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Co-existence of Goldenhar and Klinefelter Syndromes in a Patient Born Following ICSI

CASE REPORT

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ABSTRACT

Intracytoplasmic sperm injection (ICSI) is a widespread and powerful method enabling men with low sperm quantity and quality to become fathers. However, compared with naturally conceived children, there are increased risks of problems, such as congenital malformations, chromosomal abnormalities, infertility, epigenetic diseases, and delayed neuropsychological development in the offspring. We present the case of 6-year-old male patient born following ICSI with clinical and radiological features of Goldenhar syndrome as well as a history of surgery for unilateral cryptorchidism. His karyotyping showed a chromosomal constitution of 47, XXY. Clinicians should be aware of the risks of an increasing number of patients born following ICSI to maximize children's health and welfare.

Keywords: Goldenhar syndrome, Klinefelter syndrome, intracytoplasmic sperm injection

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INTRODUCTION

Craniofacial Microsomia is a rare condition with congenital abnormalities. It includes a spectrum of malformations, primarily involving structures derived from the first and second branchial arches. Facial asymmetry, mandibular hypoplasia, preauricular or facial skin multiple tags and/or pits, auricular anomalies (from anomalies in the size and shape of the external auricle to anotia) and hearing loss are the characteristic findings in patients with this syndrome. Vertebral, renal, cardiac, and limb anomalies are also observed as clinical features. Most cases are sporadic, and various etiologies, such as chromosome abnormalities, single-gene mutations, vascular disruption, teratogens, and very rarely, maternal use of assisted reproductive techniques (ART) have been implicated for their occurrence (1).

CASE REPORT

The proband was a 6-year-old male referred to the Medical Genetics clinic in Pamukkale University, because of facial dysmorphism and bicuspid aorta (Figure 1. a-c). He was the first child of non-consanguineous parents. The mother and father were 26- and 34- years-old at the time of gestation, respectively. The pregnancy was induced by ICSI with ejaculated sperm in another center because of severe oligospermia. Amniocentesis was recommended at the 16th week of pregnancy, but the family refused it. The patient was born at 26 weeks of gestation with cesarean section. He had a birth weight of 810 g. When he was 1-year-old, he was operated for right cryptorchidism. He had normal stages of motor development. On physical examination performed at our clinic, his weight was 17 kg (3-10th centile), height was 112 cm (25-50th centile), and head circumference was 51.2 cm (25-50th centile). Dysmorphic features included prominent glabella, asymmetric face, right malarial hypoplasia, three skin tags in the left ear and one in the right ear, right microtia and cleft earlobe, upslanting palpebral fissures, broad nasal root, narrow ala nasi, prominent columella, short neck, shoulder asymmetry, bilateral 5th clinodactyly, bilateral partial cutaneous syndactyly between the 2nd and 3rd toes, and left testis in the inguinal canal. The child had normal brain MRI and abdominal ultrasound findings. Echocardiography showed a bicuspid aortic valve. On auditory examination, conductive hearing loss of the right ear was detected. Skeletal radiographies revealed fusion at the C6-C7 vertebrae, height loss in all cervical vertebrae, and hemivertebrae at C5 and C6. Chromosomal analysis of the patient indicated 47, XXY, while his parents had normal karyotypes. Fluorescent in situ hybridization with X and Y alpha satellite probes showed no signs of mosaicism in the patient. Written informed consent was obtained from patient's family.

DISCUSSION

Intracytoplasmic sperm injection (ICSI) is a widespread and useful method among ART and usually applied for treatment of couples with male factor infertility. Several studies found that there was an increased incidence of

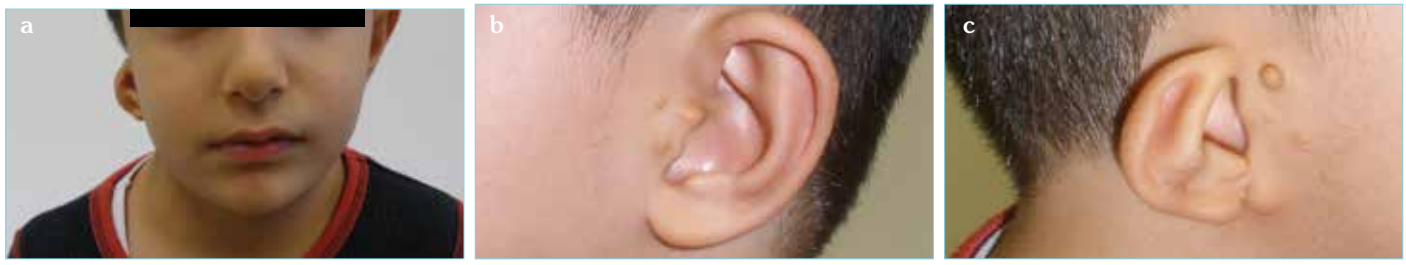

Figure 1. a-c. Facial features of the patient (a). Front view demostrating facial asymmetry, right malarial hypoplasia, and shoulder asymmetry (b). Lateral view of skin tags located in front of the left ear (preauricular) (c). Lateral view of the right microtia with one preauricular skin tag and cleft earlobe.

aneuploidies, mainly sex chromosome aberrations, among children conceived by ICSI (2). Subfertile men are considered to have higher rates of aneuploid offsprings, secondary to gametes with higher rates of chromosomal segregation errors (3). The invasive nature of the ICSI procedure may also lead to embryonic aneuploidy by disruption of the oocyte meiotic spindle or nuclear decondensation of spermatozoa (4). Goldenhar syndrome is the first reported congenital anomaly following ART; however, there are a few studies about Goldenhar syndrome following ICSI (5). To the best of our knowledge, this is the first report of a patient conceived through ICSI with co-existence of Goldenhar and Klinefelter syndromes. The exact mechanism is unclear. However, altered gamete environment due to hormonal stimulation, physical manipulation, and embryo culture during the ICSI procedure may initiate changes, such as epigenetic modifications in growth and development genes that are responsible for such adverse outcomes (6, 7). Although these syndromes as an outcome of ICSI are rare, further studies are needed to understand the molecular basis not only for healthcare professionals but also for the couples considering fertility treatment.

CONCLUSION

Intracytoplasmic sperm injection (ICSI) involves the injection of a single spermatozoon into an oocyte cytoplasm using a glass micropipette and has become the most frequently used method of fertilization in ART. Although the safety and efficiency of ICSI is improving over time, clinicians consider the existing evidence indicates that children conceived through ICSI have an increased risk of congenital malformations compared with naturally conceived children.

Informed Consent: Written informed consent was obtained from patient's family who participated in this study.

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REFERENCES

1. Bogusiak K, Puch A, Arkuszewski P. Goldenhar syndrome: current perspectives. World J Pediatr 2017; 13(5): 405-15. [CrossRef]
2. Simpson JL. Birth defects and assisted reproductive technologies. Semin Fetal Neonatal Med 2014; 19(3): 177-82. [CrossRef]
3. Watanabe H. Risk of chromosomal aberration in spermatozoa during intracytoplasmic sperm injection. J Reprod Dev 2018. Jul 7. doi: 10.1262/jrd.2018-040. [Epub ahead of print]. [CrossRef]
4. Esteves SC, Roque M, Bedoschi G, Haahr T, Humaidan P. Intracytoplasmic sperm injection for male infertility and consequences for offspring. Nat Rev Urol. 2018 Jul 2. doi: 10.1038/s41585-018-0051-8. [Epub ahead of print] [CrossRef]
5. Yovich JL, Stanger JD, Grauaug AA, Lunay GG, Hollingsworth P, Mulcahy MT. Fetal abnormality (Goldenhar syndrome) occurring in one of triplet infants derived from in vitro fertilization with possible monozygotic twinning. J In Vitro Fert Embryo Transf 1985; 2(1): 27-32. [CrossRef]
6. Sullivan-Pyke CS, Senapati S, Mainigi MA, Barnhart KT. In Vitro fertilization and adverse obstetric and perinatal outcomes. Semin Perinatol 2017; 41(6): 345-53. [CrossRef]
7. Song S, Ghosh J, Mainigi M, Turan N, Weinerman R, Truongcao M, et al. DNA methylation differences between in vitro- and in vivo-conceived children are associated with ART procedures rather than infertility. Clin Epigenetics 2015; 7: 41. [CrossRef]