Pregnancy in a Woman with Uncorrected Tetralogy of Fallot

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ABSTRACT

Tetralogy of Fallot (ToF) is the most common form of cyanotic congenital heart disease after 1 year of age, with overall incidence approaching 10% of all congenital heart disease. Natural survival (i.e. without corrective procedure) into the fourth decade is extremely rare (only about 3%), but there is a tendency of increasing number of women with cyanotic congenital heart disease living 3 to 4 decades and are becoming pregnant. Because of significant physiology adaptation and changes, pregnancy and delivery process are troublesome for mostly unhealthy women, including those with uncorrected ToF. For ToF patients, it remains an important cause of maternal morbidity (62,5%), and even mortality (10%) and has significant effects on fetal outcome.

Discussed below a case of pregnancy in a 28 year old woman with uncorrected ToF, was diagnosed to have pneumonia, ToF-class III-IV of New York Heart Association, secondary polycythemia caused by hypoxia, and uncompensated metabolic acidosis on 25th week pregnancy. Through delicate medical care, patient's condition improvement can be seen . Patient decided to continue the pregnancy. Without optimal either obstetrical or medical management, prognosis of pregnancy in patient with uncorrected ToF is poor.

Key words: *pregnancy, uncorrected tetralogy of fallot.*

INTRODUCTION

Tetralogy of fallot (ToF) is the most common form of cyanotic congenital heart disease after 1 year of age, with overall incidence approaching 10% of all congenital heart disease. The defects which can be found in patient with ToF are caused by a single developmental defect: an abnormal anterior and cephalad displacement of the infundibular (outflow tract) portion of the interventricular septum. Four anomalies arising from this defect are (1) pulmonary stenosis, (2) right ventricular hypertrophy, (3) overriding aorta, (4) nonrestrictive ventricular septum defect.[1-3]

To reach adulthood, most patients with ToF will need surgery, either palliative or reparative. However, few patients will present as adults without correction of ToF. Natural survival into the fourth decade is extremely rare (only about 3%), but there is a tendency of increasing number of women with cyanotic congenital heart disease living 3 to 4 decades and are becoming pregnant.[4,5]

Entering the pregnancy, parturition, and finally post parturition phase, healthy women will face multiple physiology changes covering all of body system, including cardiovascular changes. There are at least 7 changes during pregnancy related to cardiovascular physiology, i.e. heart position and size, blood volume, blood pressure and systemic vascular resistance, stroke volume, cardiac output, heart murmur, and blood flow.[4,6-10]

During parturition, secondary to patient's anxiety, pain and uterine contraction, oxygen consumption increases threefold; and cardiac output rises progressively owing to increase in both stroke volume and heart rate. These changes are positional related, known as supine hypotensive syndrome of pregnancy.[1,9] Post parturition, changes of cardiovascular physiology are mainly targeted to reach pre pregnancy condition,

through autotransfusion and hemoconcentration phase.[4,6,7]

All of the processes described above are troublesome for mostly unhealthy women, including those with uncorrected ToF. As a result of the fall in peripheral vascular resistance that occurs during a normal pregnancy, there may be an increase in right to left shunt, with subsequent increase in the cyanosis. Parturation is particularly hazardous time since the blood loss associated with the process may induce hypotension and eventually the right to left shunt. Thus, ToF patient may notice a deterioration during pregnancy and parturation.[11] These remain an important cause of maternal morbidity (62,5%), and even mortality (10%) and has significant effects on fetal outcome.[12] Therefore, knowledge about maternal cardiovascular physiology changes and their consequences must be known as the basic of obstetrics and medical treatment plans.

Reported below is a case of 28 year old pregnant woman with uncorrected ToF, coming with difficulty of breathing as the chief complaint. Through delicate medical care, patient's condition improvement can be seen.

CASE ILLUSTRATION

A 28 year old woman was reffered to Emergency Room with chief complaint of worsening difficulty of breathing since 2 days before admission. Patient was at sixth month of pregnancy, had a routine control by midwife since the first time the pregnancy had been known. Since the third month of pregnancy, patient had felt dyspnea on effort and seen bluish fingers and toes. These conditions improved at rest, worsened by activities. There was no orthopnea, nocturnal paroxysmal dyspnea, cough, wheezing sound during breathing, and edema. Since 2 days before admission, these conditions worsened. Dyspnea was felt constantly, independent of activities. In addition, patient had fever, cough with yellowish mucoid sputum, apparently bluish fingers and toes. Administration of mucolytic cough syrup, oral antipyretic, and antibiotics failed to improve patient's condition. Patient then was reffered to Emergency Room.

Since childhood, patient has often felt fatigue and dyspnea even during simple activities. Patient sometimes needed to squat to improve those complaints. Patient often got upper respiratory tract infections, improved with over the counter drugs. Patient was never brought to see medical help. Patient's parents assumed it was asthma.

Two years before, at the first pregnancy, conditions as described above, had been felt on seventh month pregnancy. After chest X-ray had been taken, patient was diagnosed to have congenital heart disease by an obstetrician in Solo (specific diagnosis unknown). Patient delivered a non breathing infant prematurely (on eight month pregnancy). Resuscitation was given, but failed to give improvement on infant's condition. After parturition, patient's condition improved. Since then, patient has never checked her condition to any doctor nor used contraception.

On ER, the patient was fully conscious, body weight 48 kg (pre pregnancy body weight unknown), blood pressure 120/80 mmHg, pulse rate 96x/minute, regular, respiratory rate 32x/minute, regular, symmetric, and body temperature 37,8 ^{o}C. Patient's lips, distal fingers and toes were cyanotic, clubbing fingers and toes were seen. Physical examination of chest revealed augmentation of right and left fremitus, dull sound on percussion. Vesicular sound and rales on were heard on both sides of the lungs. Normal heart sound, without gallop and murmur, was heard on auscultation of the heart. Obstetric examination revealed uterine fundal height was 24 cm, fetal heart sound was 128 beats/minute, inspection, inspeculo and vaginal touché were within normal limit.

On admission, laboratory examination demonstrated her hemoglobin 25,5 g/dL, haematocrite 82%, WBC 17.400/ìl, platelet count 90.000/ìl. Arterial gas analysis showed pH: 7,307, pCO_2: 25,9 mmHg, pO_2: 38,6 mmHg, saturation of O_2: 65,8%, HCO_3^-: 12,6 mEq/l; appropriate with uncompensated metabolic acidosis. Blood chemistry, urine analysis, and electrolyte test were within normal limit.

Chest X-ray showed cardiomegaly (enlargement of right ventricle), infiltrate on both lungs are appropriate with pneumonia, and coin lesion on left parahiler. (Figure 1)

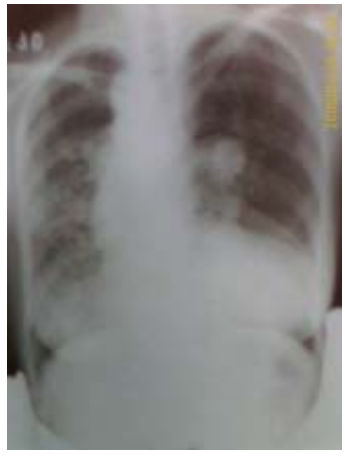

Figure 1. Patient's chest X ray on admission

Electrocardiogram showed sinus rhytm, QRS rate 85 x/minute, normal QRS axis, normal p wave, PR interval 0,2" , QRS duration 0,06" , incomplete right bundle branch block. Echocardiogram showed normal position, balance four chamber, hypertrophy of interventricular septum and right ventricle, large VSD, R to L shunt, overriding aorta ± 50%, minimal aorta regurgitation, small MPA, minimal flow. Good PA size (20 mm). Left aortic arch, no coarctation of the aorta, no collateral from descendent aorta. Ejection fraction 81%. This result accord with Tetralogy of Fallot.

Based on all the data above, the patient was diagnosed to have pneumonia, ToF-class III-IV of New York Heart Association (NYHA), secondary polycythemia caused by hypoxia, and uncompensated metabolic acidosis on 25th week pregnancy. Observation of patient's vital sign, saturation of O_2, diuresis, and fetal heart rate were done regularly. Sputum was planned to be taken for microorganism culture and resistance test. Total bed rest in Intensive Care Unit/ High Care Unit was planned for this patient. The management of this patient was with injection of ceftriaxone 2x1 gram, oral administration of azithromycin 1x500 mg, paracetamol 4x500 mg, ambroxol 3x1 teaspoon, fluid and calorie intake 2.000 cc and 1.600 kcal respectively. Phlebotomy 300 cc/ day for each two days was planned, with previous administration of 5.000 U heparin. Phlebotomy was done with hematocrit target 48-52%. Education about patient's and fetus' condition, risks and benefits between pregnancy continuation and termination, next pregnancy protection by contraception usage were given to patient and her spouse.

Unfortunately, there was no place in ICU and HCU. Patient and family agreed to get medical care in ER and continue the pregnancy with agreement of emergency caesarian section if patient's condition was worse. Twelve hours after admission, there was improvement of patient conditions, reduction of dyspnea, respiratory rate 24 x/minute (with 4L/minute O_2), body temperature 37,5 ^oC. Arterial gas analysis showed pH: 7,38, pCO_2: 27,4 mmHg, pO_2: 46,0 mmHg, saturation of O_2: 81,4%, HCO_3^-: 16,3 mEq/l; being appropriate with compensated metabolic acidosis. On the first and second day, significant improvements were observed. On the third day, patient felt well, with minimal dyspnea, respiratory rate 24 x/minute (with 4L/minute O_2), body temperature 36,7 ^oC, minimal rales on both lungs, and cyanosis on lips and extremities. Patient forced to be discharged and planned to get medical care in Solo. Take home medications given were azithromycin 1x500 mg, paracetamol 4x500 mg, and ambroxol 3x1 teaspoon. Patient was then highly recommended to get continuous medical care.

DISCUSSION

A 28 year old pregnant woman came with difficulty of breathing as chief complaint. First thing that must be determined regarding this complaint is whether this is a physiological or pathological complaint. Dyspnea in a pregnant woman physiologically could have happened as the result of (1) uterus enlargement that pushes diaphragm upward, narrowing thorax space, restricting pulmonary expansion during inspiration, then finally causes hyperventilation, tachypnea as compensation; and (2) hormonal changes, especially increment of progesterone level, causing loosening of respiratory tract muscle and hyperventilation.[13] However, dyspnea which is severe enough to limit activity is not normal during pregnancy and should lead to further evaluation.[5]

In this patient, dyspnea was felt severe enough to limit activity, with cyanosis on lips and extremities. These conditions show that there was an abnormal condition that needed further evaluation. This pathological condition could be caused by abnormalities in pulmonary-respiration system (e.g. pneumonia, asthma, COPD), cardiovascular system (e.g. congestive heart failure, cardiac valve abnormality, congenital heart disease), kidney-metabolic disturbance (e.g. metabolic acidosis), hematology disturbance, etc. Should also be considered abnormality that is exclusively present on pregnancy, e.g. massive uterus enlargement which can be found in polyhydramnion and lung edema to be found in severe preeclampsia that is usually present on late second or third trimester of pregnancy.

Based on clinical presentation, laboratory findings, and chest X-ray result, the patient could be diagnosed as pneumonia since it meets American Thoracic Society 2001 criteria for pneumonia diagnosis.[14] One interesting question is about the safety of X-ray test for pregnant woman. Many literatures recommend avoiding this test whenever possible, although this test is actually save enough to be performed especially if specific protection to mother's abdomen is given. Otake, et al, showed that radiation dose which is given to patient when chest X-ray test is performed, is only 0,02-0,07 mrad. Dose which is needed to be given to bring mental retardation for 16-25 week old fetal is approximately 60-150 rad. It means that the dose which is given is 3 billion times smaller than the detrimental dose.[15] In conclusion, X-ray test in this case is out of harm's way.

Apart from pneumonia, patient's chest X-ray also shows enlargement of right ventricle. If this finding is connected with patients clinical presentation (cyanotic lips and extremities, history of congenital heart disease diagnosis, squatting to improve complaint [dyspnea and

fatigue], recurrent upper respiratory tract infections), ToF anomaly can be suspected.[1,2] Echocardiography confirmation and electrocardiography test then confirm the diagnosis. [1,2,16]

Metabolic disturbance can't also be excluded although there was neither history of vomiting nor diabetes mellitus that possibly complicated with ketoacidosis. Metabolic disturbance can be present as the complication of pneumonia and cyanotic congenital heart disease. Arterial gas analysis confirms the diagnosis.

Now, let's discuss the relationship between all conditions which are described above, their impact on maternal and fetal conditions, monitoring and treatment needed to be taken to improve patient's condition. Figure 2 schematically describes correlation of patient's clinical presentations. The proper understanding of maternal physiology changes during pregnancy is needed for further discussion.

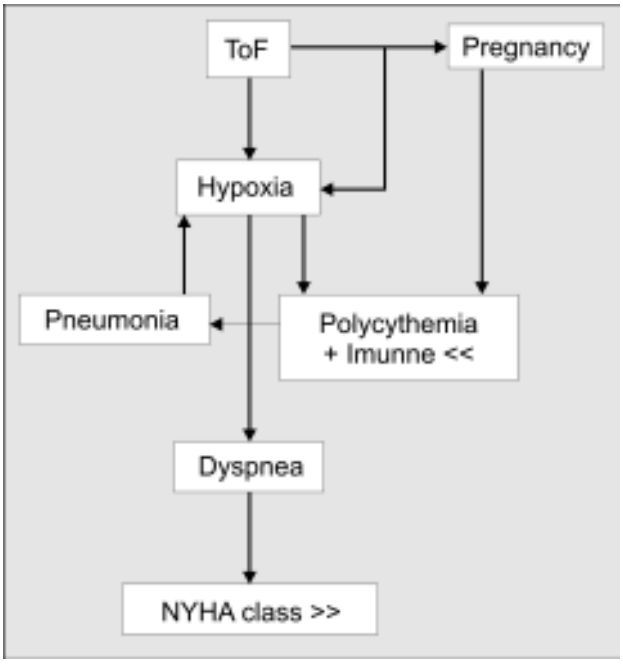

Figure 2. Correlation of patient's clinical presentations

From many changes during pregnancy, cardiovascular changes that most closely worsen condition of pregnant woman's with uncorrected ToF is reduction of peripheral vascular resistance. Reduction of peripheral vascular resistance causes expansion of right to left shunt blood flow, finally causes expansion of aorta blood flow. Inversely, there is reduction of pulmonary blood flow. End result of this condition is reduction of arterial O_2 pressure and its saturation. Patient falls into deeper hypoxia than previously occured in non pregnant condition.[3,4,17]

Chronic hypoxia that usually present is triggering factor for secondary polycythemia. This is a physiology mechanism for compensating the low tissue O_2 distribution.[16] The effect of chronic polycythemia (excessive erythropoiesis) is depression of thrombopoiesis in bone marrow, causing low platelet count.[18] The low platelet count that worsens is equivalent to the worsening of hypoxia throughout pregnancy.

Both hypoxia and polycythemia are risk factor for upper respiratory tract infection (URTI). As both of the conditions worsen, the URTI develops into pneumonia. In addition, pregnant woman is vulnerable for infection because of physiologically decreasing of either specific or non specific immune response.[6]

Pneumonia then acts as a vicious circle with hypoxia. Pneumonia reduces lung-blood O_2 diffusion, worsening hypoxia. Hypoxia sensitizes chemoreceptor, bringing dyspnea sensation. Patient unable to do any activity even the simple one is appropriate with class III-IV of New York Heart Association (NYHA). All this phenomena are felt appropriate with the reduction of peripheral vascular resistance on the end of second trimester of pregnancy as we can see from this patient.[7]

This is a threatening condition for both mother and fetus. Maternal mortality rate reaches 10% and is classified as moderate risk for pregnancy with heart disease [2A] with mortality rate reaches 5-15% according to FIGO category 1992.[16] For fetus, there is increment of death risk (45-50% for all cyanotic congenital heart disease[4,12]) and premature delivery (30-50% for all cyanotic congenital heart disease[10]). Neill and Swanson (1961) and Presbitero, et.al. (1994), revealed that with increasing maternal hypoxia, as reflected by mother's hemoglobin and maternal oxygen saturation, the percentage of live-born infants fell and when hypoxemia is intense enough to stimulate a rise in haematocrite above 65%, pregnancy wastage is virtually 100 percent.[11,17] If the fetus is born, fetus will show delayed intrauterine growth and development as a result of intrauterine hypoxemia. Incidence of cardiac defects reported in born infant ranges between 3 and 17%.[9] Therefore, comprehensive management is needed to overcome this problem.

The basic problems found in this patient are pregnancy and ToF. Therefore, management has to be focused on both basic problems, besides solving pneumonia and polycythemia. Pneumonia is managed by administration of double antibiotics (i.e. a β-lactam and a macrolide), appropriate with the recommendation of Infectious Diseases Society of America/American Thoracic Society Consensus 2007 for pneumonia

treatment in patient with comorbidities such as chronic heart disease (strong recommendation; level I evidence).[19] In case of pregnant woman, the safety of antibiotic usage both for mother and fetus must be considered. Both ceftriaxone and azythromycin are classified into "B" category of pregnancy safety US FDA. Polycythemia is managed by tapping process, i.e. phlebotomy 250-500 cc/ day using blood donor collection set for each two days until haematocrite target ≤ 42% (for woman) is reached.[20]

For management of ToF, there is no literature which recommends repairing process of cardiac anomalies during pregnancy. Therefore, the only way to overcome this problem is by managing the pregnancy. European Society of Cardiology (ESC) and some literatures state that pregnant woman with class III-IV of NYHA is highly recommended for pregnancy termination as soon as possible. Pregnancy can proceed with total bed rest and supportive care, and is classified as high risk pregnancy.[8,13,17] This patient in fact chooses the second choice, so the next things to be discussed are items which are needed to be monitored during pregnancy, labor-delivery and post parturition.

During pregnancy, in maternal side, the additional observations which are needed to be done besides routine obstetrics observation is blood gas analysis (especially PO_2 and saturation of O_2). In fetal side, two items which are needed to be monitored are fetal growth and well-being. These can be done by regular uterine fundal height measurement, fetal USG, Doppler velocimetry, cardiotocography, and fetal heart-placenta dynamic function observation.[21-23]

Many literatures prefer vaginal birth to caesarian section for delivery mode in woman with ToF. Caesarian section is indicated only for obstetrical indications.[4,24-27] The reasons are bleeding amount that theoretically will be lesser if vaginal birth mode is chosen (400-500 cc, compared with 800-1.000 cc) and usage of anesthetic drugs that possibly will cause hypotension. If caesarian section is indicated, general anesthesia is chosen to avoid hypotensive effect of regionally administration of anesthetic drugs. Administration of massive loading fluid before procedure is recommended to avoid hypotensive effect that possibly happens. [22,24,26,27]

In first phase of delivery, it is recommended to avoid the usage of uterotonic agents, although some writers suggest the usage of low dose epidural analgesia for reducing oxygen consumption. Patient is recommended to take left lateral decubitus position to prevent supine hypotensive syndrome of pregnancy.[22] Oxygen is preferably given and every 15 minute observation is recommended.[25] In second phase of delivery, forceps usage is recommended. In this phase, delivery is recommended to be assisted by a cardiologist. In third phase of delivery, it is recommended to limit the bleeding amount. Patient, especially with class III-IV of NYHA, is not recommended to give breastfeeding, considering the hypotensive effect of oxytocin which is produced during breastfeeding process.[25] Another problem to be considered is infective endocarditis risk during delivery process. American Heart Association (2005) categorizes delivery process in women with uncorrected ToF as high-relative risk procedure that potentially causes infective endocarditis. Therefore, patient should be given prophylactic antibiotic, i.e. 2 gram ampicillin given intravenously and 1,5 mg/kg body weight gentamicin 30 minutes before the procedure plus 1 gram ampicillin 6 hours after the procedure.[28]

The born infant has an apnea risk as a result of intrauterine asphyxia, therefore despite routine observation (every 15 minutes for first active phase of delivery and every 5 minutes for second phase of delivery based on American College of Obstetricians and Gynecologist 1995), it is recommended that doctor, who assists the delivery process, has optimal neonatal resuscitation ability.[23]

Education about reparative procedure after this pregnancy is needed to be given, instead of contraception method to prevent another pregnancy before reparative process is done. Each patient then should be assessed before conception with careful history taking to determine functional status, exercise capacity, and the presence or absence of other lesions.[11] Finally, it can be said that without optimal or obstetrical or medical management, prognosis of pregnancy in patient with uncorrected ToF is poor.

CONCLUSION

A case of pregnancy in patient with uncorrected ToF has been discussed above. The patient was diagnosed to have pneumonia, ToF-class III-IV of NYHA, secondary polycythemia caused by hypoxia, and uncompensated metabolic acidosis on 25th week pregnancy. The management of this patient was with total bed rest, injection of ceftriaxone, oral administration of azythromycin, paracetamol, ambroxol, phlebotomy 300 cc/ day for each two days, with previous administration of heparin. Significant improvements were observed. The patient decided to continue the pregnancy. Without optimal either obstetrical or medical management, prognosis of pregnancy in patient with uncorrected ToF is poor.

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