Pseudotrisomy 13 Syndrome : A Case Report

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Abstract : **We report on a male baby with microcephaly, holoprosencephaly of alobar type with single ventricle, cyclopia, proboscis, poorly developed testes, and clenched hands without polydactyly, suggestive of trisomy 13 syndrome. However, the cytogenetic study disclosed 46,XY. The case presented here very well represents pseudotrisomy 13 syndrome and signifies the value of cytogenetic study and genetic counseling.**

เรื่องย่อ : **กลุ่มอาการโครโมโซม ๑๓ เกินลวง : รายงานผู้ป่วย ๑ ราย**
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รายงานเด็กชายแรกคลอด ๑ ราย ที่มีความผิดปกติหลายอย่างของกลุ่มอาการโครโมโซม ๑๓ เกิน ได้แก่ ศีรษะเล็กกว่าปกติ, สมองไม่แบ่งซีก, มีตาเดียวตรงกลาง, มีงวงเหนือคิ้ว, นิ้วมือกำเข้าหากันแต่ไม่พบนิ้วเกิน น้ำหนักตัว, การเจริญเติบโตและอัณฑะเจริญน้อยกว่าปกติ ผลการตรวจโครโมโซมพบเป็น ๔๖,XY ถือเป็นกลุ่มอาการโครโมโซม ๑๓ เกินลวง ที่ไม่พบนิ้วเกิน ซึ่งมีการถ่ายทอดทางกรรมพันธุ์ได้ นับเป็นตัวอย่างหนึ่งซึ่งชี้ให้เห็นความสำคัญของการตรวจโครโมโซม และการให้คำปรึกษาเกี่ยวกับโรคทางพันธุกรรม

INTRODUCTION

The clinical recognition of trisomy 13 syndrome denotes the definite diagnosis in most patients. Many authors[1-11] have reported on cases that clinically resembled trisomy 13 syndrome but had normal chromosomes, and have proposed the term *pseudotrisomy 13 syndrome*. Some authors[2] put forth a clinical diagnostic criteria of holoprosencephaly and polydactyly to establish the diagnosis, while other authors[3,4] showed that neither holoprosencephaly nor polydactyly are obligatory manifestations of this condition. We report on a case with alobar holoprosencephaly, cyclopia, proboscis, poorly developed testes, clenched hands, and absence of polydactyly.

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CLINICAL REPORT

This 1,960 gram, 40 week gestation, Thai male infant was delivered as a viable neonate with Apgar scores 1,1 at 0 and 5 minutes after birth, respectively. Due to the trisomy 13 diagnosed prenatally, he received no resuscitation. The mother was 35 years old, gravida 4, para 2, and abortion 1. She had an uneventful antenatal course and presented with labor pain. The ultrasonography, performed on the day of admission, revealed a single viable fetus with cephalic and multiorgan anomalies. The findings included holoprosencephaly, clenched hands without polydactyly, proboscis and two-vesseled umbilical cord suggestive of trisomy 13 syndrome. The labor progressed and the cesarean section had to be performed due to placenta previa totalis. At birth, the baby weighed 1,960 grams (< 2SD) and measured 37.5 cm (< 2SD). Head circumference and chest circumference were 31.5 (< 2SD) and 27 cm (< 2SD), respectively.

The autopsy showed microcephaly (brain weight 74.5 grams), holoprosencephaly of alobar type with absence of corpus callosum and septum pellucidum, single ventricle, cyclopia, proboscis, low-set malformed ears with right microtia, micrognathia, clenched hands, poorly developed testicular tissue, micropenis, cryptorchidism, Meckel's diverticulum, and single umbilical artery.

DISCUSSION

Apparently, the clinical phenotype, which was easily recognizable, made the diagnosis of trisomy 13 most likely. However, the cytogenetic study of postmortem cord blood revealed 46,XY leading to the diagnosis of an autosomal recessive syndrome, ***"Pseudotrisomy 13 syndrome"*** (so called "holoprosencephaly-polydactyly") (HSP). Pseudotrisomy 13 syndrome seems to represent a separate genetic entity characterized by holoprosencephaly, facial anomalies, polydactyly, and other visceral defects[1]. Some authors[2] have suggested that the term pseudotrisomy *13* be restricted to "karyotypically normal individuals whose most prominent abnormalities are holoprosencephaly and polydactyly." On the contrary, Lurie and Wulfsberg[3] considered that the presence of holoprosencephaly or polydactyly was not essential for diagnosis. They proposed the following diagnostic criteria for the HSP. The diagnostic criteria for sporadic cases would be:

I. a normal karyotype;

II. a) a combination of holoprosencephaly and postaxial polydactyly with or without other characteristics; or

b) a combination of holoprosencephaly with other characteristics but without polydactyly; or

c) a combination of postaxial polydactyly, brain defects (microcephaly, hydrocephaly, and agenesis of corpus callosum) and other characteristics.

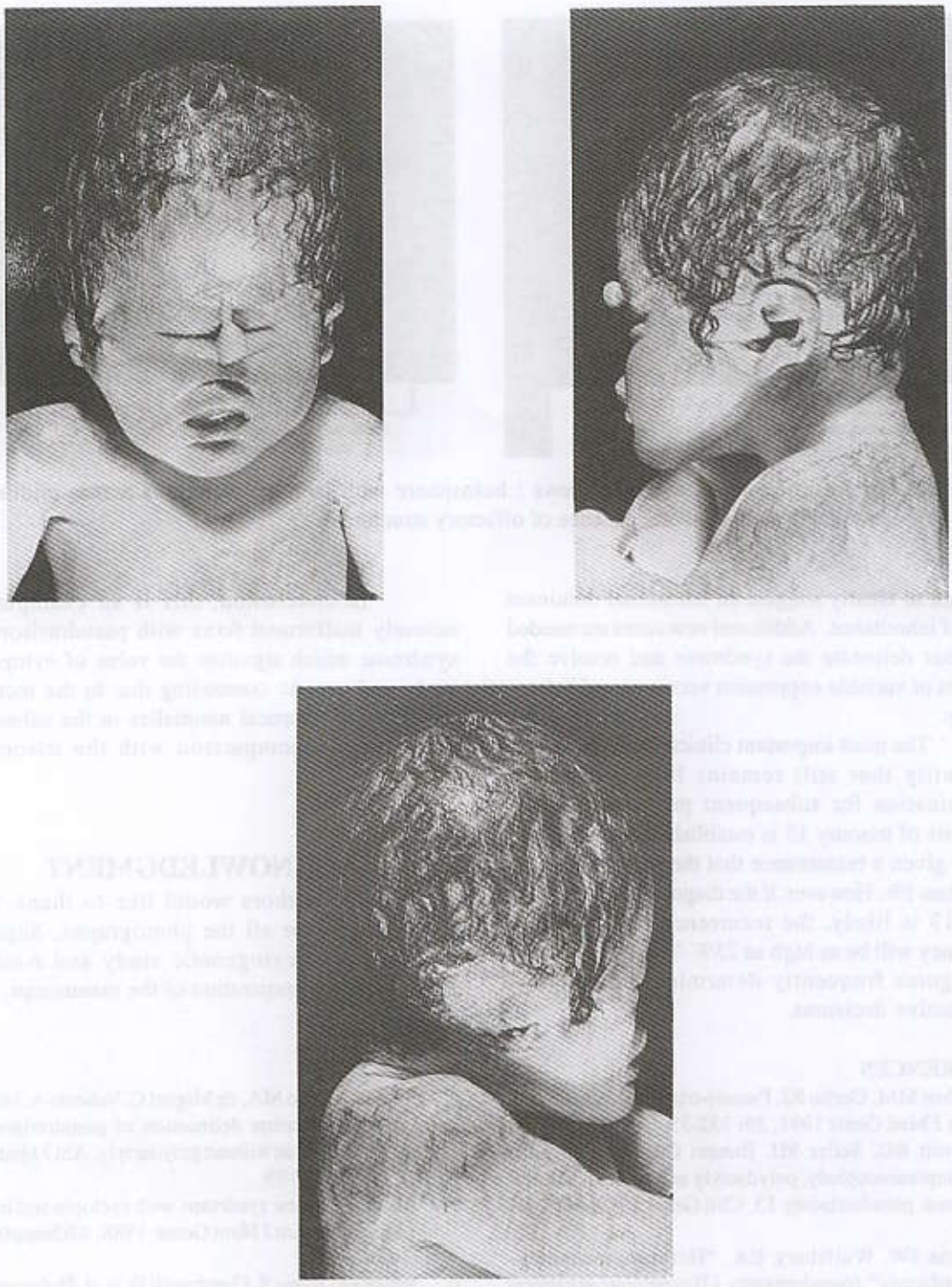
The diagnostic criteria for familial cases would be:

I. a normal karyotype in at least one affected sib; and

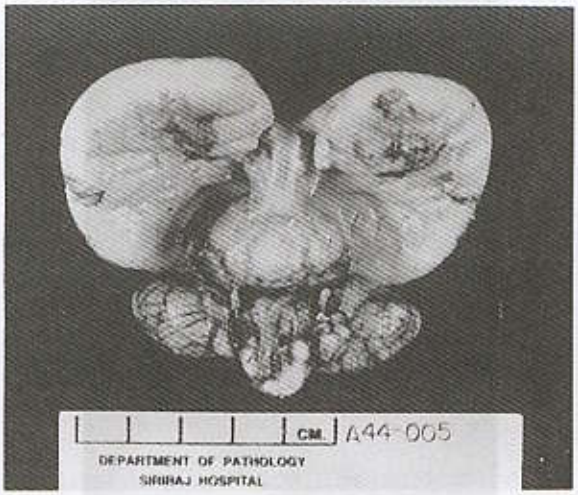
II. diagnostic criteria IIa, b, or c in at least one affected sib if the other sibs have no abnormalities contradicting the diagnosis.

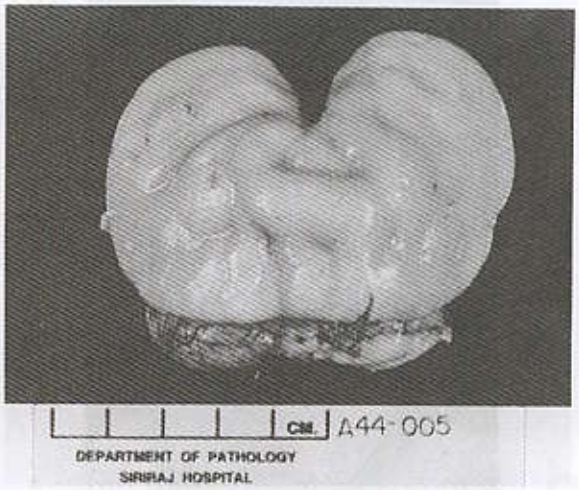
In comparison of the clinical manifestations of our case with the criteria described above, the baby we mention here showed most manifestations of the trisomy 13 syndrome, but he did not have polydactyly. Ramos-Arroyo et al[4] have reported a case with holoprosencephaly, median cleft lip, cardiac and genital anomalies, normal upper limbs, and a 46,XX karyotype. They also reviewed 22 karyotypically normal cases whose clinical features resembled trisomy 13 syndrome and compared them with the case they presented. Different skeletal manifestations of the syndrome had been previously reported, and they concluded that the cases might represent phenotypic variability of the pseudotrisomy syndrome, although genetic heterogeneity could not be ruled out presently.

The cause of pseudotrisomy 13 syndrome is still under debate. Many authors[5-10] suggested autosomal recessive inheritance as a cause of the syndrome. On the other hand, Martinez-Frias et al.[11] pointed out that data on parental ages were suggestive of autosomal dominant inheritance. However, Ramos-Arroyo et al.[4] had analyzed parental age using data from the cases they reviewed and presented, and concluded that, although the number of cases was still limited, epidemiological data did



Figures 1-3. Facial anomalies, front and lateral views: microcephaly, cyclopia, proboscis and abnormal external ears.





Figures 4-5. Brain, inferior and superior views : holosphere with large convolutions across midline; no interhemispheric fissure; absence of olfactory structures.

not seem to clearly suggest an autosomal dominant mode of inheritance. Additional new cases are needed to further delineate the syndrome and resolve the problem of variable expression versus causal heterogeneity.

The most important clinical issue related to this entity that still remains is accurate risk determination for subsequent pregnancy. If the diagnosis of trisomy 13 is established, then couples will be given a reassurance that the recurrent risk is lower than 1%. However, if the diagnosis of pseudotrisomy 13 is likely, the recurrence risk in future pregnancy will be as high as 25%. These contrasting risk figures frequently determine the couples' reproductive decisions.

In conclusion, this is an example of a severely malformed fetus with pseudotrisomy 13 syndrome which signifies the value of cytogenetic study and genetic counseling due to the increased incidence of identical anomalies in the subsequent pregnancy in comparison with the trisomy 13 syndrome.

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