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# Genetic mos 46,X, idic(Y)(q12)[9]/45,X[6].ish idic(Y)(SRY+,DYZ3++,SRY+): A Case of Mixed Gonadal Dysgenesis in a Child with Cryptorchidism and Hypospadias from Ouagadougou, Burkina Faso

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## Abstract

Disorders of sexual development arise from a disparity between chromosomal, gonadal, or phenotypic characteristics. Despite their rarity, these disorders hold significant clinical and multidisciplinary importance. In this context, we present a case involving mixed gonadal dysgenesis (MGD) due to mosaicism, with a karyotype of mos 46,X, idic(Y)(q12)[9]/45,X[6], in a child named OKA. The child's legal sex is registered as male in the civil registry, exhibiting normal psychomotor development for his age, as well as appropriate growth in height and weight according to the growth curve. However, physical examination reveals certain anomalies within the external genitalia—including labia majora, a micropenis in lieu of a clitoris. These observations prompted genetic analyses, including postnatal constitutional karyotyping and FISH techniques utilizing a specific SRY locus probe and the centromeric probe of the Y chromosome. These analyses confirm the presence of mos 46,X, idic(Y)(q12)[9]/45, X[6].ish idic(Y)(SRY+, DYZ3++, SRY+). An abdominopelvic ultrasound aimed at identifying internal genitalia in OKA revealed bilateral cryptorchidism, along with an uncomplicated right inguinoscrotal hernia. Subsequently, orchidopexy was recommended. Mixed gonadal dysgenesis, mosaicism, and cryptorchidism

were diagnosed in this case.

## Keywords

Mixed Gonadal Dysgenesis, idic(Y)(q12), Disorders of Sex Development, Mosaicism, Karyotype, FISH

## 1. Introduction

The typical pattern of human sexual development is a finely regulated and dynamic process governed by intricate genetic activity and orchestrated by endocrine mediators in the form of steroid and peptide hormones [1] [2]. Normal sex development depends on the precise spatiotemporal sequence and the coordination of mutually antagonistic activating and repressing factors [3]. Following Jost's groundbreaking paradigm, the initial stage of sexual development is marked by the establishment of chromosomal sex (*i.e.*, the presence of a Y or X chromosome) during fertilization [4] [5]. Subsequently, chromosomal sex exerts its influence on gonadal sex determination, directing the differentiation of the bipotential gonadal crest into either testes or ovaries.

The gene responsible for initiating testicular development within the fetal gonad is denoted as the testis determining factor (TDF), often identified as the same gene known as the "sex determining region of the Y chromosome" (SRY) [6]. The presence and expression of the SRY gene, located on the distal region of the short arm of the Y chromosome (Yp), play a pivotal role in determining the gonadal sex of an embryo. It achieves this by orchestrating the differentiation of the bipotential embryonic gonad into the testes, leading to the formation of Sertoli and Leydig cells [7]. The differentiation of male testicles triggers the secretion of distinct hormones responsible for translating the gonadal sex into the male internal and external genitalia (sex phenotype) [1] [8]. Any disruption that occurs during this intricate process of sex differentiation could potentially result in a misalignment between chromosomal, gonadal, and phenotypic sexes. This misalignment, often characterized as disorders of sex development (DSD), can give rise to various anomalies [9] [10].

Sex development disorders (DSD) are classified into three groups based on sex chromosome constitution: sex chromosome DSD, 46,XY DSD, and 46,XX DSD. The mos 45,X/46,XY karyotype, involving either a structurally normal or abnormal Y chromosome, corresponds to mixed gonadal dysgenesis (MGD). This condition can manifest with a range of phenotypes, from female with gonadal streaks to atypical external genitalia or male with bilateral testes, often associated with cryptorchidism and hypospadias, as well as clinical features of Turner syndrome. The presence of testes in MGD is influenced by the distribution of the Y chromo-some cell line and the presence of at least one copy of the SRY gene in the pre-Sertoli cells, which is essential for Sertoli and Leydig

cell differentiation.

According to genetic mechanisms, mutations in the SRY gene influence male sex determination and can cause mixed gonadal dysgenesis. A new SRY mutation can cause asymmetrical activation of the SOX9 gene involved in sexual differentiation, resulting in mixed gonadal development without mosaicism. Approximately 15% of 46, XY gonadal dysgenesis cases are found to have mutations in the SRY gene, with most of these mutations located within the HMG domain [11] [12]. In addition to SRY, other genes and sex-determining transcription factors, such as SOX9, NR5A1, GATA4, DAX1, and DHH, play a role in inducing subsequent stages of testicular maturation [11].

Disorders of sexual differentiation are increasingly being recognized and warrant particular attention, although they represent relatively uncommon genetic disorders. These disorders can involve numerical or structural abnormalities affecting the X and/or Y chromosomes. Notable clinical manifestations of sex chromosome abnormalities include Turner syndrome, Klinefelter syndrome, 47,XXX syndrome, mosaicism, and structural variations [13].

Therefore, in this clinical case report, we present a case of mixed gonadal dysgenesis (MGD) with mosaicism (mos 46,X, idic(Y)(q12)[9]/45,X[6]) in a child who underwent consultation at the age of 8 months, with a male sex designation recorded in the civil registry.

## 2. Case Presentation

The subject of this study was a child named OKA, of undetermined sex, born on April 15, 2022, and admitted at the age of 8 months to Hospital Saint Camille de Ouagadougou, Burkina Faso, due to a disorder of sexual development. The child OKA exhibited signs of mixed gonadal dysgenesis, with a karyotype showing mosaicism: mos 46,X, idic(Y)(q12)[9]/45,X[6].

OKA is the sole offspring of his parents and the result of a pregnancy without pathological particularities. No genetic antecedents are known to be involved in either the father's or mother's family. A disorder of sexual differentiation was identified at birth, leading to the assignment of a gender-neutral first name. On May 27, 2022, at the age of one month, the child underwent inguino-scrotal hernia repair.

Upon admission, psychomotor development was normal for OKA's age, and growth was according to the staturoponderal growth curve. Anthropometric parameters, including weight (6.9 kg), height (66 cm), and arm circumference (13 mm), were within the normal range, though the weight-height index was slightly below the median. Physical examination of the external genitalia revealed labia majora, a micropenis in place of the clitoris, and the presence of a scrotum (**Figure 1** and **Figure 2**).

These findings prompted the performance of further paraclinical examinations. An abdomino-pelvic ultrasound aimed at identifying internal genitalia concluded

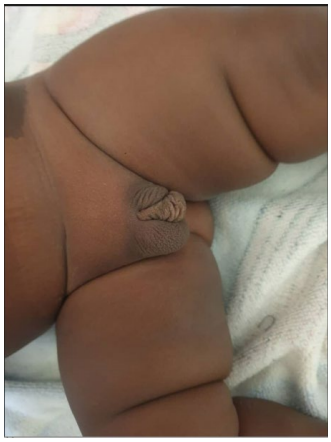

**Figure 1.** Visual inspection of genital organ phenotype in the OKA child. Absence of a visible penis. Presence of labia majora and scrotum. Source: Prof. TM Zohoncon

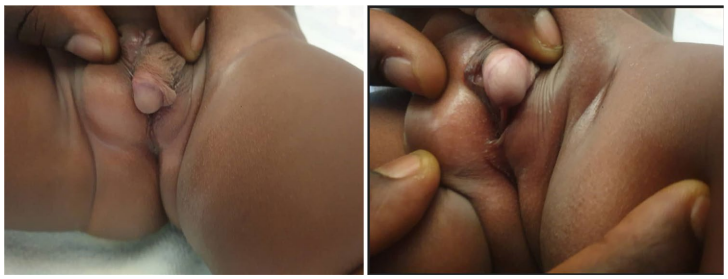

**Figure 2.** Phenotypic visualization of concealed micropenes in OKA children. Observation of labia majora with a micropenis in place of the clitoris. Source: Prof. TM Zohoncon

with the diagnosis of bilateral cryptorchidism, accompanied by an uncomplicated right inguino-scrotal hernia. The testicles were observed to be positioned within the inguinal region, displaying normal size and uniform, well-vascularized echogenicity in color Doppler, measuring 10 × 5 mm on the right and 12 × 5 mm on the left. A parietal defect in the right inguinal area, allowing a small loop to pass through the mobile right bursa during exertion, was also visualized. No visualization of female genitalia (such as the uterus or ovaries) was observed during the examination.

As part of the management plan, orchidopexy was performed, and biopsies were taken during the procedure to evaluate the histological composition of the testes. The biopsy showed a macroscopic appearance of a 0.3 cm greyish biopsy fragment. Microscopic examination revealed testicular parenchyma consisting of Sertoli tubes of variable size, with no germline cells. These tubes are distributed within fibrotic interstitial tissue. Leydigian islets were absent. Overall, the biopsy showed a histological appearance of immature testicular tissue. Further follow-up included ultrasound monitoring to detect early signs of gonadal dysgenesis or tumorigenesis.

## 3. Methodology

The postnatal constitutional karyotype was performed on 5 mL of peripheral venous

whole blood collected from the OKA child in a sterile lithium heparin vacutainer tube. The karyotype, conducted using conventional techniques, was supplemented with fluorescence in situ hybridization (FISH), a molecular cytogenetic technique, to identify chromosomal rearrangements or detect submicroscopic chromosomal abnormalities. Through a fee-for-service agreement, Hôpital Saint Camille de Ouagadougou (HOSCO) sent the sample to the Centre d'Études et de Recherches en Biologie Appliquée (CERBA) in France for cytogenetic and FISH analysis. The study protocol was approved by the Institutional Ethics Committee of Hôpital Saint Camille de Ouagadougou (HOSCO) under deliberation no. 2022-12-010 dated December 8, 2022. Written informed consent was obtained from the parents prior to AKO's inclusion in the study, and data confidentiality was maintained.

## 4. Results

Through conventional cytogenetics and molecular cytogenetics, following the ISCN 2020 nomenclature, the findings were as follows: mos 46,X, idic(Y)(q12)[9]/45,X[6].ish idic(Y)(SRY+,DYZ3++,SRY+).

The postnatal constitutional karyotype, conducted through conventional cytogenetics, exhibited two distinct cell lines: one with 46 chromosomes characterized by a rearranged Y chromosome in the form of an isodicentric structure, displaying a breakpoint and symmetry at q12 (observed in 9 out of 15 cells); and another cell line with 45 chromosomes, featuring a gonosomal formula of X (seen in 6 out of 15 cells). These observations provide an explanation for the child's presented disorders of sexual development. Further confirmation of the diagnosis was attained through FISH techniques, employing a specific probe targeting the SRY locus and the centromeric probe of the Y chromosome. The FISH study encompassed the following probes, and the number of cells examined: Loci LSI SRY in Yp11.3 and DXZ1 in Xp11.1-q11.1 (Vysis) in 10 mitoses, as well as satellite alpha probes of the X and Y chromosomes (DXZ1 and DYZ3) using XA AneuScore III (Metasystems).

Subsequent to these investigations, genetic counseling was conducted. The OKA child continues to receive care under the supervision of a pediatric surgeon. At the age of 12 months, a follow-up assessment with the pediatric surgeon was conducted, leading to the scheduling of an orchidopexy for the OKA child. Thus, in June 2024, at the age of 2, the child OKA underwent orchidopexy and a gonadal biopsy, the histological examination of which revealed immature testicular tissue. Histologically, the testicular parenchyma consisted of Sertoli cell-only tubules of varying sizes, distributed within fibrotic interstitial tissue, without germ cells; lacking Leydig cell clusters.

Chromosomal aberrations can impact the number or structure of chromosomes. Mosaicism involving 45,X/46,XY is associated with mixed gonadal dysgenesis (MGD). In this case, the presence of both 46,X,idic(Y)(q12) and 45,X cells highlights the complexity of this disorder, with the Y chromosome cell line contributing to partial testicular formation, while the 45,X cell line may result in dysgenesis. The absence of critical spermatogenic genes, such as AZFc, on the idic(Y)

chromosome could contribute to infertility in adulthood. Additionally, the risk of gonadoblastoma and dysgerminoma due to the presence of TSPY in a dysgenetic gonad necessitates ongoing monitoring through biopsy and ultrasound follow-ups.

Mosaicism, which involves both numerical and structural variations in chromosomes, can lead to disorders of sexual development (DSD). In the case of the child OKA, the postnatal constitutional karyotype and FISH analysis revealed a mosaicism pattern described as mos 46,X, idic(Y)(q12)[9]/45,X[6].ish idic(Y)(SRY+, DYZ3++, SRY+), following the ISCN 2020 nomenclature. This pattern reveals the presence of two distinct cell lines: one with 46 chromosomes, featuring a rearranged Y chromosome with a breakpoint at q12, and another with 45 chromosomes, with a gonosomal formula of X. Notably, the child is SRY+ and presents with cryptorchidism and hypospadias. The manifestation of masculine traits is frequently seen in SRY-positive patients [14].

Several scenarios can give rise to discrepancies between chromosomal, gonadal, and phenotypic sexes. One such scenario is the emergence of an isodicentric Y chromosome, as seen in this case. This occurs when a break happens in one of the Y chromatids during mitosis or meiosis, followed by fusion of the broken ends of sister chromatids. This process can result in a mosaicism pattern involving the loss of the Y chromosome in some cells, leading to a 45,X cell line [6]. The presence of 45,X cells contributes to gonadal dysgenesis, while the presence of 46,X,idic(Y) cells results in partial testicular formation.

Beyond the case of mosaicism in OKA, it shows that a significant proportion, ranging from 80% to 90%, of 46,XX males arise from a Y-to-X translocation event during meiosis [14]. Interestingly, the development of testes can occur even in the absence of the SRY gene, leading to categorization into SRY-positive and SRY-negative groups. The SRY gene plays a crucial role as the primary regulator of the testis determination pathway, governing the expression of SOX9 within Sertoli cell precursors. Some 46, XY DSD individuals with a mutation or deletion of the SRY gene show sex reversal leading to infertility, as a defect in this gene leads to a block in male differentiation. Also, a deletion or mutation of the SOX9 gene could cause sex reversal. Deletion of the DMRT1 gene would also cause sex reversion in XY patients presenting a female phenotype. Other genes such as SOX3, DAX1, WT1, FGF9, and SF1 are also involved in the complex sex determination cascade [14].

In the OKA child, the presence of a 45,X cell line indicates monosomy X, which often arises from paternal meiotic errors and accounts for more than 50% of reported cases. Mitotic errors can lead to mosaic patterns, as seen here [15]. Mixed gonadal dysgenesis is the most common chromosomal anomaly associated with ambiguous genitalia, frequently characterized by 45,X/46,XY mosaicism. This condition can manifest with phenotypes ranging from typical male external genitalia to ambiguous genitalia or features resembling Turner syndrome [16].

Cryptorchidism and hypospadias, as observed in the OKA child, are well-docu-

mented in other chromosomal abnormalities. In some cases, patients with a 46,XX karyotype may present with male external genitalia, often accompanied by small testes, cryptorchidism, hypospadias, azoospermia, and other conditions [14]. Table 1 presents a review of genotype-phenotype correlations in reported patients with mos 45,X/46,X, idic(Y)(q12).

The present study describes a child with a mosaic karyotype of 46,X,idic(Y)(q12)[9]/45,X[6], with phenotypic manifestations including labia majora, a micropenis in lieu of a clitoris, hypospadias, and cryptorchidism. These findings are consistent with the presence of mixed gonadal dysgenesis (MGD), a condition often associated with mosaicism involving abnormal Y chromosomes. In comparison to other cases reported in the literature, this case shares several features, while some differences can also be noted (**Table 1**).

**Table 1.** Literature review of genotype-phenotype correlations in reported patients with mos45,X/46,X,dic(Y)(q12).

| Article references | Karyotype/FISH | Phenotype | Sex | Age (years) |
|---|---|---|---|---|
| Martin DesGroseilliers *et al.* [17], 2002 | 47,X,idic(Y)(q12) × 2[123]/45,X[9] | Global psychomotor delay atrioseptal defect, radio-ulnar synostosis, bilateral fifth finger clinodactyly, premature closure of the anterior fontanel | F | 2.3 |
| Martin DesGroseilliers *et al.* [18], 2006 | 46,X,idic(Y)(q12)[226].ish idic(Y)(q12)(wcpY +,SRY + +,DYZ3 + +)/45,X[21]/47,X,idic(Y) (q12) × 2[3].ish idic(Y)(q12) × 2(wcpY +,SRY+ +,DYZ3 + +) × 2 | Dysmorphic features, mild language delay, small uterus | M | 4 |
| Willis, M. J. H *et al.* [19], 2006 | 45,X [14],/46,X, psu dic (Y)(q12)[5], (SRY + +) | Normal | M | Infant |
| James Pascual *et al.* [20], 2009 | 45,X[8]/46,X,idic(Y)(q12)[12] | Ambiguous genitalia | M | Infant |
| Melanie Beaulieu Bergeron *et al.* [21], 2011 | 46,X,idic(Y)(q12)[138]/45,X[36]/46,X,del (Y)(q12)[1] | Pure gonadal dysgenesis | F | unknown |
| Yin H *et al.* [22], 2023 | 45,X[8]/46,X,idic(Y)(q12)[32] | Short stature, mircopenis, hypospadias and cryptorchidism | M | 8 |
| Present study | 46,X,idic(Y)(q12)[9]/45,X[6] | Labia majora, a micropenis in lieu of a clitoris, hypospadias and cryptorchidism | M | Infant |

Martin DesGroseilliers *et al.* [17], 2002 reported a case of 47,X,idic(Y)(q12) × 2[123]/45,X[9], with a phenotype involving global psychomotor delay, atrioseptal defect, and radio-ulnar synostosis in a 2.3-year-old female patient. While both cases involve a mosaic karyotype with isodicentric Y chromosomes, the phenotypic differences are notable. Our case does not present with the same systemic anomalies or developmental delays, highlighting the variable expressivity of the condition. Similarly, Martin DesGroseilliers *et al.* [18], 2006 described a male patient with a 46,X,idic(Y)(q12)[226]/45,X[21] mosaicism who exhibited dysmorphic

features and mild language delay, along with a small uterus at 4 years of age. This case, unlike our patient, involved dysmorphic features and a small uterus, indicating that phenotypic presentations can range from purely genital anomalies to more systemic dysmorphisms.

In contrast, the case presented by Willis *et al.* [19], 2006 involved an infant male with a 45,X/46,X, psu dic(Y)(q12) karyotype, who showed normal physical development. This highlights a more benign presentation compared to the cryptorchidism, micropenis, and hypospadias observed in our patient. This further emphasizes the variability in clinical presentation even among patients with similar karyotypes.

The case described by James Pascual *et al.* [20], 2009 is more closely aligned with the present study. This patient, also an infant male with 45,X/46,X,idic(Y)(q12) mosaicism, exhibited ambiguous genitalia, a presentation similar to the labia majora, micropenis, and hypospadias seen in OKA. However, our patient additionally presented with cryptorchidism, which was not noted in Pascual's case, underscoring the variability in gonadal development in such cases. Beaulieu Bergeron *et al.* [21], 2011 reported a case of 46,X,idic(Y)(q12)/45,X, but the patient presented with pure gonadal dysgenesis, classified as female. This case differs significantly from our patient, as the latter exhibited male external genitalia. The variance in gonadal and external genital development between the two cases could be attributed to differences in the distribution and expression of the Y chromosome cell line. The recent case by Yin H *et al.* [22], 2023 involved a male patient with 45,X/46,X, idic(Y)(q12) mosaicism who presented with short stature, micropenis, hypospadias, and cryptorchidism. This case closely mirrors the phenotype observed in our patient, reinforcing the typical presentation of genital anomalies, including micropenis and cryptorchidism, in cases involving idic(Y) mosaicism. The similarities between these cases further substantiate the association of these phenotypic features with this chromosomal abnormality.

The care for the OKA child requires a multidisciplinary approach [23]. In countries with limited socioeconomic resources, where prenatal diagnosis is unavailable and technical capabilities are insufficient, achieving comprehensive medical and surgical management becomes challenging. One major issue is disclosing such a condition to parents at birth and providing continuous familial support as the child grows. In cases like OKA's, where both 46,X,idic(Y) and 45,X cells are present, Turner syndrome management protocols should be applied to the 45,X cell line, following current recommendations in the literature. Another concern is the potential for fertility issues during adolescence. Depending on the severity of the clinical manifestations, phenotypes such as sexual dysplasia, infertility, and behavioral disorders can manifest in cases of mosaicism [13]. Further studies are necessary to determine the exact breakpoint in the idic(Y)(q12) chromosome, particularly to understand the retention or loss of key spermatogenic regions like AZFc, which can influence fertility outcomes. In the absence of prenatal diagnosis in countries with limited resources, multidisciplinary management of DSD is

crucial to support the patient and their family throughout development [23].

## Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Ethical Approval

All procedures met the ethical standards of the responsible committee and were approved by the Institutional Ethics Committee of Saint Camille Hospital of Ouagadougou (HOSCO) in its deliberation N° 2022-12-010 of du 8/12/2022.

## Consent

The parents of the child OKA granted their free and informed consent for the genetic analyses and the publication of this clinical case. They have also given their authorization for the case description and the inclusion of the external photograph within this article.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Martinez de LaPiscina, I. and Flück, C.E. (2021) Genetics of Human Sexual Development and Related Disorders. *Current Opinion in Pediatrics*, **33**, 556-563. https://doi.org/10.1097/mop.0000000000001066

[2] Hiort, O., Birnbaum, W., Marshall, L., Wünsch, L., Werner, R., Schröder, T., *et al.* (2014) Management of disorders of sex development. *Nature Reviews Endocrinology*, **10**, 520-529. https://doi.org/10.1038/nrendo.2014.108

[3] Witchel, S.F. (2018) Disorders of Sex Development. *Best Practice & Research Clinical Obstetrics & Gynaecology*, **48**, 90-102. https://doi.org/10.1016/j.bpobgyn.2017.11.005

[4] Jost, A., Vigier, B., Prépin, J. and Perchellet, J.P. (1973) Studies on Sex Differentiation in Mammals. In: Greep, R.O., Ed., *Proceedings of the 1972 Laurentian Hormone Conference*, Elsevier, 1-41. https://doi.org/10.1016/b978-0-12-571129-6.50004-x

[5] Nagahama, Y., Chakraborty, T., Paul-Prasanth, B., Ohta, K. and Nakamura, M. (2021) Sex Determination, Gonadal Sex Differentiation, and Plasticity in Vertebrate Species. *Physiological Reviews*, **101**, 1237-1308. https://doi.org/10.1152/physrev.00044.2019

[6] Han, Y., Wu, J., Tan, F., Sha, J., Zhang, B., Zhai, J., *et al.* (2023) 45, X/46, X, Psu Idic (Y) (q11.2) Mosaicism in a Primary Amenorrhea Girl with Swyer Syndrome. *Case Reports in Genetics*, **2023**, Article ID: 9127512. https://doi.org/10.1155/2023/9127512

[7] Koopman, P., Gubbay, J., Vivian, N., Goodfellow, P. and Lovell-Badge, R. (1991) Male Development of Chromosomally Female Mice Transgenic for Sry. *Nature*, **351**, 117-121. https://doi.org/10.1038/351117a0

[8] Kim, S.S. and Kolon, T.F. (2009) Hormonal Abnormalities Leading to Disorders of

Sexual Development. *Expert Review of Endocrinology & Metabolism*, **4**, 161-172. https://doi.org/10.1586/17446651.4.2.161

[9] Hughes, I.A. (2008) Disorders of Sex Development: A New Definition and Classification. *Best Practice & Research Clinical Endocrinology & Metabolism*, **22**, 119-134. https://doi.org/10.1016/j.beem.2007.11.001

[10] Hughes, I.A., Houk, C., Ahmed, S.F. and Lee, P.A. (2006) *Journal of Pediatric Urology*, **2**, 148-162. https://doi.org/10.1016/j.jpurol.2006.03.004

[11] Bashamboo, A. and McElreavey, K. (2015) Human Sex-Determination and Disorders of Sex-Development (DSD). *Seminars in Cell & Developmental Biology*, **45**, 77-83. https://doi.org/10.1016/j.semcdb.2015.10.030

[12] McCann-Crosby, B. and Sutton, V.R. (2015) Disorders of Sexual Development. *Clinics in Perinatology*, **42**, 395-412. https://doi.org/10.1016/j.clp.2015.02.006

[13] Guo, N., Cai, M., Lin, M., Xue, H., Huang, H. and Xu, L. (2022) Positive Predictive Value of Noninvasive Prenatal Testing for Sex Chromosome Abnormalities. *Molecular Biology Reports*, **49**, 9251-9256. https://doi.org/10.1007/s11033-022-07754-x

[14] Terribile, M., Stizzo, M., Manfredi, C., Quattrone, C., Bottone, F., Giordano, D.R., *et al.* (2019) 46, XX Testicular Disorder of Sex Development (DSD): A Case Report and Systematic Review. *Medicina*, **55**, Article 371. https://doi.org/10.3390/medicina55070371

[15] Popescu-Hobeanu, G., Riza, A., Streață, I., Tudorache, Ș., Comănescu, A., Tănase, F., *et al.* (2022) Cytogenetic Analysis of Sporadic First-Trimester Miscarriage Specimens Using Karyotyping and QF-PCR: A Retrospective Romanian Cohort Study. *Genes*, **13**, Article 2246. https://doi.org/10.3390/genes13122246

[16] Carreño-Martínez, A.C., Mendoza Rojas, V.C., Gil Forero, J.A., Figueroa, V.H. and Contreras-García, G.A. (2021) 45, X/46, XY Mosaicism with Male Phenotype: Case Report. *Urologia Internationalis*, **106**, 533-536. https://doi.org/10.1159/000519368

[17] DesGroseilliers, M., Lemyre, E., Dallaire, L. and Lemieux, N. (2002) Tetrasomy Y by Structural Rearrangement: Clinical Report. *American Journal of Medical Genetics*, **111**, 401-404. https://doi.org/10.1002/ajmg.10591

[18] DesGroseilliers, M., Beaulieu Bergeron, M., Brochu, P., Lemyre, E. and Lemieux, N. (2006) Phenotypic Variability in Isodicentric Y Patients: Study of Nine Cases. *Clinical Genetics*, **70**, 145-150. https://doi.org/10.1111/j.1399-0004.2006.00654.x

[19] Willis, M.J.H., Bird, L.M., Dell'Aquilla, M. and Jones, M.C. (2006) Natural History of Prenatally Diagnosed 46, X, Isodicentric Y. *Prenatal Diagnosis*, **26**, 134-137. https://doi.org/10.1002/pd.1352

[20] Pascual, J., McMann, L.P., Gallagher, T. and Pinsker, J.E. (2009) Ambiguous Genitalia in a Newborn with 45, X/46, X, Idic(y) Ovotesticular Disorder of Sex Development. *Endocrine Practice*, **15**, 732-736. https://doi.org/10.4158/ep09060.crr

[21] Bergeron, M.B., Brochu, P., Lemyre, E. and Lemieux, N. (2011) Correlation of Intercentromeric Distance, Mosaicism, and Sexual Phenotype: Molecular Localization of Breakpoints in Isodicentric Y Chromosomes. *American Journal of Medical Genetics Part A*, **155**, 2705-2712. https://doi.org/10.1002/ajmg.a.34260

[22] Yin, H., Xie, H., Zou, J., Ye, X., Liu, Y., He, C., *et al.* (2023) A Mosaic Karyotype of 45, X/46, X, Psu Idic(Y)(q12) in a Ten-Year-Old Boy: Integrating High-Throughput Sequencing with Cytogenetic Technique for Precise Diagnosis and Genetic Counselling. *BMC Pediatrics*, **23**, Article No. 104. https://doi.org/10.1186/s12887-023-03872-y

[23] Ahmed, S.F., Achermann, J., Alderson, J., Crouch, N.S., Elford, S., Hughes, I.A., *et al.*

(2021) Society for Endocrinology UK Guidance on the Initial Evaluation of a Suspected Difference or Disorder of Sex Development (Revised 2021). *Clinical Endocrinology*, **95**, 818-840. https://doi.org/10.1111/cen.14528