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Received 20 Sep 2016.
Revised 19 Oct 2016.
Accepted 02 Nov 2016.
Published online 09 Dec 2016

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Trisomy 8 Mosaicism in a Malay Boy – A Case Report

Abstract— Warkany syndrome 2 or Trisomy 8 mosaicism (T8M) is a very exceptional, chromosomal defect affecting males more than females. Due to its extreme phenotype variations and symptoms most patients go undiagnosed. Here we report, a 4-year old boy with T8M who underwent chromosomal study after being diagnosed with ambiguous genitalia at birth.

***Keywords*— Warkany syndrome 2, Trisomy 8 mosaicism, chromosomal defect**

1 INTRODUCTION

Trisomy 8 is a condition where every cell of an individual presents with an extra copy (three copies of chromosome 8). This disorder occurs when a pair of chromosomes fail to divide evenly, resulting in cells containing more than two chromosome 8 [1]. It is a condition that has severe effects on the developing fetus, and usually causes early lethal condition to the fetus [2]. Trisomy 8 mosaicism (T8M) is a variant of trisomy 8 where only some of the cells present with three copies of chromosome 8 and other remaining cells exhibit normal copy number of cells.

Individuals with TM8 have a better survival outcome and are expected to survive into childhood and adulthood compared to those all cells having trisomy 8 [3]. They also exhibit an identifiable pattern of developmental abnormalities [4]. In most cases they will present with distinct, recognizable phenotype defects. Medical problems, such as kidney and urinary conditions [5,6,7], congenital heart conditions [1], and corpus callosum disorders [8], have been reported in people with T8M.

2 CASE REPORT

The patient was born on 12th September 2012. The mother is 20-year-old while the father is 21-year. This is a non-consanguineous marriage. Both parents are of Malay ethnic group.

At birth, the baby weighed 3.2 kg and was 32 cm in length. The baby was born via spontaneous vaginal delivery. The baby exhibited bilateral hydrocele and hypospadias with bifid spectrum. It was also noted that the baby had ambiguous genitalia, therefore a chromosomal study was done.

For ante-natal history, the mother had a history of previous miscarriage during the second trimester of unknown reasons in the year 2010. She experienced late onset pregnancy-induced hypertension while pregnant with the patient but she was not on regular follow-up. She was also diagnosed with maternal obesity during the pregnancy, costochondritis at 16 weeks and vaginal candidiasis at 37 weeks. She also gave a family history of diabetes mellitus.

Chromosome analysis was conducted at the Genetics Laboratory, Advanced Medical and Dental Institute (AMDI), Universiti Sains Malaysia. The results showed there were two (2) cell lines found: The major cell line exhibited normal male karyotype in the metaphase spreads, whereas the minor cell line showed trisomy 8 in four (4) of the metaphase spreads, hence the karyotype was (47,XY,+8[4]/46,XY[45]) (Figures 1 and 2). Patient also showed SRY positive for the Y chromosome by PCR gene analysis (Figure 3). The patient was discharged after relevant management was instituted.

Two (2) months later, the infant was admitted due to prolong fever and productive cough four days earlier. He was found to exhibit hypospadias with bilateral testis descent and managed by surgically by the paediatrics surgical team and discharged well. At nine (9)

months of age he was again admitted for acute bronchiolitis. During this time, examination showed he was developing normally. He weighed 7.5 kg and length was 71 cm tall. He was able to sit without support, crawl, performed a palmar grasp and able to babble. There was normal head and neck development. He did not demonstrate any typical clinical presentations of T8M. He is now on regular follow-up.

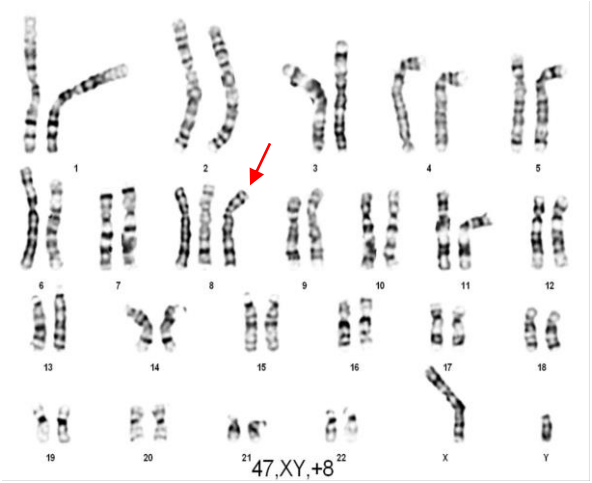

Figure 1: The karyotype results show the presence of a third chromosome 8, (trisomy 8)

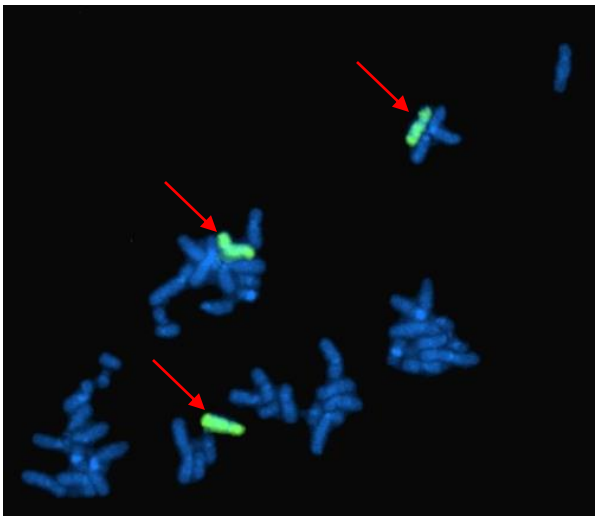

Figure 2: Fluorescence in situ hybridization result (FISH) shows chromosome 8 in green; the three copies are indicative of trisomy 8

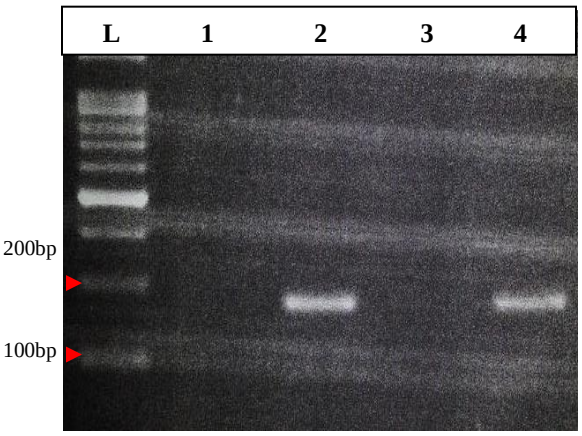

Figure 3: Electrophoresis gel result shows a positive band of SRY gene. SRY gene is found in Y chromosome and used as sex determination

Lane	Description	Product size
L	Ladder	100bp ladder
1	Negative control	-
2	Positive control (Male)	~160bp
3	Positive control (Female)	-
4	Patient's sample (SG008/13)	~160bp

3 DISCUSSION

Warkany syndrome was named after Dr. Josef Warkany, a pediatrician from USA. He first described the condition together with the underlying cause in the 1960s [9]. He published the first observation of chromosome Trisomy 8 in 1971. T8M is a very rare disorder which affects only one in every 25,000-50,000 live births [10]. Most T8M patients show some recognizable phenotypes, including a short neck with irregular extra skin folds, a long slim body which comes together with a narrow chest, deep plantar and palmar creases, and pear-shaped facial appearance [5,11,12,7]

Trisomy 8, found in hematological disorders, notably in malignant myeloid disorders such as acute myeloid leukemia (AML), myelodysplastic syndromes, and myeloproliferative neoplasms are known as acquired trisomy 8 [13,14]. It was noted that Trisomy 8 in patients with AML is associated with decrease in overall survival compared with patients with normal cytogenetics since this worsen the outcomes [15].

Medical problems, such as kidney and urinary conditions [5,6,7], congenital heart

conditions [1], and corpus callosum disorders [8], have been also reported in people with T8M. Effects on learning, speech, and development have been widely reported as well.

Contradictory to previously discussed T8M case reports, the patient in this report shows none of the characteristic features that were previously reported in patients with T8M. However, the patient's very young age might explain the lack of clinical presentation of these features. The described features such as delayed motor development, severe ability to learn and speak could appear as he gets older. Further follow-up is needed for this patient to monitor his progress.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

ACKNOWLEDGEMENT

The authors would like to acknowledge the parents of the child and the staffs of Genetics Laboratory, AMDI for the support and technical assistance.

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