

Patau Syndrome: A case report

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Abstract: Patau syndrome is a congenital disorder associated with trisomy 13. The extra chromosome 13 causes numerous fetal structural defects specially of the central nervous system, cardiovascular system and urogenital system. Major structural anomalies are occasionally identified in the late first or early second trimester. Other anomalies will be visible on ultrasound done around 20 weeks. Any discovery of multiple structural anomalies in a foetus increases the chances of chromosomal anomalies and women should be offered amniocentesis or other invasive tests to establish the foetal karyotype. Following a confirmed prenatal diagnosis of Patau syndrome, the decision to be made is either to terminate the pregnancy or to manage it conservatively. Most pregnancies will result in miscarriage or death in utero but some survive the first few weeks of life. Here we present a case of Patau syndrome which was diagnosed prenatally due to the presence of omphalocele and congenital cardiac abnormalities. This was followed by amniocentesis which confirmed the diagnosis. Pregnancy termination was offered to her but declined. Ultimately the foetus died in utero and delivered later without any complications.

Keywords: Patau syndrome, Trisomy 13, congenital anomalies.

INTRODUCTION

Patau syndrome is caused by a chromosomal abnormality in which some or all of the cells of the body contain extra genetic material from chromosome 13. The extra genetic material disrupts normal development, causing multiple and complex organ defects which is lethal to developing embryo. Most cases of trisomy 13 are inherited and result from random events during the process of gametogenesis in healthy parents. Incidence of Patau syndrome is approximately 1 case per 8,000-12,000 live births [1]. Significant racial or geographic differences in frequency are not evident. Stillbirth and in utero fetal demise are common pregnancy outcomes. But the fetal development can proceed to live birth. Median survival age with Patau syndrome is only 2.5 days; 82% die within 1 month and 95% die within 6 months [1]. Its importance is due to its association with numerous malformations of the central nervous system, the cardiovascular system and the urogenital system. Central nervous system malformations are important

predicting factors of the survival of a child who bear this syndrome [2].

There is some non-invasive prenatal testing for the diagnosis of Patau syndrome. A mid-pregnancy ultrasound scan which is most commonly done can show up the foetal structural abnormalities. On further evaluation of these abnormalities by some invasive tests like amniocentesis can confirm the diagnosis. Here we have presented a case which was diagnosed in this way but ultimately the fetus died in-utero.

CASE REPORT

A 30 years old Malay housewife, gravida 2, para 1+ 0 got admitted to a tertiary care hospital of Malaysia on 27.12.2016 at 9:15 am for induction of labour due to intrauterine death of foetus. It was a planned pregnancy and her LMP was on 30.03.2016 and accordingly EDD on 06.01.2017. Antenatal booking was done at 8 weeks; all the routine antenatal investigations were done which revealed no abnormality. The early booking ultrasound revealed no

abnormality. Her blood group was O positive. She had regular antenatal check-up. But anomaly scan done at 20 weeks of pregnancy revealed multiple structural abnormality i.e. omphalocele and cardiac anomalies. For this reason, she was advised amniocentesis for karyotyping. She did amniocentesis and karyotyping on 20.10.2016 (30 weeks of gestation) and it revealed the foetus to be trisomy 13 (Patau syndrome). Modified oral glucose tolerance test was also done which was normal and Hb electrophoresis done on 14.09.2016 showed her to be Hb E trait.

Due to presence of chromosomal anomaly she was advised for delivery but she refused. Her pregnancy continued but there was sudden cessation of foetal movement on 21.12.2016 and ultrasound scan (USS) done thereafter showed intra uterine death of the foetus. She was then advised for admission and delivery.

Her past obstetric history revealed that she is para one. It is a female baby weighing 3.2 kg delivered vaginally in April 2014 at term without any complications. The baby was growing well. Her marriage was non-consanguineous. She had no history of any medical diseases.

Upon admission to the hospital she had no labour pain, leaking liquor or per vaginal bleeding. Physical examination revealed her weight 78 kg, Body mass index 30.46 kg/m², pulse 78/min, blood pressure 125/78 mm of Hg. Per abdominal examination showed symphysio-fundal height of 34 cm. A single foetus in longitudinal lie with cephalic presentation was palpable. Foetal head was 5/5 palpable and foetal heart sound was absent. Per vaginal (p/v) examination revealed cervix 2 cm, soft, posteriorly placed, os- 2 cm and station -3.

Prior to induction some investigations were done. Hb% 11.7 gm/dL, platelet 178 x 10⁹ /L, prothrombin time 11.2 second (control - 12.4 second), APTT patient 27 second (control - 28.3 second); renal functions and serum electrolytes were normal.

She was decided to be induced mechanically first. Under all aseptic precaution Foley's catheter was introduced intracervically on 27.12.2016 at 10 am and the balloon was inflated with 75 cc normal saline. Labour pain started at 11 am and intensity gradually increased. At 2 pm p/v examination showed os 9 cm, station - 0 and membrane ruptured. Labour progressed normally and she delivered a macerated male baby per vaginally at 02:58 pm. Placenta and membrane were expelled out spontaneously. Blood loss was about 300 cc. Examination of the baby showed that weight was 2890 gm, length 49 cm, and head circumference 30 cm. Spalding sign was positive. There was hypotelorism of eyes, flat nose, low set ears, polydactyly of both hands and feet, omphalocele and hypospadias.

Postnatally there was no problem. She was prescribed tab cabergolin for suppression of lactation. She was discharged on 28.12.2016 with advice for follow-up after six weeks.

DISCUSSION

Patau syndrome is the least common but most severe of the viable autosomal trisomy. It was first observed by Thomas Bartholin in 1657 but the chromosomal nature of the disease was ascertained by Dr. Klaus Patau, a German geneticist in 1960 [3]. This condition occurs due to the presence of a full extra copy of chromosome 13 or an extra partial copy of chromosome 13 (Robertsonian translocation) or because of mosaic chromosomal pattern. Full trisomy 13 is caused by nondisjunction of chromosome during meiosis and the mosaic form is caused by random error during cell division early in fetal development. Like all other nondisjunction (such as Down and Edward syndrome) the risk of this syndrome in the offspring increases with maternal age at pregnancy with about 31 years being the average [4]. The age of our patient is 30 years. The sex ratio at birth is slightly skewed towards female presumably because of decreased survival among male. A significant number of cases that are trisomy for chromosome 13 end in spontaneous abortion, fetal demise, or stillbirth [5]. In our case the foetus was a male who died in utero.

There are no known risk factors of Patau syndrome except previous history of any affected foetus. So suspicion only arises if a routine mid-trimester ultrasound scan shows multiple fetal structural anomalies when cytogenetic investigation is advised, which may reveal the diagnosis. Among the structural anomalies, 80% are cardiac defects which include patent ductus arteriosus, ventricular septal defect, atrial septal defect and dextrocardia. Another common defect is holoprosencephaly in which the brain does not divide completely into halves. The facial defects are hypotelorism, microphthalmia, anophthalmia, absent or malformed nose or proboscis, cleft lip or cleft palate. There may be capillary hemangioma or polycystic kidney disease. If prenatal diagnosis is escaped then the newborn typically presents with low Apgar scores with various structural birth defect like cleft lip, cleft palate, polydactyly, omphalocele, neural tube defect and microcephaly with poor neurological performance. In Our case routine mid-trimester ultrasound scan first revealed structural anomalies i.e. omphalocele and cardiac anomalies. Then she underwent amniocentesis and it showed trisomy 13.

In addition to conventional cytogenetics, fluorescent in-situ hybridization (FISH) on interphase cells could be used to obtain a more rapid diagnosis. There is also a new noninvasive prenatal testing using cfDNA from maternal blood. This has got high sensitivity and specificity. Positive predictive values also appear to be much higher than for standard prenatal

aneuploidy screening [6]. Unlike Edward syndrome and Down syndrome, the quad screen does not provide a reliable means of screening for this disorder. A significant number of cases can be detected through the use of first trimester screening [ultrasonography measurement of the nuchal translucency, pregnancy associated plasma protein A (PAPPA), and free β hCG]. In England and Wales during 2008–09, there were 172 diagnoses of Patau syndrome, with 91% of diagnoses made prenatally [7]. There were 111 elective abortions, 14 stillbirth/miscarriage/fetal deaths, 30 outcomes unknown, and 17 live births. Approximately 4% of Patau syndrome with unknown outcomes are likely to result in a live birth, therefore the total number of live births is estimated to be 18 [7].

The structural anomalies in our reported foetus had (evident after birth): hypotelorism of eyes, flat nose, low set ears, polydactyly of both hands and feet, omphalocele and hypospadias. A multi-state, population-based study by Springett and colleagues on 240 live-born infants with trisomy 13 showed that the prevalence of anomalies were as follows: cardiac anomalies, 57%; nervous system anomalies, 39%; eye anomalies, 30%; polydactyly, 44%; and orofacial cleft, 45% [8].

Once a diagnosis of Patau syndrome is made, pregnancy management varies according to the gestational age at diagnosis. At pre viable gestational age, pregnancy termination is an option. When patient choose not to terminate specially when pregnancy has reached a viable gestational age as happened in this case, labor may be induced at term. In our case the fetus was dead; if the fetus is alive, prior to onset of labor there should be a focused discussion on neonatal resuscitation. Neonatal attendant should be informed about the patient's wishes for her child. Infants who survive the neonatal period have an average length of stay in a neonatal ICU of 10.8 days [9]. Surgical interventions are generally withheld for the first few months of life because of the high mortality rates of babies with Patau syndrome.

Regarding future pregnancy parents should be referred to a geneticist or genetic counselor for appropriate counseling regarding recurrence risks, etiology and prognosis. Recurrence risks depend on the details of the chromosome abnormality and the mother's age. In general, for freestanding trisomy 13, the recurrence risk is approximately 0.5% above the mother's age-related risk for autosomal trisomy. Recurrence risks for Robertsonian and other structural rearrangements widely vary; these risks can be as high as 100% in rare cases in which a parental translocation occurs involving both copies of chromosome 13 [1]. Parental cytogenetic studies are required if

Robertsonian translocation or other structural chromosome abnormalities are found. In each subsequent pregnancy, the woman should be offered a prenatal diagnostic study. Such studies are also indicated when either parent is known to carry any structural chromosome abnormalities.

Patau syndrome is definitely a severe form of viable autosomal trisomy. Pregnancy management of such a grieving patient need vast experience in this field. Some delivering hospitals are more experienced in the management of pregnancies complicated by known lethal fetal birth defects. For this reason, when possible pregnancy with Patau syndrome should be delivered at such centers.

CONCLUSION

All the pregnancy must be evaluated by mid-trimester USS for fetal structural anomalies. If needed cytogenetic study should be done as soon as possible. As the prognosis is very poor for the neonate identified with Patau syndrome, so pregnancy termination should be done if diagnosed in pre-viable stage.

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