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Case Report
Fatality Cases Congenital Anomaly in Trisomy-Isochromosome: A Case Report

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Abstract

Severe congenital anomaly was a problem in the field of fetal medicine and there was always controversy in the subsequent management. Some countries have standard rules regarding the management of congenital abnormalities but in Indonesia when congenital abnormalities are found to be often controversial to determine the termination of pregnancy. Termination of pregnancy survival fetus was often a dilemma but in some cases with an intrauterine fetal death prognosis or lethal soon after birth. Currently in Indonesia a justifiable reason for terminate of pregnancy only case of life threatening or emergency in the mother or fetus. Clinicians may only be able to give advice and consideration to the couple from a medical standpoint but the social and religious sociocultural factors in some nations or adherents of the faith in the world have views that are not in line with their beliefs about the termination of a living fetus. In this article 3 cases were explained with a poor prognosis of intrauterine death or shortly after delivery, i.e., cases of edward syndrome, isochromosome 18 and tumors on the face covering the mouth and nose.

Key words: Congenital anomaly, termination, fetus, poor prognosis, edward syndrome, isochromosome 18

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Congenital anomalies are important causes of infant and childhood deaths, chronic illness and disability. Management of pregnancy complicated by fetal abnormalities poses challenges for obstetricians and pediatricians. Problem to decide terminate pregnancy was a matter of professional debate, political policy, public policy and religion. Some opinions expect that prenatal diagnosis can prevent late pregnancy cessation. Currently in Indonesia a justifiable reason for terminate of pregnancy only case of life threatening or emergency in the mother or fetus[1]. A case could be lethal also if the institution no have any facilities that can correct or cure anomaly. The primary issue involves the complexity surrounding the decision-making process regarding the treatment strategy immediately following birth in newborns diagnosed with trisomy 18.

Clinicians have long recognized that infants born with serious congenital anomalies i.e., more frequently than in fantsborn without anomalies. Several anomalies could be lethal that can be detected during pregnancy[2-4] include as follows:

- Nerve tubes anomaly (anencephaly, encephalocele, holoprosencephaly, myelomeningocele)
- Kidney agenesis
- Organs develop outside the body cavity (gastroschisis, ectopia cordis)
- Caudal Regression Syndrome (coccygeal teratoma)
- Dysplasia skeletal (thanatophoric dysplasia with very narrow chest cavity)
- Severe cardiac abnormalities
- Chromosomal abnormalities (trisomy 13, trisomy 18, trisomy 21)
- Fetal tumors

It is well known that trisomy 18 pregnancies have a high risk of fetal loss and stillbirth. The life prognosis of trisomy 18 was controversial as the outcome is usually lethal. Patients with long-term survival of trisomy 18 exhibited severe psychomotor developmental delay. Cytogenetic investigation was an essential step towards the accurate diagnosis of individuals with clinical suspicion of a genetic anomaly. Also, this type of investigation could offer critical information to the practitioner for prognosis of patient and the correct appreciation of the recurrence risk of a certain genetic condition.

CASE PRESENTATION

The incidence of congenital aberration year of 2017 in Dr. Hasan Sadikin general hospital bandung Indonesia was 357: 100,000 deliveries, in this article submitted 3 cases that threaten intrauterine death or shortly after birth.

Case 1: Edwards syndrome: A case report with multiple prenatal abnormalities obtained associated with Edwards syndrome. G5P3A1, 43 years old, feeling 8 months pregnant came with a shortness of breath, carrying a referral letter from a network hospital with polyhydramnios description. History of labor 3 times spontaneously without congenital abnormalities, normal weight, smallest child age was currently 8 years. There was a history of curettage for indications of abortion, no tissue examination.

Regular menstrual cycle 28-30 days, no pain and ordinary amount. History of diabetes mellitus, hypertension, tuberculosis or previous fevers, use drugs or herbs were denied. history of congenital abnormalities in a partner's family was denied. There was a history of taking folic acid for 1 month during a young pregnancy.

Ultrasound examination obtained a single pregnancy biometry according to gestational age 30-31 weeks, singleton, with multiple abnormalities e.g., hypoplasia of nasal bone, micrognathia, omphalocele, single umbilical artery, clenched hand and polyhydramnios. Evaluation based on clinical symptoms show a poor prognosis.

After counseling and preparation, performed amnioreduction of polyhydramnios indication. Amniotic fluid successfully removed as much as 1500 cc. The liquid was sent to the Advanced Biomedical Laboratory of Faculty of Medicine Padjadjaran showed trisomy 18 (Fig. 1). The parents requests for termination of the pregnancy but was not approved by clinical meeting staff. Patient was discharged 1 day later and asked to control 1 week later.

Patient came back 2 weeks after the amnioreduction action, with the complaint not feeling child's movement since 1 day before entering the hospital. An ultrasound confirmed Intrauterine fetal death. Pregnancy was terminated by oxytocin induction. Born baby with no signs of life weighing 1350 g, body length 38 cm, male, with grade 3 maceration and appearance of low set ear, micrognathia, omphalocele, clenched hand and rocker bottom feet (Fig. 1).

Case 2: Isochromosome 18: A 36-year-old woman, G2P1A0 was referred to Hasan Sadikin Hospital with a G2P1A0 gravid 28-29 weeks, AVSD and Spina Bifida Occulta. History of

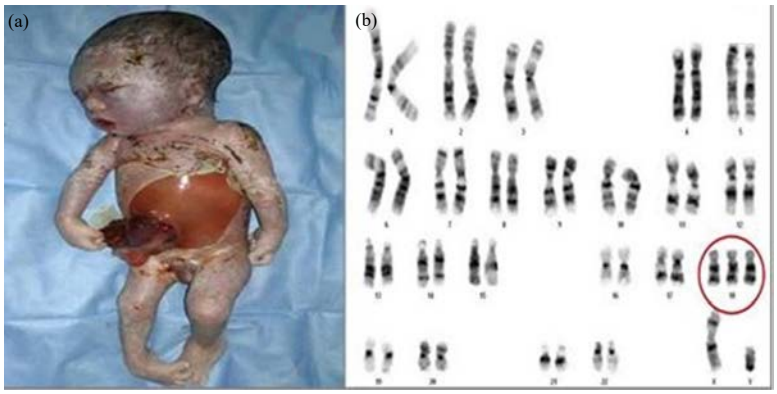

Fig. 1(a-b): Neonate with omphalocele (a) Postnatal and (b) Karyotyping result Trisomy 18

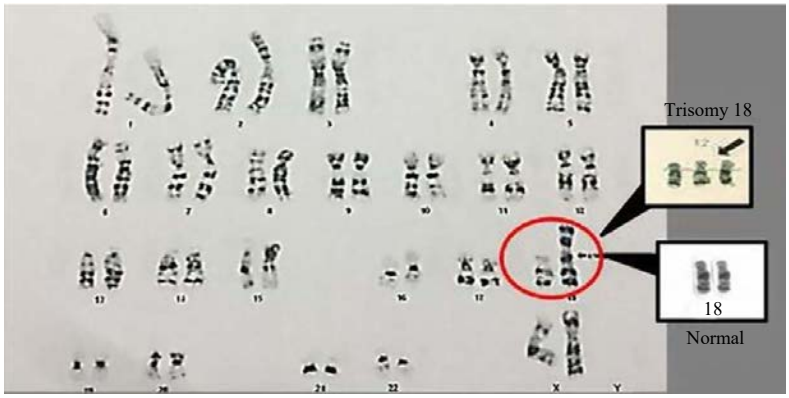

Fig. 2: Karyotyping result isochromosome 18

previous antenatal examinations was performed twice in obstetric and gynecology specialists. History diabetes melitus, hypertension and chronic disease in the mother denied. Ultrasound examination was obtained by a singleton gravid life, head location, according to gestational age 26-27 weeks, estimated weight of fetus 832 gr, micrognathia, microtia, AVSD, spina bifida occulta, polihidramnios AFI 32,6 cm.

The defect in the ventricular septum of pars membranacea was 0.92cm wide and there was no visible septum primum and secundum in the atrium. The mitral and tricuspid valves can still be identified so that they are included in the incompatible AVSD category. AVSD was also called an atrioventricular canal (AV canal) defect or endocardial cushion defect.

Spina bifida occulta was a posterior arcus abnormality and was a mild form of spina bifida called a closed spina bifida and does not involve the spinal nerve. Cytogenetic examination of a karyotyping from amniocentesis results using the FISH method was found 46, xx, i(18q) i.e., the isochromosome in the short arm of chromosome 18 (Fig. 2). Termination becomes a dilemma because gestational age has made it possible to live, even though the family requested it but was not approved by clinical meeting staff despite poor prognosis.

At 29-30 weeks or 1 week after amniocentesis the patient had prematurely ruptured membranes, his spontaneous birth and the birth of a baby girl weighing 900 g, body length 38 cm, apgar value 5/3 and baby died 4 h after delivery.

Case 3: Facial tumor: Description of mother's age 39 years old came to prenatal diagnostic clinic at 18 weeks' gestation. Ultrasound image shows the upper part of the face and upper chest covered by the tumor with no visible nose and mouth (Fig. 3). This was a lethal case at the time of postpartum because neonate could not be breath, mouth and nose pressed by a massive tumor. Pregnancy was decided to terminate because of a poor prognosis after delivery, beside request of the patient.

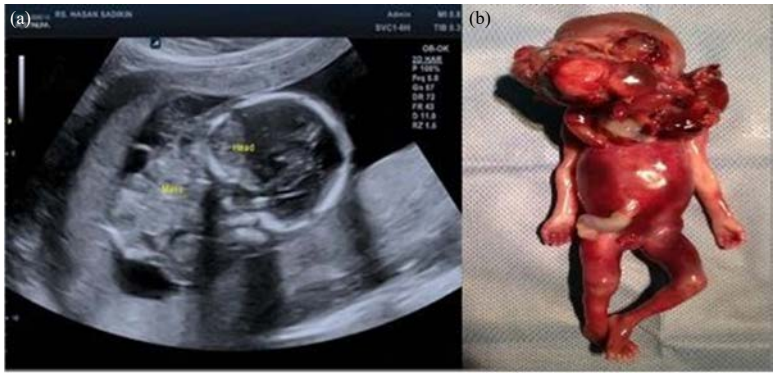

Fig. 3(a-b): Irregular mass in area fetal face, (a) Ultrasound examination and (b) Postnatal

DISCUSSION

In this study, the prognosis of 2 cases chromosome 18 abnormalities identified by ultrasound and karyotyping. It was clinically associated with various major and minor multi system anomalies, including cardiovascular, brain with neurological, renal, gastrointestinal and skeletal malformations. The aim of the present study was to clarify the prognosis for each trisomy 18 case and to compare and consider the life prognosis. Two cases chromosomes 18 abnormalities prenatally diagnosed and all cases have a bad prognosis because multiple anomalies. All of the cases were fatal cases, one of case intrauterine death happened 2 week after amniocentesis and the other baby died 4 h after delivery.

Edwards syndrome was a genetic disorder included in the major trisomy and characterized by an extra chromosome 18. Prevalence was 1 / 6000-8000 live births and 1: 2500-3000 in the form of abortion and fetal death.[1] These extra chromosomes often come from maternal, associated with an increase in maternal age and more than 80% are meiotic nondisjunction. The incidence of recurrence in couples giving birth to trisomy 18 was 1%. The prevalence of trisomy 18 in the female fetus was greater than in male but less mortality cases. Further reported female fetuses with trisomy 18 had a higher chance of survival when compared with a male fetus[1-4].

The trisomy on chromosomes 21, 18 and 13 was important because of the reason for the severe and life-threatening disability of the infant. The researcher states that there is a misconception of the public view that trisomy 18 is a lethal condition so that efforts to help fetus and parents become not optimal. The patient's parents need genetic counseling in the face of such a situation and get a complete explanation of the recurrence of abnormalities for subsequent reproductive processes[5].

A seminal population study in the United Kingdom in 1996 reported an overall prevalence Edward syndrome of 1/4272 and a liveborn prevalence of 1/8333, overall frequency detected in Hawaii from a similar study was 1/2123 with a liveborn frequency[5] of 1/7900. Research shows 37-58% AVSD was associated with chromosomal anomalies, especially trisomy[6-8] 21 and 18. Therefore, a fetal karyotype examination should be examined when AVSD was discovered. AVSD can also be part of other syndromes such as Elis-Van Creveld, VACTRL, CHARGE, etc[1,5]. Nava *et al.*[9] reported that aneuploidy was a strong predictor if AVSD as a single defect. Yıldırım *et al.*[10]. reported that fetuses with isolated AVSD defects had a higher incidence of karyotype abnormalities than those with complex defects.

Imataka studied about trisomy 18 have a result approximately >90% of new borns did not survive beyond 1 years of age with intensive care support. Medical intervention during postnatally improving periods of life neonatal with[11] trisomy 18. EUROCAT (European Surveillance of Congenital Anomalies) recorded a total prevalence of major congenital anomalies of 23.9/1,000 births for 2003-2007, 80% were live births. 2.5% of live births with congenital anomaly died in the 1st week of life. 2.0% were stillbirths or fetal deaths from 20 weeks gestation. 17.6% of all cases were terminations of pregnancy following prenatal diagnosis[12].

The 3rd case was a very rare facial tumor covered entire face including mouth and nose. Currently, in Indonesia this case as a poor prognosis because reconstruction require extraordinary efforts at a cost that was not in accordance with the expected results, so the termination of pregnancy was chosen by parents. Among neonatal patients, teratomas were the most common, benign neoplasm, however facial teratomas are encountered in less than 1:250,000 live births. These facial teratomas continue to be associated with significant morbidity and mortality due to the risk of airway compromise, the complexity of surgical resection and the risk of both recurrence and malignant conversion[13].

In some cases with a poor fetal prognosis should be considered for termination of pregnancy because possibility risk of the pregnancy equal to normal pregnancy although the benefits obtained by the family was minimal because fatal possibility. Termination considerations of pregnancy are often a problem as some parents may accept the presence of a predicted child was disabled based on a prenatal diagnosis. Termination consideration was the prerogative rights of the couple because it was accountable as a parent. Medical considerations assessing severe and lethal abnormalities only aggravated the mother's condition and the best advice in terms of reproductive function was termination and good preparation when pregnant in the future to prevent recurring severe defects.

Sociologically, the medical treatment for the neonatal to infantile periods with disabilities was found to be different for various countries depending on factors such as culture, religion, human rights, law and views on bioethics. Traditionally, a non-intervention approach in the newborn management of trisomy 18 and 13 has been previously utilized. Clinicians may only be able to give advice and consideration to the couple from a medical standpoint but the social and religious sociocultural factors in some nations or adherents of the faith in the world have views that are not in line with their beliefs about the termination of a living fetus. The termination decision in cases of severe congenital abnormalities that have a fetal death prognosis may have to be based on medical interests and partner's beliefs about that matter.

CONCLUSION

Trisomy chromosome or isochromosome 18 was a lethal case. The decision to determine the termination of pregnancy in severe cases will be faster with the results of ultrasound alone. Medical considerations assessing severe and lethal abnormalities aggravated the mother's condition and the best advice in terms of reproductive function were termination and good preparation when pregnant in the future to prevent recurring severe defects.

SIGNIFICANCE STATEMENT

This study discover the link between ultrasound findings with the karyotyping, that can be beneficial for clinicians include obstetricians. This study will help the researcher to uncover the critical areas of the necessity karyotyping in obstetrics. Thus a new theory on maternal fetal medicine especially diagnosis prenatal area.

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