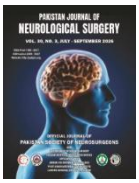

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Case Report

A Rare Pediatric Case of Twins with 46XY Karyotype, Swyer Syndrome, Associated with Intraventricular Hemorrhage (IVH) and Post-hemorrhagic Hydrocephalus (PHH): A Case Report and Literature Review

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ABSTRACT

Objective: The aim was to identify the underlying causes of phenotypic sex differences and potential difficulties that determine the twins' 46XY chromosomes.

Case Presentation: A 37-year-old woman who delivered twin premature neonates of 29 and 30 weeks of gestation. At the Morozoskaya Children Hospital in Moscow, Russia. She had a history of hereditary thrombophilia (heterozygous Leiden mutation). Microintestinal growth factor (MGF), intrauterine growth factor (IGF), and fetal growth factor (FGF) all showed abnormalities between 24 and 25 weeks. The neurosonography showed male and female twins diagnosed with a confirmed fetal karyotype 46, XY; Swyer syndrome, with Stage 3 intraventricular hemorrhage, obstructive post-hemorrhagic hydrocephalus, and multifocal structural epilepsy with multicystic transformation of the brain hemispheres, movement and tone dysfunction. The management was follow-up with insertion of the extracranial ventricular shunt. After a few weeks, the VP subgaleal shunt was relocated, and the baby was evaluated and monitored by UCI.

Conclusion: In this case, it is a rare condition that was not only accompanied by intraventricular hemorrhage and post-hemorrhagic hemorrhage in the twin prenatally, which were controlled, but the female neonate passed away after all the efforts by the colleagues, while the 46XY male twin survived.

Keywords: Swyer Syndrome 46, XY Pure Gonadal Dysgenesis, Intraventricular Hemorrhage, Posthemorrhagic.

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INTRODUCTION

Swyer syndrome was first described and reported by Swyer in 1955. Also known as 46, XY pure gonadal dysgenesis, it is a very uncommon disorder with aberrant anatomy or disturbance of the sexual gonads, with chromosomal development in both male and female premature infants. Swyer syndrome is a very uncommon disorder. 46, XY and pure gonadal dysgenesis, often known as Swyer syndrome, was first described in 1955. Swyer described it as aberrant anatomy with an abnormality chromosomal, with sexual gonadal development. Patients with Swyer syndrome often have typical female external genitalia, and the prevalence is 1 in 80,000.[1] The SRY gene area is deleted in 10% to 20% in female with Swyer syndrome; in 80% to 90% of instances, the SRY gene is typically normal but has mutations in MAP3K1, DHH, and NR5A1, genes, and the another's diagnostic determinants.[2] Thus far, it has been established that the SRY gene is found on the Y chromosome; As a result, the testicles are activated by several genes, some of which may be found on chromosomes 17 and chromosomes 9. Even in the presence of a Y chromosome, testicular differentiation will fail if the SRY gene or another gene that controls testicular development later mutates, leading to the gonads' female development.[3] The twins in this case study are an example of 46, XY gonadal dysgenesis, often known as Swyer syndrome. With cell lines on chromosome 45, X, in the gonads, disruption of genes like DSS/DAX1, particularly duplication, may disrupt male sex determination and result in cryptic mosaicism. Nevertheless, the male phenotype cannot be explained by the genetic mutation. Therefore, the expression of the mutant gene would determine the creation of a gonad with a contralateral testis.[4] Skin fibroblasts were stained with GTG for karyotyping. In tests conducted on 75 metaphases with 325 interphase nuclei, reports of 25 metaphases were examined using in situ hybridization with the fluorescent probe DYZ3 (Vysis, Downers Grove, IL). The probe binds to the alpha-satellite region of the short arm of the Y chromosome. The male twin's phenotype will be consistent with mixed gonadal dysgenesis, which is typically linked to the karyotypes 46, XY and/or 46, XY/45, X [5,3]

Case Report

A 37-year-old mother gave birth to twins prematurely at 29 and 30 weeks of gestation. At the Morozoskaya Children Hospital in Moscow, Russia. The mother is Rh positive and has blood type O (I). Genetic thrombophilia (heterozygous Leiden mutation and hyperhomocysteinemia) is part of her mother's medical history. Uterine curettage was one of the surgical treatments. Five years ago, at 7 weeks of pregnancy was not viable. In early studies of 46, XX uterine cavity with curettage was used as a surgical operation. Three years ago, a late-induced spontaneous abortion occurred at 20 weeks of gestation. The features of the pregnancy course included congenital abnormalities of the fetus: the cartilaginous portion of the nose was not clearly delineated in a facial abnormality. The chin was moderately hypoplastic. The fetal sample was subjected to clinical exome sequencing at the Genomed laboratory; no pathogenic or likely pathogenic mutations were found (Figure 1). Her Pregnancy history included seven births. In the first trimester, the pregnancy was healthy, but an abnormal fetal

genital structure was identified during a second-trimester scan. Amniocentesis was therefore carried out at 21 weeks. The fetal karyotype was 46, XY. Two male and female germ cell clones were identified by GCA. Fetal growth factor (FGF), microintestinal growth factor (MGF), and intrauterine growth factor (IGF) anomalies were found between weeks 24 and 25 **(Figure 2)**. Workplace advancement: The first stage's duration: The second stage's duration: Surgeries include placental insufficiency, intrauterine growth restriction, intrahepatic cholestasis, and fetal deterioration in a pregnant woman at 29–30 weeks. Suprapubic transverse laparotomy. Cesarean section using a transverse incision in the lower uterine region. myomectomy. Reinfusion of autologous erythrocytes. 6-7 is the Apgar score. Blood type of the mother: O (I). Rh factor for mother: (+) positive. Blood type for infants: B (III). Rh factor for infants: (+) positive. Rh phenotype in infants: CEce. Post-Neurosonography: Larger post-hemorrhagic ventriculomegaly; no other notable dynamics. IVH sequelae, ventriculomegaly with likely occlusion at the fourth ventricle's median aperture, and growing widespread leukomalacia of the periventricular white matter of the cerebral hemispheres and cerebellum are all seen on magnetic resonance imaging. The cerebral hemispheres exhibit widespread cystic-glial change, which is primarily cystic, according to computed tomography. Diagnosis: The twins' (male and female) fetal karyotype is 46, XY pure gonadal dysgenesis (Swyer syndrome). Severe brain damage caused by hypoxia and hemorrhage. Intraventricular hemorrhage in stage three. Obstructive hydrocephalus following hemorrhage. The cerebral hemispheres undergo multicystic change. Structural epilepsy with several foci. Syndrome of movement and tone disorders. After a few weeks following the implantation of an extracranial ventricular shunt, the status was changed to VP subgaleal. With a postoperative diagnosis of bilateral grade 3 intraventricular hemorrhage (non-traumatic) in both the pregnancy and the infant, only the boy fetus survived. All of the brain's hemispheres showed cystic-glial change, which was primarily cystic. There was rhinorrhea, or leakage of cerebrospinal fluid (CSF). An extraventricular shunt was inserted. The patient had sporadic nystagmus while in the

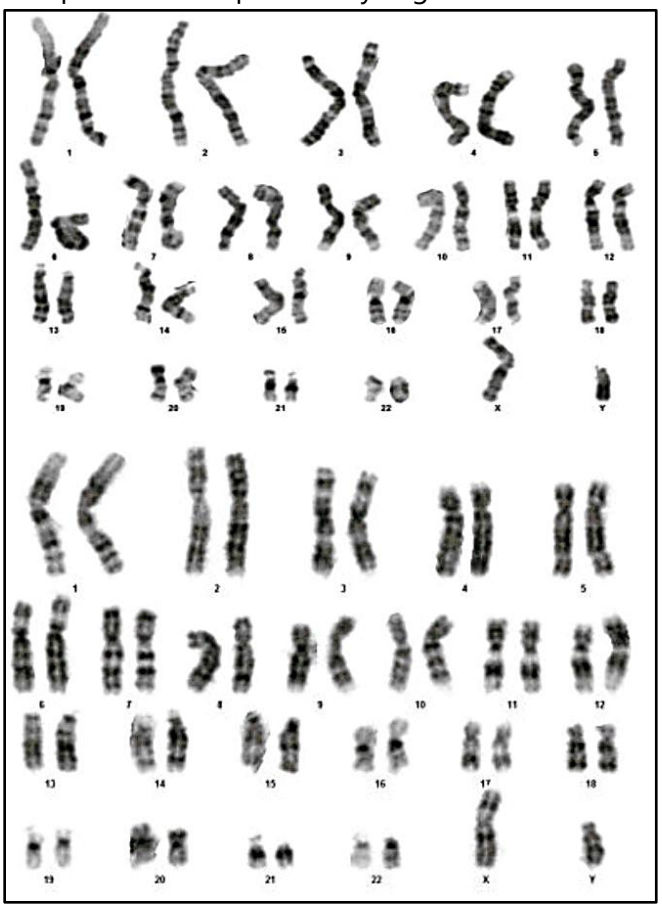

Figure 1: *Karyotype 46XY, Swyer syndrome.*

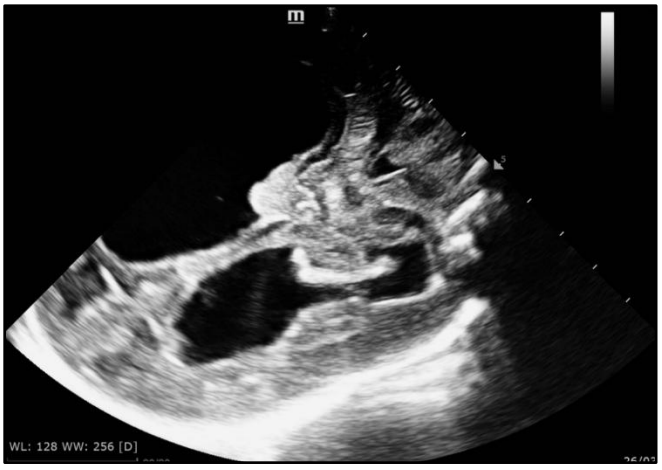

Figure 2: *Evidence of Intraventricular hemorrhage and post-hemorrhagic hydrocephalus (Image added with patient's permission).*

intensive care unit. The seizures were limited to the intensive care unit and did not recur. The right ventriculoatrial shunt was implanted. We recommended follow-up after 1 month, with a combination of the pediatrics, gynecology, neurology, and neurosurgery departments monitoring and developing the patient after the removal of the right subgaleal drain.

DISCUSSION

Swyer syndrome is characterized by a female phenotype and a male genotype; the gonads are dysgenetic, the uterus is often hypoplastic, and the external genitalia, including the vagina, appear normal. The most prevalent symptom is primary amenorrhea, which is treated with hormone replacement therapy and estrogen therapy to trigger puberty. The reproductive years are when the most troublesome clinical presentation happens. Twin pregnancies are extremely uncommon, and patients with Swyer syndrome are unlikely to become pregnant. This is due to the non-functioning and infertile gonads in Swyer syndrome. However, individuals may be able to conceive through in vitro fertilization using donor eggs with the help of contemporary assisted reproductive technology and proper uterine control.[6]

Due to the high incidence of gonadal cancer in patients with Swyer syndrome, an early diagnosis is essential. Karyotype analysis and gonadal exploration are advised if the patient is a teenager with primary amenorrhea since extended treatment will be necessary for survival and surgical excision of the gonads is frequently required. An estimated 20% of people have 46XY gonadal dysgenesis, which is caused by a deletion of the short arm of the Y chromosome that affects the SRY gene and inhibits or mutates SRY in other genes. A female patient with an XY karyotype will be diagnosed with Swyer syndrome if she shows no sexual development and has a palpable Müllerian system with female testosterone levels. Thus, in our instance, the twins, XY, showed pure or full gonadal dysgenesis at 29 and 30 weeks of gestation. [7]

Diagnostic Evaluation

If the mother is in discomfort and the uterus and ovaries an MRI should be done, followed by an MRI. A peripheral blood smear karyotype will reveal a 46XY genotype; hormonal tests will reveal high levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and low levels of testosterone and anti-Müllerian hormone (AMH).[8]

Intraventricular hemorrhage (IVH) pathogenesis

The fragility of the blood vessels in the germinal matrix makes it a complicated pathological process. As a result, reduced mean arterial pressure in situations of germinal hemorrhage results in changed cerebral blood flow, which affects neonates' brain control and causes clinical disturbance. These symptoms raise the possibility of vascular rupture, which can result in germinal matrix bleeding that spreads to the nearby lateral ventricle.[9] Erythropoiesis is triggered by conditions such as fetal hypoxia, which increases the release of growth factors that support neovascularization, such as angiopoietin and vascular endothelial growth factor. Blood vessels lack pericytes and are weak or delicate once they develop. Astrocytes may be lacking in glial fibrillary acidic protein, or the cells in the capillary walls contain low amounts of fibronectin in the juvenile basal lamina. The bleeding process is accelerated in newborns with underlying platelet and coagulation disorders. A hemorrhagic parenchymal infarction results from a hematoma that blocks a vein and reduces white matter perfusion.[10,11,12]

Post-hemorrhagic hydrocephalus (PHH)

Modern treatments involve draining cerebrospinal fluid (CSF) to reduce intracranial pressure and improve cognitive function by reducing intra-abdominal hydrocephalus (IH). Some earlier studies focused on surgical complications, primarily CSF infection, such as shunt rate, catheter obstruction, and catheter revision. These studies, lacking attention to neurological outcomes, were incomplete and only included motor and language functions. A range of neurodevelopmental disorders can occur, including motor dysfunction and intellectual disability, such as behavioral problems accompanied by memory and executive function deficits, as well as emotional problems ranging from anxiety and depression to hyperactivity disorder and visual impairment. Motor dysfunction can range from mild motor dysfunction, such as end-stage motor incoordination, to cerebral palsy.[11,13,14]

Ventriculoperitoneal shunt (VPS)

Ventricular catheter insertion is performed at Kocher's point, about 1 to 2 cm anterior to the coronal suture and 2 to 3 cm lateral to the midline. In a frontal approach, Keen's point is utilized for a parietal approach. The insertion site will be determined by the desired ventricular structure and the specific kind of hydrocephalus. After making a skin incision and continuing with a 10-14 mm burr hole in the skull, the dura mater is coagulated using electrocautery. In the frontal approach, the catheter should be advanced toward the medial canthus, parallel to the tragus, in the cranial plane, and toward the midpoint of the pupil in the coronal plane. The depth will measure 4-5 cm in young children and 3-4 cm in babies. Ventricular cannulation is validated by the cessation of resistance, the observation of unobstructed cerebrospinal fluid flow, and the placement of the catheter into the ventricle. Upon achieving sufficient cerebrospinal fluid flow, the stylet will be extracted and attached at the proximal end of the catheter to the valve of the implanted shunt system.[12,13,14]

CONCLUSION

In this case, it was an uncommon syndrome that was not only accompanied by intraventricular hemorrhage and post-hemorrhagic hemorrhage in the twin males prenatally, but the female neonate died despite the colleagues' best efforts. The 46XY male twin survived after the placement of a ventricular shunt and a galeal shunt, which was later removed. Cerebrospinal fluid (CSF) flow, and therefore intracranial pressure, was monitored. The patient was a premature infant, and the condition was complex. Take-home message: early intervention and full management by the surgeons is a highly qualified and standard procedure, as well as full postoperative management by the ICU team.

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Additional Information

Disclosures: The Authors report no conflict of interest.
Ethical Approval: The study was carried out according to the latest revision of the Helsinki Declaration regarding medical research involving human subjects. No. Reference L035'00115-77/00096790, 103, February 2, 2015.
Human Subjects: Consent was obtained from the patient included in the study.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:
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List of Abbreviations:
(FGF); Fetal growth factor.
(MGF); Microintestinal growth factor.
(IGF); Intrauterine growth factor.
(CSF); Cerebrospinal fluid.
(LH); Luteinizing hormone.
(FSH); Follicle-stimulating hormone.
(AMH); Anti-Müllerian hormone.
(IVH); Intraventricular Hemorrhage.
(PHH); Post-hemorrhagic hydrocephalus.
(IH); intrahepatic hydrocephalus.

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Software	Daniel A Encarnacion-Santos	Writing – Review & Editing	Daniel A Encarnacion-Santos
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Investigation	Daniel A Encarnacion-Santos	Project administration	Gennady Chmutin,
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