# World Journal of *Clinical Cases*

World J Clin Cases 2021 April 6; 9(10): 2160-2418





Published by Baishideng Publishing Group Inc

W J C C World Journal of Clinical Cases

#### Contents

#### Thrice Monthly Volume 9 Number 10 April 6, 2021

#### **MINIREVIEWS**

2160 Tertiary peritonitis: A disease that should not be ignored Marques HS, Araújo GRL, da Silva FAF, de Brito BB, Versiani PVD, Caires JS, Milet TC, de Melo FF

#### 2170 SARS-CoV-2, surgeons and surgical masks

Khalil MI, Banik GR, Mansoor S, Alqahtani AS, Rashid H

#### **ORIGINAL ARTICLE**

#### **Case Control Study**

2181 Iguratimod promotes transformation of mononuclear macrophages in elderly patients with rheumatoid arthritis by nuclear factor-KB pathway

Liu S, Song LP, Li RB, Feng LH, Zhu H

#### **Retrospective Study**

2192 Factors associated with overall survival in early gastric cancer patients who underwent additional surgery after endoscopic submucosal dissection

Zheng Z, Bu FD, Chen H, Yin J, Xu R, Cai J, Zhang J, Yao HW, Zhang ZT

- 2205 Epidemiological and clinical characteristics of 65 hospitalized patients with COVID-19 in Liaoning, China Zhang W, Ban Y, Wu YH, Liu JY, Li XH, Wu H, Li H, Chen R, Yu XX, Zheng R
- 2218 Comprehensive clinicopathologic characteristics of intraabdominal neurogenic tumors: Single institution experience

Simsek C, Uner M, Ozkara F, Akman O, Akyol A, Kav T, Sokmensuer C, Gedikoglu G

2228 Distribution and drug resistance of pathogens in burn patients in China from 2006 to 2019 Chen H, Yang L, Cheng L, Hu XH, Shen YM

#### **Observational Study**

2238 Impact of simethicone on bowel cleansing during colonoscopy in Chinese patients Zhang H, Liu J, Ma SL, Huang ML, Fan Y, Song M, Yang J, Zhang XX, Song QL, Gong J, Huang PX, Zhang H

#### **Prospective Study**

Effect of suspension training on neuromuscular function, postural control, and knee kinematics in anterior 2247 cruciate ligament reconstruction patients

Huang DD, Chen LH, Yu Z, Chen QJ, Lai JN, Li HH, Liu G

#### **CASE REPORT**

2259 Turner syndrome with positive SRY gene and non-classical congenital adrenal hyperplasia: A case report He MN, Zhao SC, Li JM, Tong LL, Fan XZ, Xue YM, Lin XH, Cao Y



Conton	World Journal of Clinical Cases
Conten	Thrice Monthly Volume 9 Number 10 April 6, 2021
2268	Mechanical thrombectomy for acute occlusion of the posterior inferior cerebellar artery: A case report
	Zhang HB, Wang P, Wang Y, Wang JH, Li Z, Li R
2274	Bilateral retrocorneal hyaline scrolls secondary to asymptomatic congenital syphilis: A case report
	Jin YQ, Hu YP, Dai Q, Wu SQ
2281	Recurrent undifferentiated embryonal sarcoma of the liver in adult patient treated by pembrolizumab: A case report
	Yu XH, Huang J, Ge NJ, Yang YF, Zhao JY
2289	Adult onset type 2 familial hemophagocytic lymphohistiocytosis with <i>PRF1</i> c.65delC/c.163C>T compound heterozygous mutations: A case report
	Liu XY, Nie YB, Chen XJ, Gao XH, Zhai LJ, Min FL
2296	Salvage of vascular graft infections <i>via</i> vacuum sealing drainage and rectus femoris muscle flap transposition: A case report
	Zhang P, Tao FL, Li QH, Zhou DS, Liu FX
2302	Innovative chest wall reconstruction with a locking plate and cement spacer after radical resection of chondrosarcoma in the sternum: A case report
	Lin CW, Ho TY, Yeh CW, Chen HT, Chiang IP, Fong YC
2312	Changes in sleep parameters following biomimetic oral appliance therapy: A case report
	Singh GD, Kherani S
2320	Bone remodeling in sigmoid sinus diverticulum after stenting for transverse sinus stenosis in pulsatile tinnitus: A case report
	Qiu XY, Zhao PF, Ding HY, Li XS, Lv H, Yang ZH, Gong SS, Jin L, Wang ZC
2326	Prolonged use of bedaquiline in two patients with pulmonary extensively drug-resistant tuberculosis: Two case reports
	Gao JT, Xie L, Ma LP, Shu W, Zhang LJ, Ning YJ, Xie SH, Liu YH, Gao MQ
2334	Low-grade mucinous appendiceal neoplasm mimicking an ovarian lesion: A case report and review of literature
	Borges AL, Reis-de-Carvalho C, Chorão M, Pereira H, Djokovic D
2344	Granulomatosis with polyangiitis presenting as high fever with diffuse alveolar hemorrhage and otitis media: A case report
	Li XJ, Yang L, Yan XF, Zhan CT, Liu JH
2352	Primary intramedullary melanoma of lumbar spinal cord: A case report
	Sun LD, Chu X, Xu L, Fan XZ, Qian Y, Zuo DM
2357	Proliferative glomerulonephritis with monoclonal immunoglobulin G deposits in a young woman: A case report
	Xu ZG, Li WL, Wang X, Zhang SY, Zhang YW, Wei X, Li CD, Zeng P, Luan SD



Combon	World Journal of Clinical Cases
Conten	Thrice Monthly Volume 9 Number 10 April 6, 2021
2367	Nocardia cyriacigeorgica infection in a patient with pulmonary sequestration: A case report
	Lin J, Wu XM, Peng MF
2373	Long-term control of melanoma brain metastases with co-occurring intracranial infection and involuntary drug reduction during COVID-19 pandemic: A case report
	Wang Y, Lian B, Cui CL
2380	Solitary bone plasmacytoma of the upper cervical spine: A case report
	Li RJ, Li XF, Jiang WM
2386	Two-stage transcrestal sinus floor elevation-insight into replantation: Six case reports
	Lin ZZ, Xu DQ, Ye ZY, Wang GG, Ding X
2394	Programmed cell death protein-1 inhibitor combined with chimeric antigen receptor T cells in the treatment of relapsed refractory non-Hodgkin lymphoma: A case report
	Niu ZY, Sun L, Wen SP, Song ZR, Xing L, Wang Y, Li JQ, Zhang XJ, Wang FX
2400	Pancreatic cancer secondary to intraductal papillary mucinous neoplasm with collision between gastric cancer and B-cell lymphoma: A case report
	Ma YH, Yamaguchi T, Yasumura T, Kuno T, Kobayashi S, Yoshida T, Ishida T, Ishida Y, Takaoka S, Fan JL, Enomoto N
2409	Acquired haemophilia in patients with malignant disease: A case report
	Krašek V, Kotnik A, Zavrtanik H, Klen J, Zver S



#### Contents

Thrice Monthly Volume 9 Number 10 April 6, 2021

#### **ABOUT COVER**

Editorial Board Member of World Journal of Clinical Cases, Deb Sanjay Nag, Senior Consultant, Department of Anaesthesiology, Tata Main Hospital, C-Road (West), Bistupur, Jamshedpur 831 001, India. ds.nag@tatasteel.com

#### **AIMS AND SCOPE**

The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

#### **INDEXING/ABSTRACTING**

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

#### **RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yan-Xia Xing, Production Department Director: Yun-Xiaojian Wu; Editorial Office Director: Jin-Lei Wang.

NAME OF JOURNAL	INSTRUCTIONS TO AUTHORS			
World Journal of Clinical Cases	https://www.wjgnet.com/bpg/gerinfo/204			
<b>ISSN</b>	GUIDELINES FOR ETHICS DOCUMENTS			
ISSN 2307-8960 (online)	https://www.wjgnet.com/bpg/GerInfo/287			
LAUNCH DATE	GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH			
April 16, 2013	https://www.wjgnet.com/bpg/gerinfo/240			
FREQUENCY	PUBLICATION ETHICS			
Thrice Monthly	https://www.wjgnet.com/bpg/GerInfo/288			
<b>EDITORS-IN-CHIEF</b>	PUBLICATION MISCONDUCT			
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng	https://www.wjgnet.com/bpg/gerinfo/208			
EDITORIAL BOARD MEMBERS	ARTICLE PROCESSING CHARGE			
https://www.wjgnet.com/2307-8960/editorialboard.htm	https://www.wjgnet.com/bpg/gerinfo/242			
PUBLICATION DATE	STEPS FOR SUBMITTING MANUSCRIPTS			
April 6, 2021	https://www.wjgnet.com/bpg/GerInfo/239			
COPYRIGHT	ONLINE SUBMISSION			
© 2021 Baishideng Publishing Group Inc	https://www.f6publishing.com			

© 2021 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com



W J C C World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2021 April 6; 9(10): 2259-2267

DOI: 10.12998/wjcc.v9.i10.2259

ISSN 2307-8960 (online)

CASE REPORT

# Turner syndrome with positive SRY gene and non-classical congenital adrenal hyperplasia: A case report

Mei-Nan He, Shan-Chao Zhao, Ji-Min Li, Lu-Lu Tong, Xin-Zhao Fan, Yao-Ming Xue, Xiao-Hong Lin, Ying Cao

ORCID number: Mei-Nan He 0000-0001-7520-7610; Shan-Chao Zhao 0000-0002-1052-4487; Ji-Min Li 0000-0002-8893-1840; Lu-Lu Tong 0000-0001-8425-1912; Xin-Zhao Fan 0000-0002-9811-2929; Yao-Ming Xue 0000-0003-1356-4780; Xiao-Hong Lin 0000-0003-0655-8497; Ying Cao 0000-0002-8129-7621.

Author contributions: He MN,

Tong LL, and Li JM carried out the studies, participated in collecting the data, and drafted the manuscript; He MN, Cao Y, and Zhao SC performed the statistical analysis and participated in its design; Fan XZ, Xue YM, and Lin XH helped to draft the manuscript; all authors read and approved the final manuscript.

Informed consent statement:

Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to report.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an

Mei-Nan He, Ji-Min Li, Lu-Lu Tong, Xin-Zhao Fan, Yao-Ming Xue, Ying Cao, Department of Endocrinology and Metabolism, Nanfang Hospital, Southern Medical University, Guangzhou 510515, Guangdong Province, China

Shan-Chao Zhao, Department of Urology, Nanfang Hospital, Southern Medical University, Guangzhou 510515, Guangdong Province, China

Xiao-Hong Lin, Guangzhou KingMed Center for Clinical Laboratory Co., Ltd., Guangzhou 510005, Guangdong Province, China

Corresponding author: Ying Cao, MD, Doctor, Department of Endocrinology and Metabolism, Nanfang Hospital, Southern Medical University, No. 1838 Guangzhou Avenue North, Baiyun District, Guangzhou 510515, Guangdong Province, China. nfcy123@126.com

## Abstract

#### BACKGROUND

Co-morbidity of SRY gene turner syndrome (TS) with positive SRY gene and nonclassical congenital adrenal hyperplasia (NCAH) is extremely rare and has never been reported to date.

#### CASE SUMMARY

In this article, we present a 14-year-old girl who was referred to our hospital with short stature (weight of 43 kg and height of 143 cm, < -2 SD) with no secondary sexual characteristics (labia minora dysplasia). Laboratory tests indicated hypergonadotropic hypogonadism with significantly increased androstenedione and 17-hydroxyprogesterone (17-OHP) levels. This was accompanied by the thickening of the extremity of the left adrenal medial limb. The patient's karyotype was 45,X/46,X, +mar, and cytogenetic analysis using multiplex ligation-dependent probe amplification and high-throughput sequencing indicated that the SRY gene was positive with compound heterozygous mutations in CYP21A2 as the causative gene for congenital adrenal hyperplasia. The sites of the suspected candidate mutations were amplified and verified using Sanger sequencing. The patient was finally diagnosed as having SRY positive TS with NCAH. The patient and her family initially refused medical treatment. At her most recent follow-up visit (age = 15 years old), the patient presented facial hair, height increase to 148 cm, and weight of 52 kg, while androstenedione and 17-OHP levels remained high. The patient was finally willing to take small doses of hydrocortisone (10 mg/d).



WJCC | https://www.wjgnet.com

open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: htt p://creativecommons.org/License s/by-nc/4.0/

Manuscript source: Unsolicited manuscript

Specialty type: Medicine, research and experimental

Country/Territory of origin: China

#### Peer-review report's scientific quality classification

Grade A (Excellent): 0 Grade B (Very good): B Grade C (Good): 0 Grade D (Fair): 0 Grade E (Poor): 0

Received: August 29, 2020 Peer-review started: August 29, 2020 First decision: December 28, 2020 Revised: January 10, 2021 Accepted: January 27, 2021 Article in press: January 27, 2021 Published online: April 6, 2021

P-Reviewer: Reyes TME S-Editor: Fan JR L-Editor: Wang TQ P-Editor: Xing YX



#### **CONCLUSION**

In conclusion, upon evaluation of the patient mentioned in the report, we feel that 17-OHP measurement and cytogenetic analysis are necessary for TS patients even in the absence of significant virilization signs. This will play a significant role in guiding diagnosis and treatment.

Key Words: Turner syndrome; SRY gene; Congenital adrenal hyperplasia; Tumor; Diagnosis; Endocrinology and metabolism; Case report

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: This paper reports a 14-year-old girl who was diagnosed with non-classical congenital adrenal hyperplasia (NCAH) and turner syndrome (TS) with a positive SRY gene concurrently. The combination of these three factors increases the difficulty of diagnosis and treatment but provides insights into the understanding of TS. At the same time, in the diagnosis of TS, in addition to karyotype analysis, physical examination of virilization characteristics, 17-hydroxyprogesterone detection, and even cytogenetic analysis are of vital importance, which are helpful for clinicians to identify the diagnosis and treatment of the disease and avoid missed diagnosis and misdiagnosis. This report expands clinicians' understanding of TS and NCAH.

Citation: He MN, Zhao SC, Li JM, Tong LL, Fan XZ, Xue YM, Lin XH, Cao Y. Turner syndrome with positive SRY gene and non-classical congenital adrenal hyperplasia: A case report. World J Clin Cases 2021; 9(10): 2259-2267

URL: https://www.wjgnet.com/2307-8960/full/v9/i10/2259.htm DOI: https://dx.doi.org/10.12998/wjcc.v9.i10.2259

## INTRODUCTION

Turner syndrome (TS) is the most common chromosomal abnormality in females. It has a prevalence of 1:2500, which approximates to 3% of live female births and approximately 15% of miscarriages<sup>[1,2]</sup>. TS patients are characterized by short stature, broad chest, low posterior hairline, prominent ears, narrow and acutely arched palate, lack of pubertal onset at adolescence, and presence of streak ovaries with normal intelligence<sup>[3]</sup>. Monosomy X is the most common karyotype observed in patients with TS (50%-60%), in addition to other structural abnormalities in the X chromosome or mosaicism karyotype reported<sup>[4-6]</sup>. Additionally, the presence of Y chromosome material has been reported in about 10%-18% of patients. The role of the Y chromosome in human tumorigenesis remains controversial. However, the risk of virilization during puberty, gonadoblastoma, and malignant transformation increases by 7%-10% when Y chromosome material is present in gonadal tissue or peripheral blood in TS patients<sup>[4,7,8]</sup>.

Non-classical congenital adrenal hyperplasia (NCAH) is a common autosomal recessive disorder that manifests due to P450c21 (21-hydroxylase) deficiency. NCAH is caused by mutations in the CYP21A2 gene or microconversions between CYP21 pseudogenes and active genes<sup>[9,10]</sup>. The disorder is a mild form of congenital adrenal hyperplasia (CAH) and may result in infertility, miscarriages, oligomenorrhea, hirsutism, acne, advanced bone age, and clitoromegaly in females. 17hydroxyprogesterone (17-OHP) levels could be used for diagnosis, but the gold standard is the adrenocorticotropic hormone (ACTH) stimulation test and 17-OHP measurement based on several studies and guidelines. However, the optimal cutoff for baseline 17-OHP levels or post-ACTH peak 17-OHP levels for NCAH diagnosis remains controversial<sup>[11-14]</sup>. Based on a large data set in combination with genetic diagnosis, NCAH could be diagnosed using baseline 17-OHP levels > 6 nmol/L or > 30 nmol/L after ACTH stimulation<sup>[13,14]</sup>. The diagnosis could be substantiated using CYP21A2 mutation analysis. In contrast to CAH patients, the majority of patients with NCAH are never diagnosed due to very mild symptoms. In addition, compared to the majority of patients with classic CAH requiring life-long glucocorticoid treatment for survival, NCAH patients are seldom diagnosed and treated only when



#### symptomatic<sup>[15]</sup>.

The diagnosis of CAH is difficult in females with TS. This is because of the shared common clinical features like short stature, amenorrhea, and infertility and the rare reports of the condition. Moreover, patients with a combination of TS with a positive SRY gene and NCAH have never been reported. In this article, we present a 14-yearold girl who was diagnosed with NCAH and TS with a positive SRY gene concurrently. The combination of these three factors increases the difficulty of diagnosis and treatment but provides insights into the understanding of TS. It also suggests that 17-OHP together with genetic screening is necessary for TS patients.

#### CASE PRESENTATION

#### Chief complaints

A 14-year-old girl was referred to our hospital with growth and developmental retardation.

#### History of present illness

Based on her medical history, the patient was born after a normal full-term delivery and her parents were not genetically related. She appeared to be in good health. Her height and weight were 51 cm and 3.2 kg, respectively, at birth. However, her growth rate was slow (1 cm/year) and her height was 143 cm at age 12 years (< -2 SD), which was significantly lower than normal when she visited our hospital.

#### Physical examination

On physical examination, the patient's general status was good, her vital signs were stable, and no masculine features such as hirsutism, acne, and clitoromegaly were observed. Axillary and pubic hair was absent. Breast and labia minora dysplasia was observed.

#### Laboratory examinations

Biochemistry and electrolyte analysis showed no abnormalities (Table 1). Hormone profiles indicated hypergonadotropic hypogonadism, and karyotype analysis indicated 45,X/46,X, +mar, and mosaicism with suspected Y chromosome material (Figure 1).

#### Imaging examinations

Ultrasonic gynecopathy examinations and pelvic magnetic resonance showed no development of the uterus or ovaries (Figure 2).

#### **FINAL DIAGNOSIS**

The patient's final diagnosis was SRY positive TS with NCAH.

#### TREATMENT

The patient initially refused medical treatment. At the most recent follow-up visit (one year later), the patient finally accepted low doses of hydrocortisone (10 mg/d).

#### OUTCOME AND FOLLOW-UP

At the most recent follow-up visit (patient's age was 15 years old), the electrolytes were normal. However, the patient had facial hair, her height increased to 148 cm, and her weight was 52 kg, with androstenedione and 17-OHP levels remaining high (Table 1). Human chorionic gonadotropin (HCG) stimulation test showed absence of Leydig cell function (Table 2). We will continue to follow the patient for therapeutic effects.

WJCC | https://www.wjgnet.com

#### He MN et al. SRY positive TS with NCAH

Table 1 Patient electrolyte and hormone profile								
Parameter	First visit	Follow-up (after 1 yr)	Reference range					
Serum sodium, mmol/L	138	140	135-145					
Serum potassium, mmol/L	3.82	4.38	3.50-5.30					
Serum chloride, mmol/L	102.9	103.9	137-147					
Serum calcium, mmol/L	2.40	2.40	2.20-2.65					
Serum phosphorus, mmol/L	1.36	1.40	0.81-1.45					
Serum magnesium, mmol/L	0.78	0.80	0.77-1.03					
Follicle stimulating hormone, mIU/mL	60.86	60.83	3.50-12.50					
Luteinizing hormone, mIU/mL	19.98	23.88	2.40-12.60					
Estradiol, pg/mL	< 5.00	11.96	12.40-233.00					
Progesterone, ng/mL	0.101	0.722	0.00-0.89					
Testosterone, ng/mL	0.200	0.310	0.025-0.481					
Free testosterone, pg/mL	3.48	4.12	0.00-4.20					
17Hydroxyprogesterone, ng/mL (first time)	24.70	27.26	0.05-1.02					
17Hydroxyprogesterone, ng/mL (second time)	12.10	-	0.05-1.02					
Dehydroepiandrosterone, µg/dL	4.15	4.77	4.30-22.40					
Androstenedione, ng/mL	7.12	8.18	0.30-3.30					
Adrenocorticotropic hormone, pg/mL	39.74	51.06	7.20-63.30					
Cortisol (8:00), nmol/L	15.32	13.20	1.65-9.23					
Cortisol (16:00), nmol/L	4.96	-	3.44-16.76					
Cortisol (0:00), nmol/L	1.83	-	-					
AMH, ng/mL	< 0.06	-	-					

AMH: Anti-Mullerian hormone.

Table 2 Human chorionic gonadotropin stimulation test results								
Parameter	0 min	24 h	48 h	72 h				
Testosterone, ng/mL	0.250	0.300	0.260	0.290				
Androstenedione, mmol/L	8.18	-	-	4.86				
Dihydrotestosterone	35.59	-	-	28.90				

#### DISCUSSION

As mentioned previously, CAH diagnosis is difficult in females with TS. The majority of previously reported cases with concomitant TS and CAH were diagnosed as TS. They had ambiguous genitalia or their NCAH was misdiagnosed as TS<sup>[9,16-26]</sup>. Although our patient was of short stature with no virilization signs and ambiguous genitalia, Larizza *et al*<sup>[21]</sup> reported that the frequencies of both abnormal 17-OHP response to ACTH stimulation test and CYP21 gene mutation carriers were prominently higher in patients with TS than in healthy controls. Next, Linglart *et al*<sup>[27]</sup> found that the proportion of 21-hydroxylase deficiency carriers in TS patients was up to 21.6%, which was significantly higher than that in the general Italian population<sup>[27]</sup>. Based on previous studies and the labia minora dysplasia observed in our patient, we measured 17-OHP levels and performed karyotyping and cytogenetic analysis. Our results demonstrated that 17-OHP levels were significantly increased and karyotype and cytogenetic analysis demonstrated 45,X/46,X, +mar with a positive SRY gene with compound heterozygous mutations in CYP21A2, suggesting it to be the causative gene for CAH.



Baishidena® WJCC | https://www.wjgnet.com



Figure 1 Computed tomography scan and Karyotype analysis indicated 45,X/46,X, +mar, and mosaicism with suspected Y chromosome material. A-D: Magnetic resonance imaging showed no uterus or ovary; E: Computed tomography of the adrenal gland indicated left adrenal hyperplasia; F: The patient's karyotype is 45,X/46,X, +mar.

The reason for the absence of typical clinical manifestations despite the presence of the causative gene mutation for CAH is the wide phenotypic variability of the nonclassical form. This is due to different enzymatic activity levels induced by several gene mutations in the CYP21A2, as well as microconversions between CYP21 pseudogenes and active genes<sup>[25]</sup>. To-date, > 200 CYP21A2 inactivating mutations have been recorded in the Human Gene Mutation Database (www.hgmd.org). New et al<sup>[26]</sup> extensively investigated the genotype-phenotype correlation in 1507 patients with CAH and demonstrated the presence of genotype-phenotype discordance. Moura-Massari et al<sup>[28]</sup> investigated the correlation between genotypes and the severity of hyperandrogenic phenotype in a cohort of 114 NCAH patients. Their results demonstrated that CYP21A2 genotypes do not predict the severity of hyperandrogenic manifestation in the non-classical form of CAH<sup>[28]</sup>.

Gonadal dysgenesis observed in TS patients is associated with gonadoblastomas and malignant transformation when Y-chromosome-derived genetic material is present in the genome<sup>[4]</sup>. If the presence of Y chromosome fragments in TS patients







Figure 2 The sequences of the patients and her parents. A, C, and E: The patient's sequence; B and D: The sequence of the patient's father; F: The sequence of the patient's mother.

> could be detected at an early stage, the incidence of gonadoblastomas could be reduced or even prevented. Treatment of TS could be guided with prophylactic gonadectomy considered<sup>[29]</sup>.

Regrettably, our patient refused laparoscopic exploration to further determine the



Raishideng® WJCC | https://www.wjgnet.com

presence and nature of gonadal tissue and determine whether she was at risk for gonadoblastoma. HCG stimulation test showed the absence of Leydig cell function. We will assess disease progression during follow-up.

#### CONCLUSION

In conclusion, upon evaluation of the patient mentioned in the report, we feel that 17-OHP measurement and cytogenetic analysis are necessary for TS patients even in the absence of significant virilization signs. This will play a significant role in guiding diagnosis and treatment.

#### ACKNOWLEDGEMENTS

The authors are grateful to Professors Ying Cao, Shan-Chao Zhao, and Yao-Ming Xue for their assistance in providing insights to the diagnosis and reviewing this manuscript. In addition, we are thankful to Jin-Min Li, Lu-Lu Tong, and Xin-Zhao Fang who were involved in the patient's care and cytogenetic analysis. We also thank the patient and her family for their cooperation and permission.

#### REFERENCES

- Kurnaz E, Çetinkaya S, Savaş-Erdeve Ş, Aycan Z. Detection of the SRY gene in patients with Turner 1 Syndrome. J Gynecol Obstet Hum Reprod 2019; 48: 265-267 [PMID: 30685428 DOI: 10.1016/j.jogoh.2019.01.012]
- Ibrahim MN, Laghari TM, Hanif MI, Khoso ZA, Riaz M, Raza J. Comparison of Classical and Non-2 Classical Turner Syndrome at NICH Karachi. J Coll Physicians Surg Pak 2018; 28: 840-843 [PMID: 30369375 DOI: 10.29271/jcpsp.2018.11.840]
- Kavoussi SK, Christman GM, Smith YR. Healthcare for adolescents with Turner syndrome. J Pediatr 3 Adolesc Gynecol 2006; 19: 257-265 [PMID: 16873029 DOI: 10.1016/j.jpag.2006.05.012]
- 4 Baer TG, Freeman CE, Cujar C, Mansukhani M, Singh B, Chen X, Abellar R, Oberfield SE, Levy B. Prevalence and Physical Distribution of SRY in the Gonads of a Woman with Turner Syndrome: Phenotypic Presentation, Tubal Formation, and Malignancy Risk. Horm Res Paediatr 2017; 88: 291-297 [PMID: 28618411 DOI: 10.1159/000477240]
- Bispo AV, Dos Santos LO, Burégio-Frota P, Galdino MB, Duarte AR, Leal GF, Araújo J, Gomes B, 5 Soares-Ventura EM, Muniz MT, Santos N. Effect of chromosome constitution variations on the expression of Turner phenotype. Genet Mol Res 2013; 12: 4243-4250 [PMID: 23546984 DOI: 10.4238/2013.March.13.13
- 6 Saenger P, Wikland KA, Conway GS, Davenport M, Gravholt CH, Hintz R, Hovatta O, Hultcrantz M, Landin-Wilhelmsen K, Lin A, Lippe B, Pasquino AM, Ranke MB, Rosenfeld R, Silberbach M; Fifth International Symposium on Turner Syndrome. Recommendations for the diagnosis and management of Turner syndrome. J Clin Endocrinol Metab 2001; 86: 3061-3069 [PMID: 11443168 DOI: 10.1210/jcem.86.7.7683]
- 7 Gravholt CH, Fedder J, Naeraa RW, Müller J. Occurrence of gonadoblastoma in females with Turner syndrome and Y chromosome material: a population study. J Clin Endocrinol Metab 2000; 85: 3199-3202 [PMID: 10999808 DOI: 10.1210/jcem.85.9.6800]
- Freriks K, Timmers HJ, Netea-Maier RT, Beerendonk CC, Otten BJ, van Alfen-van der Velden JA, Traas MA, Mieloo H, van de Zande GW, Hoefsloot LH, Hermus AR, Smeets DF. Buccal cell FISH and blood PCR-Y detect high rates of X chromosomal mosaicism and Y chromosomal derivatives in patients with Turner syndrome. Eur J Med Genet 2013; 56: 497-501 [PMID: 23933507 DOI: 10.1016/j.ejmg.2013.07.008]
- Mishra VV, Pritti K, Aggarwal R, Choudhary S. Nonclassic congenital adrenal hyperplasia 9 misdiagnosed as Turner syndrome. J Hum Reprod Sci 2015; 8: 239-241 [PMID: 26751945 DOI: 10.4103/0974-1208.170416
- Araújo RS, Mendonca BB, Barbosa AS, Lin CJ, Marcondes JA, Billerbeck AE, Bachega TA. 10 Microconversion between CYP21A2 and CYP21A1P promoter regions causes the nonclassical form of 21-hydroxylase deficiency. J Clin Endocrinol Metab 2007; 92: 4028-4034 [PMID: 17666484 DOI: 10.1210/jc.2006-2163
- 11 Trapp CM, Oberfield SE. Recommendations for treatment of nonclassic congenital adrenal hyperplasia (NCCAH): an update. Steroids 2012; 77: 342-346 [PMID: 22186144 DOI: 10.1016/i.steroids.2011.12.009
- 12 Speiser PW, Azziz R, Baskin LS, Ghizzoni L, Hensle TW, Merke DP, Meyer-Bahlburg HF, Miller WL, Montori VM, Oberfield SE, Ritzen M, White PC; Endocrine Society. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice



guideline. *J Clin Endocrinol Metab* 2010; **95**: 4133-4160 [PMID: 20823466 DOI: 10.1210/jc.2009-2631]

- 13 Livadas S, Dracopoulou M, Dastamani A, Sertedaki A, Maniati-Christidi M, Magiakou AM, Kanaka-Gantenbein C, Chrousos GP, Dacou-Voutetakis C. The spectrum of clinical, hormonal and molecular findings in 280 individuals with nonclassical congenital adrenal hyperplasia caused by mutations of the CYP21A2 gene. *Clin Endocrinol (Oxf)* 2015; 82: 543-549 [PMID: 25041270 DOI: 10.1111/cen.12543]
- 14 Savaş-Erdeve Ş, Çetinkaya S, Abalı ZY, Poyrazoğlu Ş, Baş F, Berberoğlu M, Sıklar Z, Korkmaz Ö, Buluş D, Akbaş ED, Güran T, Böber E, Akın O, Yılmaz GC, Aycan Z. Clinical, biochemical and genetic features with nonclassical 21-hydroxylase deficiency and final height. *J Pediatr Endocrinol Metab* 2017; 30: 759-766 [PMID: 28672743 DOI: 10.1515/jpem-2017-0088]
- 15 Falhammar H, Nordenström A. Nonclassic congenital adrenal hyperplasia due to 21-hydroxylase deficiency: clinical presentation, diagnosis, treatment, and outcome. *Endocrine* 2015; 50: 32-50 [PMID: 26082286 DOI: 10.1007/s12020-015-0656-0]
- 16 Maciel-Guerra AT, Guerra G Jr, Marini SH, Matias Baptista MT, Marques-de-Faria AP. Female pseudohermaphroditism due to classical 21-hydroxylase deficiency in a girl with Turner syndrome. *Clin Genet* 1997; **51**: 351-353 [PMID: 9212186 DOI: 10.1111/j.1399-0004.1997.tb02487.x]
- 17 Atabek ME, Kurtoğlu S, Keskin M. Female pseudohermaphroditism due to classical 21-hydroxylase deficiency and insulin resistance in a girl with Turner syndrome. *Turk J Pediatr* 2005; 47: 176-179 [PMID: 16052861]
- 18 del Arbol JL, Soto Más JA, Fernández-Abril JA, Raya Muñoz J, Martínez Tormo F, Gómez Rodríguez J, Gómez Capilla JA, Peña Yáñez A. [Turner syndrome caused by deletion of the long arm of the X chromosome associated with adrenogenital syndrome caused by partial deficiency of 21hydroxylase]. *Rev Clin Esp* 1983; 171: 67-71 [PMID: 6606833]
- 19 Montemayor-Jauregui MC, Ulloa-Gregori AO, Flores-Briseño GA. Associated adrenogenital and Turner's syndrome mosaicism. *Plast Reconstr Surg* 1985; 75: 877-881 [PMID: 4001208 DOI: 10.1097/00006534-198506000-00021]
- 20 Cohen MA, Sauer MV, Lindheim SR. 21-hydroxylase deficiency and Turner's syndrome: a reason for diminished endometrial receptivity. *Fertil Steril* 1999; 72: 937-939 [PMID: 10561003 DOI: 10.1016/s0015-0282(99)00378-7]
- 21 Larizza D, Cuccia M, Martinetti M, Maghnie M, Dondi E, Salvaneschi L, Severi F. Adrenocorticotrophin stimulation and HLA polymorphisms suggest a high frequency of heterozygosity for steroid 21-hydroxylase deficiency in patients with Turner's syndrome and their families. *Clin Endocrinol (Oxf)* 1994; 40: 39-45 [PMID: 8306479 DOI: 10.1111/j.1365-2265.1994.tb02441.x]
- 22 Jia HY, Sun SY, Chen YH, Yang ZW, Zhang J, Qi Y, Zhang YW, Wang WQ, Ning G. A case of 21hydroxylase deficiency in Turner's syndrome and literature review. *Zhonghua Neifenmi Daixie Zazhi* 2017; 33: 760-764 [DOI: 10.3760/cma.j.issn.1000-6699.2017.09.011]
- 23 Kendirci HN, Aycan Z, Çetinkaya S, Baş VN, Ağladıoğlu SY, Önder A. A rare combination: congenital adrenal hyperplasia due to 21 hydroxylase deficiency and Turner syndrome. J Clin Res Pediatr Endocrinol 2012; 4: 213-215 [PMID: 23261864 DOI: 10.4274/jcrpe.767]
- 24 Lee KF, Chan AO, Fok JM, Mak MW, Yu KC, Lee KM, Shek CC. Late presentation of simple virilising 21-hydroxylase deficiency in a Chinese woman with Turner's syndrome. *Hong Kong Med J* 2013; 19: 268-271 [PMID: 23732434 DOI: 10.12809/hkmj133717]
- 25 Fu R, Lu L, Jiang J, Nie M, Wang X, Lu Z. A case report of pedigree of a homozygous mutation of the steroidogenic acute regulatory protein causing lipoid congenital adrenal hyperplasia. *Medicine* (*Baltimore*) 2017; 96: e6994 [PMID: 28538409 DOI: 10.1097/MD.00000000006994]
- 26 New MI, Abraham M, Gonzalez B, Dumic M, Razzaghy-Azar M, Chitayat D, Sun L, Zaidi M, Wilson RC, Yuen T. Genotype-phenotype correlation in 1,507 families with congenital adrenal hyperplasia owing to 21-hydroxylase deficiency. *Proc Natl Acad Sci USA* 2013; 110: 2611-2616 [PMID: 23359698 DOI: 10.1073/pnas.1300057110]
- Linglart A, Cabrol S, Berlier P, Stuckens C, Wagner K, de Kerdanet M, Limoni C, Carel JC, Chaussain JL; French Collaborative Young Turner Study Group. Growth hormone treatment before the age of 4 years prevents short stature in young girls with Turner syndrome. *Eur J Endocrinol* 2011; 164: 891-897 [PMID: 21398400 DOI: 10.1530/EJE-10-1048]
- 28 Moura-Massari VO, Bugano DD, Marcondes JA, Gomes LG, Mendonca BB, Bachega TA. CYP21A2 genotypes do not predict the severity of hyperandrogenic manifestations in the nonclassical form of congenital adrenal hyperplasia. *Horm Metab Res* 2013; 45: 301-307 [PMID: 23322511 DOI: 10.1055/s-0032-1330007]
- 29 Hersmus R, Stoop H, Turbitt E, Oosterhuis JW, Drop SL, Sinclair AH, White SJ, Looijenga LH. SRY mutation analysis by next generation (deep) sequencing in a cohort of chromosomal Disorders of Sex Development (DSD) patients with a mosaic karyotype. *BMC Med Genet* 2012; 13: 108 [PMID: 23157850 DOI: 10.1186/1471-2350-13-108]

WJCC | https://www.wjgnet.com



## Published by Baishideng Publishing Group Inc 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA Telephone: +1-925-3991568 E-mail: bpgoffice@wjgnet.com Help Desk: https://www.f6publishing.com/helpdesk https://www.wjgnet.com

