DAHİLİ BİLİMLER / *MEDICAL SCIENCES*
Olgu Sunumu / Case Report

A Greig Syndrome Case Diagnosed In One Of The Singleton Of Twin Preterm Who Were Obtained By Assisted Reproduction

Yardımcı Üreme Tekniği İle Olan Preterm İkiz Eşinde Tanımlanmış Bir Greig Sendromu Olgusu

Gonca Sandal, Nurdan Uraş, Ömer Erdeve, Şerife Suna Oğuz, Uğur Dilmen

Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi Yenidoğan Kliniği

Greig cephalopolysyndactyly is a rare multiple congenital anomaly characterized by clinical triad of polysyndactyly, macrocephalia and hypertelorism. In general, although it is characterized with autosomal dominant inheritance, there is also autosomal recessive inheritance pattern. Here, we aimed to discuss an infant who was born from multiple gestations arising from assisted reproduction techniques and suspected to be Greig syndrome with no familial history. Best of our knowledge this is the first case related with assisted reproduction technique.

Key Words : ***Greig Cephalopolysyndactyly, Assisted Reproduction Technique***

Greig sefalopolisindaktili sendromu klinik olarak polisindaktili, makrosefali ve hipertelorizm triadı ile karakterize nadir multipl konjenital bir anomalidir. Genelde otozomal dominant kalıtımla karakterize olmasına rağmen, otozomal resesif geçiş paterni de vardır. Biz burada aile öyküsü olmaksızın Greig sendromu olduğundan şüphelenilen, yardımcı üreme tekniği ile olan çoğul gebelikten doğan bir yenidoğanı tartışmayı amaçladık. Yardımcı üreme tekniği ile ilişkili bizim bildiğimiz ilk vakadır.

Anahtar Sözcükler: ***Greig Sefalopolisindaktili, Yardımcı Üreme Tekniği***

The Greig cephalopolysyndactyly syndrome (GCPS) is a pleiotropic, multiple congenital anomaly syndrome. It is rare, but precise estimates of incidence are difficult to determine, as ascertainment is erratic. The primary findings include hypertelorism, macrocephaly with frontal bossing, and polysyndactyly. The polydactyly is most commonly preaxial of the feet and postaxial in the hands, with variable cutaneous syndactyly, but the limb findings vary significantly (1, 2). Other low frequency findings include central nervous system (CNS) anomalies, hernias, and cognitive impairment it was first described by Greig (1926) in an affected mother and daughter (1). Mutations in the GLI3 gene located on chromosome 7p3 are responsible (3). In addition to mutations, translocations that interrupt the gene, microdeletions, and cytogenetically detectable deletions have been described (3). In literature, several reports have been published describing variable expression of this syndrome (4-6). However, association with assisted reproduction technique was not reported. Here, we aimed to discuss an infant who was born from multiple gestations arising from assisted reproduction techniques and suspected to be Greig syndrome with no familial history.

Case Report

One of the twins who were born from first pregnancy of the 25-year old mother at 28th gestational week with birth weight of 1180 gram was hospitalized to neonatal intensive care unit due to dyspnea. The pregnancy was result of assisted reproduction technique. Considering physical examination findings, birth weight was 1180 gram (50p), height was 42 cm (90p) and head circumference was 32 cm(>90p). General status was intermediate, face had dysmorphic appearance, forehead was wide and hypertelorism was present (Fig 1). In cardiovascular examination, 2/6 systolic murmur was present.

Başvuru tarihi: 28.01.2010 • Kabul tarihi: 08.06.2010

İletişim

Dr. Gonca Sandal
Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi
Yenidoğan Kliniği
GSM : 0 505 487 10 27
E-Posta Adresi : kocabasgonca@mynet.com

Partial subcutaneous syndactyly was present at bilateral hand and foot index fingers and there was one accessory finger with normal development at hands and feet (Fig 2). Findings of other system examinations were normal. In echocardiographic examination, patent ductus arteriosus was found. In cranial USG, width of right lateral ventricle was 10 mm and width of left lateral ventricle was 12 mm that ventriculomegaly was observed. Triventricular hydrocephalus was found in cranial CT. Chromosome analysis showed a normal 46, XY karyotype. Further genetic investigations have not been performed due to technical difficulties. We performed cranial USG and head circumference measurements weekly. At postnatal 21th day cranial ultrasonografi revealed that hydrocephalus was increased and intraparanchymal hemorrhage was developed. As head circumference increased 2.3 cm/week, he was discharged for shunt operation at another center at postnatal 47th day. We did not detect any clinical convulsion and rapid increase in head circumference at the follow up period. The patient is on follow up with pediatric neurology and neurologic surgery units.

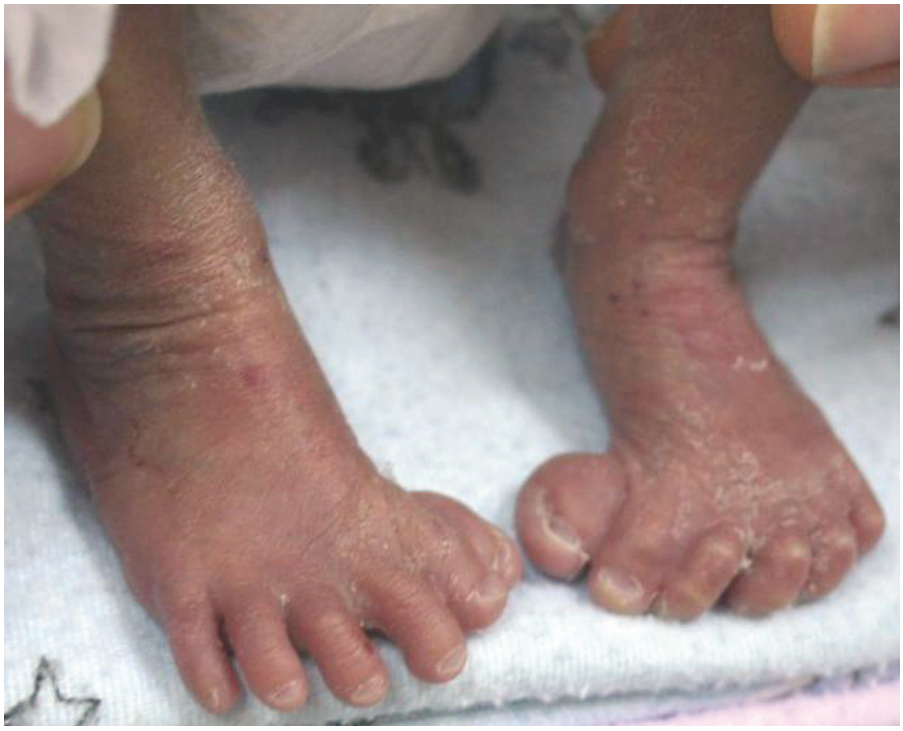

Figure 1: Feet of the patient. The feet display bifid toes and partial subcutaneous syndactyly.

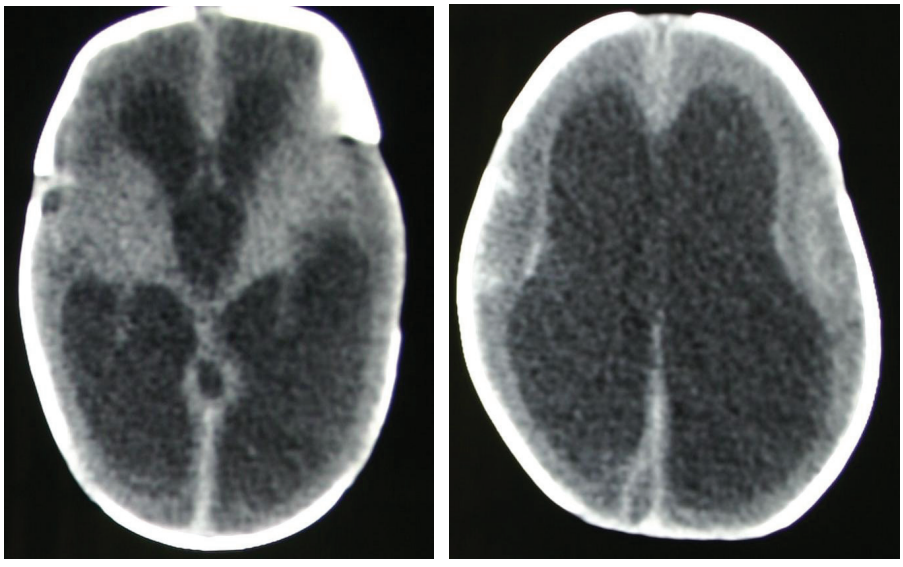

Figure 2a-2b: Cranial USG of the patient showed ventriculomegaly

Discussion

Greig cephalopolysyndactyly is a rare multiple congenital anomaly characterized by clinical triad of polysyndactyly, macrocephalia and hypertelorism (2). Incidence is estimated as 1-9/1.000.000. As molecular diagnosis methods are not widely used, it is difficult to definitely estimate incidence. At least 75 % of cases with clinical diagnosis of cephalopolysyndactyly had GL13 gen mutation. GL13 mutation has a wide spectrum. In general, although it is characterized with autosomal dominant inheritance, there is also autosomal recessive inheritance pattern (2, 3). Many families with Greig polysyndactyly syndrome were reported. Risk of non-GCPS individuals within involved families to have child with GCPS is less than 1% per each conception. In our case, there was no other individual with GCPS in the family (5, 7). When we search the London Dysmorphology Data-base using his multiple signs, the Greig cephalopolysyndactyly syndrome was the most compatible diagnosis for the boy. Twin sibling of our patient born by in vitro fertilization was also normal. As there was no familial history, the condition found in our patient suggested first mutation.

Polydactyly found in Greig syndrome is typically defined as preaxial and it may occur in any of four extremities. Most common findings are present of postaxial polydactyly in hands and preaxial polydactyl in foot. Type of polydactyly may vary between individuals as well as between extremities of same individual. Particularly dual fingers, hypoplastic accessory fingers as well as accessory fingers with complete development can be observed. Variability of cutane-

ous syndactyly is also high. Large part of patients with cutaneous syndactyly has partial cutaneous syndactyly in several fingers(2,4,6). However, there are also cases with complete cutaneous syndactyly in all fingers. Our case had partial cutaneous syndactyly in bilateral foot and hand thumb and index fingers and polydactyly.

In this syndrome, cranio-facial manifestations may also vary. Most cases have hypertelorism with or without telechantus. In our case, hypertelorism was present without telechantus. Macrocephalus not related with central nervous system is found in many cases. In our case, hydrocephalus associated by triventricular hydrocephalus and secondary macrocephalus were present. Although rare, craniocynostosis mental retardation, corpus callosum agenesis, umbilical and diaphragmatic hernia may also be present in Greig syndrome. Our case manifested none of above mentioned findings.

Teebi hypertelorism syndrome, Carpender syndrome and Gorlin syndrome are found among differential diagnosis. In Teebi syndrome, plolydactyly is typically not preaxial. Carpenter syndrome is characterized by polysyndactly, craniocynostosis and mental retardation. Gorlin syndrome (nevoid basal cell carcinoma syndrome) is characterized by macrocephalus and particularly hypertelorism and polydactyly. Moreover, mutations were found in genes related with PTCH1 and GLI-SHH pathways (6,8,9).

Factors related to infertility of both partners, quality of sperm and oocyte cell, age of couple and tozin exposure increased secondary to advanced age are among factors causing genetic disorders in assisted reproduction technique pregnancies. Quality of sperm and oocyte cells may particularly increase incidence of chromosome anomaly diagnosed during antenatal period as well as congenital malformations found in live births (10-13). Nevertheless, our case led to inquire relationship between assisted reproduction techniques and chromosomal disorders, although there is no definitive relationship between assisted reproduction techniques and chromosomal disorders .

REFERENCES

1. Biesecker LG. The Greig cephalopolysyndactyly syndrome. Orphanet J Rare Dis 2008; 24:10.
2. Balk K, Biesecker LG.The Clinical Atlas Of Greig Cephalopolysyndactly Syndrome. Am J Med Genet A 2008; 146: 548-57.
3. Biesecker LG.What you can learn from one gene : GL13. J Med Genet 2006; 43: 465-69.
4. Winter RM, Huson SM. Greig Cephalopolysyndactly Syndrome: A possible mouse homologue (xt- extratoes). Am j Med. Genet 1998; 31:93-8
5. Marafie MJ, Temtamy SA, Rajaram U, al-Awadi SA, el-Badramany MH, Farag TI. Greig cephalopolysyndactyly syndrome with dysgenesis of the corpus callosum in a Bedouin family. Am j Med Genet 1996; 66: 261-64
6. Wang CH, Tsai FJ, Shi YR. Greig Cephalopolysyndactly Syndrome in a family. Acta Paediatr Taiwan 2006; 447: 97-9.
7. Kunze J, Kaufmann HJ (1985). Greig cephalopolysyndactyly syndrome. Report of a sporadic case. Helv Paediatr Acta 1985; 40:489-95.
8. Williams PG, Hersh JH, Yen FF, Barch MJ, Kleinert HE, Kunz J, Kalff-Suske M. Greig Cephalopolysyndactly Syndrome : Altered phenotype of a microdeletion syndrome due to presence of a cytogenetic abnormality. Clin Genet 1997; 52:436-41
9. Biesecker LG. Polydactyly : How many disorders and how many genes ? Am J Med Genet 2002; 112: 279-283.
10. Clementi E, Palka C, Lezzi L, Stuppia L, Franchi P, Tiboni G M. Prevalence of chromosomal abnormalities in 2078 infertile couples referred for ART. Human Reprod 2005; 20:437-42.
11. Buckett WM, Tan SL. Congenital abnormalities in children born after assisted reproductive techniques: how much is associated with the presence of infertility and how much with its treatment? Fertil Steril. 2005 Nov;84(5):1318-9
12. Simpson JL. Registration of congenital anomalies in ART populations: pitfalls. Hum Reprod. 1996 Dec;11 Suppl 4:81-8.
13. Nancy S. Green Risks of Birth Defects and Other Adverse Outcomes Associated With Assisted Reproductive Technology Pediatrics Vol. 114 No. 1 July 2004, pp. 256-259.