation. Physical examination revealed the presence of arachnodactyly and spine deformity. The patient underwent an emergency cesarean section with general anesthesia. Breathing problem appeared the next day after cesarean section, the patient was intubated in the ICU. Chest X-ray depicted bilateral pulmonary edema. A mechanical ventilator was set up and fluid restriction had been done. The patient was extubated after showing breathing improvement in the second week in the ICU. The diagnosis of MFS in this patient was defined based on the revised Ghent Nosology. MFS with spine deformity causes breathing problems because of the altered geometry of the thoracic cavity. MFS in pregnancy may worsen the breathing problem due to autotransfusion that leads to pulmonary edema. A mechanical ventilator with a specific setting accompanied by fluid restriction is recommended to reduce the fluid overload in the lungs. **Conclusion:** Mechanical ventilators with specific settings and fluid restriction are effective perioperative management to reduce pulmonary edema on MFS in pregnancy and congestive heart failure.

Keywords: Cardiovascular disease; Marfan Syndrome; Perioperative management; Pregnancy; Preventable death.

ABSTRAK

Pendahuluan: Mutasi pada fibrillin-1 (FBN1) menyebabkan kondisi dominan autosom yang dikenal sebagai Sindrom Marfan (MFS). Kehamilan dengan MFS dapat meningkatkan morbiditas dan mortalitas terkait kehamilan dan persalinan. **Tujuan:** Laporan kasus ini akan menganalisa manajemen perioperatif Marfan Syndrome dengan gravida dan gagal jantung kongestif. **Laporan kasus:** Seorang wanita 27 tahun dengan hamil 38-39 minggu dengan diagnosis G1P0A0 dan skoliosis dan gagal jantung. Pasien mengeluh sesak disertai keringat dingin sejak trimester 2. Pemeriksaan fisik ditemukan araknodaktili dan deformitas tulang belakang. Kemudian dilakukan *section caesarea* segera dengan anestesi total. Sehari pasca operasi, pasien mengeluh sesak dan diputuskan untuk dilakukan intubasi di ICU. Rontgen thorax menunjukkan edema paru bilateral. Dilakukan pengaturan ventilator yang tepat dan restriksi cairan. Pasien di ekstubasi pada minggu kedua di ICU setelah menunjukkan perbaikan pernafasan. Penegakan diagnosis MFS pada pasien ini berdasarkan Nosologi Ghent yang telah direvisi. MFS yang disertai dengan kelainan tulang belakang dapat menimbulkan masalah pernafasan akibat berubahnya bentuk dan lapang rongga dada. MFS pada kehamilan juga memperparah masalah penafasan akibat autotransfusi yang dapat menyebabkan edema paru. Pengaturan ventilator yang disesuaikan dengan derajat keparahan ARDS serta restriksi cairan yang tepat dapat mengurangi penumpukan cairan pada paru. **Kesimpulan:** Pengaturan ventilator yang spesifik dan restriksi cairan yang tepat merupakan manajemen perioperative yang efektif untuk mengatasi edema paru pada MFS dengan gravida dan gagal jantung kongestif.

Keywords: Penyakit Kardiovaskular; Sindroma marfan; Manajemen perioperatif; Kehamilan; Kematian yang dapat dicegah.

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INTRODUCTION

A mutation in fibrillin-1 (FBN1) leads to the autosomal dominant condition known as Marfan Syndrome (MFS). This syndrome has various manifestations including aortic aneurysm that can be followed by ectopia lentis, aortic dissection, and other systemic abnormalities. Cardiovascular abnormalities findings, such as progressive aneurysm of the aortic root are considered the highest mortality risk for Marfan Syndrome (MFS). The progressive aneurysm of the aortic root could lead to aortic dissection and rupture if the corrective surgery was not performed (1). The diagnosis of MFS depends on specific clinical criteria (updated Ghent nosology), although this can be complicated because aspects of the disease change based on the patient's age, while others are seen regularly in the general population, with significant phenotypic diversity. Certain manifestations of MFS also overlap with other connective tissue diseases (2).

Although MFS is an uncommon condition (1:5.000), the prevalence is estimated to be substantially higher among athletes, particularly in sports where height and longer limbs provide them a significant advantage. Voley ball is one of the examples, which is classified as a moderate dynamic and a low static sport (3). However, this does not rule out the possibility that it will occur in pregnant women. Goland described AoD in 29 of 39 cases of pregnancy-related difficulties, including the ascending aorta (19 cases), descending aorta (8 cases), or both (2 cases). Eight of these women had not been diagnosed with MFS before the emergence of aortic issues. (5).

“These patients need anesthesia treatment either for heart surgery or other operations. Patients who are diagnosed with cardiac disease should be referred to a higher center with adequate monitoring facilities and professionals for peripartum and perinatal care. The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. The anesthesiologist has to understand the history of the patient and possible side effects of the surgical procedure, this aims to assess the risks and suitable anesthesia treatment for the patient.” (6). Because of a greater prevalence of maternal problems and fetal involvement in pregnancy with Marfan syndrome (MFS), healthcare professionals and patients face unique obstacles (4). Therefore, in this case report, the authors will conduct an analysis of the perioperative management of Marfan syndrome in pregnancy and congestive heart failure (CHF).

CASE REPORT

A 27-year-old primigravida with 38-39 weeks gestation presented to the emergency obstetrics and gynecology department of Dr. Soedono General Hospital with a referral letter from Dolopo General Hospital. The patient was referred with G1P0A0 with scoliosis and peripartum cardiomyopathy. The patient complained of persistent uterine contraction for the past two days. The patient was referred from the previous hospital due to pulmonary edema and a high risk of cardiovascular disease. The patient complained of shortness of breath accompanied by cold sweat since the second trimester of gestation. Shortness of breath gets worse with activity and doesn't get better with lying down. Previously, the patient had been receiving treatment since she was 11 years old due to her complaint of shortness of breath. It was suspected by the doctor at that time that the patient had a heart condition and scoliosis, so

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she had to take regular medication forever. However, the patient did not take medication regularly. The patient has no history of allergies and surgery.

The patient appeared short of breath and was first seen with a thin and tall stature with a sunken chest. Physical examination revealed the presence of arachnodactyly and spine deformity. The patient's consciousness is *compos mentis*, blood pressure was 128/94 mmHg, and the pulse was increasing to 118 beats per minute. The patient had a temperature of 37,5ºC, oxygen saturation of 98% (in 3 liters per minute of the nasal cannula), and was tachypneic with a respiratory rate of 34 breaths per minute. The obstetric examination resulted in a fundal height of 26 cm and a fetal heart rate of 124 beats per minute. Cervical exam revealed ± 1 cm dilated, 25% effaced, and -1 station. Chest X-ray showed normal lungs and heart radiographic appearance and severe thoracolumbar scoliosis with right convexity.

Complete blood count test showed Hemoglobin 11.2 g/dL, platelets $371x10^3/\mu L$, Hematocrite 43.1%, total leucocytes count $10.53x10^3/\mu L$, erythrocytes count 5.69 thousand/cm, MCV 75.7 fL, MCH 22.5 pg, MCHC 29.7 g/dl. The coagulation test showed PT 8.7 second (Control 11.9) and APTT 26.5 The liver function test showed albumin 2.94 g/dl (N 3.5-5), SGOT 20 U/L (N 8-31), SGPT 18 U/L (N 6-31). The kidney function test showed blood urea 6 mg/dl (N 10-20), and creatinine 0.56 mg/dl (N 0.6-1.1). A random blood glucose test showed 112 mg/dl (N 136-145). The electrolytes blood test showed natrium 132 mmol/L (N 136-145), calium 4.90 mmol/L (N 3.5-5.1), and calcium ION 1.03 mmol/L (N 1.12-1.32). The immunological test showed anti-HIV non-reactive and HbsAg Negative.

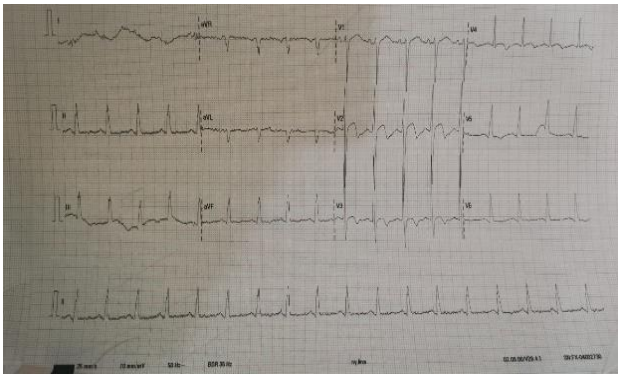

Figure 1. The Electrocardiography Showed Sinus Rhythm and Left Ventricle Hypertrophy

Treatment

The patient was diagnosed with G1P0A0, 38/39 weeks inpartu *latent phase* with scoliosis dan peripartum cardiomyopathy. The patient had planned an emergency cesarean section with general anesthesia. There was no problem during the surgery and the patient was moved to the maternity ward in stable condition. Post SC treatment was Ringer Lactate infusion of 20 drops per minute, Ketorolac injection of 30 mg/8 hours, and Ondancetron injection of 4 mg/8 hours.

Result and Follow-Up

The next day after the C-Section procedure, the patient complained of shortness of breath and then was given 3 liters/minute oxygenation with a nasal cannula. The complaint was getting worse that night, and the anesthesiologist decided to undergo intubation for indications of persistent shortness of breath due to suspicion of pulmonary edema. The patient was then referred to the Intensive Care Unit (ICU) to have a ventilator which was set to BIPAP FiO_2 70%, PEEP 5 cmH_2O, PIns 8 cmH2O, PSupp 8 cmH_2O. Mean Arterial Pressure (MAP) was maintained above 65 mmHg and a fluid deficit of 2000-4000 cc per day. Echocardiography and chest X-ray were planned for the next day. Intravenous drugs were prescribed by the anesthesiologist;

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Aminofluid infusion 500cc/ 24 hours, nutritional milk on nasogastric tube 6x100cc, Cefotaxime injection 1gr/8hr, Pantoprazole injection 40mg/12hr, Paracetamol 500mg/8hr (if needed), Dobutamin on syringe pump 4mcg/hr, Vasoconstrictor on syringe pump 50nn/hr, Furosemide injection 10mg/hr. Cripsa 2,5mg/24hr and Caralan 5mg/12hr were given as oral medications.

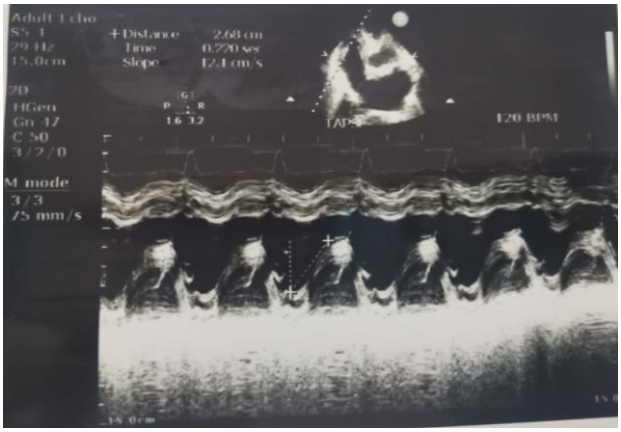

Figure 2. Echocardiography

Echocardiography revealed the systolic function of the Left Ventricle (LV) was normal with an Ejection Fraction (EF) of 56% and the diastolic function of the LV was impaired relaxation. The function of the Right Ventricle (RV) was normal. The result of blood gas examination showed that pH 7.33, PCO2 70 mmHg, PO2 149 mmHg, Bicarbonate (HCO3) 37.6 mmol/L, Excess Base (EB) 9.5 mmol/L, Oxygen Saturation (SO2) 99.0%, and temperature 36,0 ºC

On the sixth day of follow-up in the ICU, the shortness of breath was diminished and the condition showed improvement in breathing. Another anteroposterior chest X-ray was planned for further evaluation and the result showed normal lungs and heart radiographic appearance and severe thoracolumbar scoliosis with right convexity.

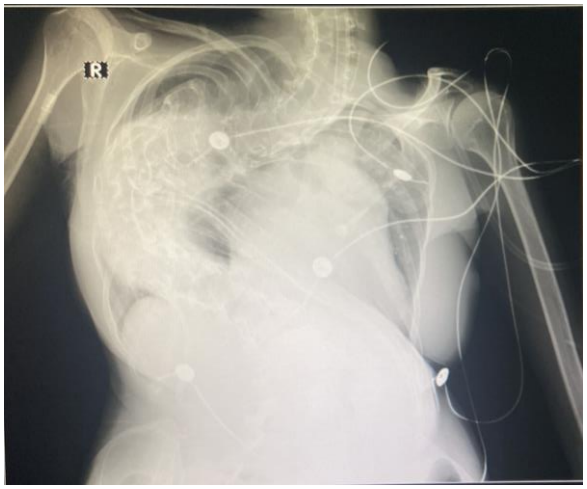

Figure 3. Chest X-ray Depicting Bilateral Pulmonary Edema

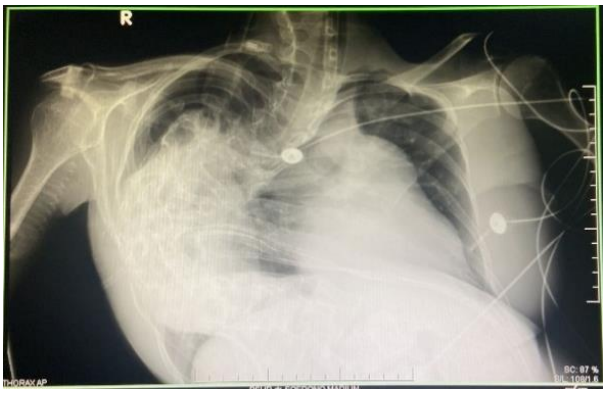

Figure 4. Radiological evaluation Chest X-rays on the sixth day in the ICU

After the evaluation, ventilator weaning was demonstrated gradually and MAP was maintained above 60 mmHg. On day 14 in ICU, the patient's condition showed improvement, and shortness of breath was completely diminished so that the patient could be extubated and moved to the High Care Unit (HCU) for monitoring, then moved to the maternity ward for 5 days before discharge.

DISCUSSION

New diagnostic guidelines for patients with or without a family history of Marfan syndrome have been provided in the 2010 revised Ghent nosology. In the absence of an established family history of Marfan's

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syndrome, the diagnosis might be made using one of the following methods:

1. Regardless of the presence or absence of systemic features, the diagnosis of Marfan syndrome can be made in the presence of aortic root dilatation or dissection and ectopia lentis, unless there are indications for Sphrintzen-Goldberg syndrome (SGS), Loeys-Dietz syndrome (LDS), or vascular Ehlers-Danlos syndrome (vEDS).
2. The presence of aortic root dilatation or dissection and FBN1 mutation) is sufficient to establish the diagnosis even when ectopia lentis is absent.
3. The presence of aortic root dilatation or dissection with no ectopia lentis and FBN1 status is either unknown or negative, the diagnosis of Marfan syndrome is confirmed by the presence of other systemic findings (≥7 points, according to the new scoring system). However, signs suggestive of SGS, LDS, or vEDS should be ruled out and suitable alternative genetic tests (TGFBR 1/2, collagen biochemistry, COL3A1, and other relevant genetic tests when indicated) should be performed.
4. Before diagnosing Marfan syndrome in the presence of ectopia lentis without aortic root dilatation or dissection, an FBN1 mutation previously associated with aortic disease must be identified. If the FBN1 mutation is not linked to cardiovascular illness, the patient should be labeled as having "ectopia lentis syndrome" (7).

In this case, the physical examination of this patient revealed a sunken chest/pectus deformity, arachnodactyly, and spinal deformity as severe thoracolumbar scoliosis. Ectopia lentis as one of the clinical signs of MFS appeared in this patient accompanied by high myopia. The diagnosis of MFS can be established by the following clinical signs according to Ghent Nasology diagnostic criteria with a total systemic score of 10 (8).

The patient has severe thoracolumbar scoliosis. This is one of the musculoskeletal manifestations caused by the abnormalities of the connective tissues as a result of the mutation of FBN1. The musculoskeletal manifestations in MFS include spinal deformities, chest wall deformities, and low back pain. This patient suffered from breathing difficulty because of her severe scoliosis. Scoliosis affects the geometry of the chest and reduces the three-dimensional range of motion of the thoracic cage and spine during breathing. This may result in reduced lung capacities, limited diaphragmatic excursion, and inefficiency of the chest wall muscles (9).

Mechanical ventilation may help to overcome the breathing problem. Another breathing problem in this patient came from bilateral pulmonary edema that was caused by autotransfusion in pregnancy. Approximately ±20-30% of blood volume enters the circulation as the result of uterine contractions (10). There is an increase in cardiac output of 60 to 80% and also an increase in peripheral resistance in the lungs (10). The presence of MFS prompted the occurrence of pulmonary edema. The connective tissues in the lungs become looser and the movement of fluid from intravascular to interstitial becomes faster rather than the condition without MFS (9).

A mechanical ventilator was used in this case to reduce the pulmonary edema and to overcome the breathing problem. The severity of acute respiratory distress syndrome (ARDS) caused by pulmonary edema needs to be considered before setting up the ventilator. According to the severity, ARDS is classified into three based on the following criteria (11):

1. Mild: 200 mm Hg < Pao2/Fio2 ratio ≤ 300 mm Hg with positive end-expiratory

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pressure (PEEP) or continuous positive airway pressure ≥ 5 cm H2O.
2. Moderate: 100 mm Hg < Pao2/Fio2 ratio ≤ 200 mm Hg with PEEP ≥ 5 cm H2O.
3. Severe: Pao2/Fio2 ratio ≤ 100 mm Hg with PEEP ≥ 5 cm H2O

In this case, the patient was classified into moderate ARDS, and the following recommendations for mechanical ventilator-specific settings are:

1. ARDS should be started at lower tidal volumes (6 mL per kg) instead of at traditional volumes (10 to 15 mL per kg),
2. Higher positive end-expiratory pressure values (12 cm H_2O) should be considered for initial mechanical ventilation in patients with ARDS,
3. Prone positioning for 12 to 16 hours per day,
4. Prophylaxis for venous thromboembolism should be given to all patients,
5. Enteral feeding should be initiated if a patient is anticipated to be on a ventilator for 72 hours,
6. Spontaneous breathing trials guided by a ventilator liberation (weaning) protocol should be initiated once a patient with ARDS begins to improve. (11)

Fluid therapy, in addition to the ventilator setting, must be explored in this patient. The goal is to maintain tissue perfusion, integrity, and function while restoring intravascular volume to maximize hemodynamic parameters. (12). It is matched with Malbrain's statement that also recommend the ROSE concept of fluid balance therapy, which shows the relationship between positive fluid balance and overload fluid in critically ill patients (13).

The administration of loop diuretic drugs in this case may reduce fluid overload. The mechanism of action of the drug is by inhibiting the co-transporter Na+/2Cl-/K+ in the thick ascending loop of Henle where one-third of the filtered sodium will be reabsorbed. This process can decrease sodium and chloride reabsorption and increase diuresis (14). Loop diuretic drugs may increase the synthesis of prostaglandins which cause kidney and venous dilation. This effect will indirectly reduce pulmonary wedge pressure. Loop diuretic drugs may also decrease electrolytes such as potassium, magnesium, calcium, and chloride. Furosemide can be given 20-40 mg twice a day with a maximum dose of 600 mg per day (14).

Patients with heart failure should avoid excessive fluid intake, according to European Society of Cardiology (ESC) guidelines. For severe heart failure, a fluid restriction of 1.5–2 liters per day is advised. Fluid restriction has been shown to have a favorable effect. Fluid restrictions of 1000 cc per day with explicit instructions or 2000 cc per day without specific instructions can improve quality of life. Fluid restriction is not always recommended for all patients with heart failure, but this therapy can be considered for patients with poor quality of life, low adherence to medication, and decompensated heart failure with or without hyponatremia. Fluid restriction can be adjusted based on body weight at 30 ml/kg/day (15).

CONCLUSION

Marfan Syndrome is an inherited disorder that affects connective tissue. The condition of pregnancy with MFS may increase morbidity and mortality during pregnancy and delivery. During pregnancy, many changes occur in the cardiovascular system, one of which is autotransfusion. This condition may cause an increase in cardiac output which leads to pulmonary edema and respiratory failure. A mechanical ventilator with specific settings and fluid restriction can be used to reduce the clinical symptoms.

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Conflict of Interest
The writers of this report declare no conflict of interest.

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Authors' Contributors
All authors have contributed to all processes in this research.

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