

# World Journal of *Clinical Cases*

*World J Clin Cases* 2020 February 26; 8(4): 652-853





### OPINION REVIEW

- 652 Fear can be more harmful than the severe acute respiratory syndrome coronavirus 2 in controlling the corona virus disease 2019 epidemic  
*Ren SY, Gao RD, Chen YL*

### ORIGINAL ARTICLE

#### Clinical and Translational Research

- 658 Identification of key genes and pathways in gastric signet ring cell carcinoma based on transcriptome analysis  
*Zhao ZT, Li Y, Yuan HY, Ma FH, Song YM, Tian YT*

#### Case Control Study

- 670 Risk factors for postoperative sepsis in patients with gastrointestinal perforation  
*Xu X, Dong HC, Yao Z, Zhao YZ*
- 679 Clinical observation of soft palate-pharyngoplasty in the treatment of obstructive sleep apnea hypopnea syndrome in children  
*Ding XX, Zhao LQ, Cui XG, Yin Y, Yang HA*
- 689 Application of positive behavior management in patients after breast cancer surgery  
*Hao YJ, Sun HB, Li HW, Chen BJ, Chen XL, Ma L, Li YL*

#### Retrospective Study

- 700 Breast non-mass-like lesions on contrast-enhanced ultrasonography: Feature analysis, breast image reporting and data system classification assessment  
*Xu P, Yang M, Liu Y, Li YP, Zhang H, Shao GR*
- 713 Risk factors for long-term prognosis of hepatocellular carcinoma patients after anatomic hepatectomy  
*Tian YL, Ji JJ, Chen LN, Cui XL, Liu ST, Mao L, Qiu YD, Li BB*
- 723 Upper esophageal sphincter abnormalities on high-resolution esophageal manometry and treatment response of type II achalasia  
*Huang CZ, Huang ZW, Liang HM, Wang ZJ, Guo TT, Chen YP*
- 736 Effectiveness of surgical resection for complicated liver cancer and its influencing factors: A retrospective study  
*Yu J, Wu ZZ, Li T, Xu Y, Zhao YC, Zhang BL, Tian H*

**Observational Study**

- 743 Effectiveness of a microabrasion technique using 16% HCL with manual application on fluorotic teeth: A series of studies  
*Nevárez-Rascón M, Molina-Frechero N, Edith A, Almeida E, Soto-Barreras U, Gaona E, Nevárez-Rascón A*
- 757 Prevalence and associated factors of suicide among hospitalized schizophrenic patients  
*Woottituk P, Maneeton B, Jaiyen N, Khemawichanurat W, Kawilapat S, Maneeton N*

**SYSTEMATIC REVIEW**

- 771 Lymphoepithelioma-like carcinoma of the upper urinary tract: A systematic review of case reports  
*Lai SC, Seery S, Zhang W, Liu M, Zhang G, Wang JY*

**CASE REPORT**

- 782 Extrapleural solitary fibrous tumor of the thyroid gland: A case report and review of literature  
*Suh YJ, Park JH, Jeon JH, Bilegsaikhan SE*
- 790 Must pilots permanently quit flying career after treatment for colorectal cancer? - Medical waiver for Air Force pilots with colorectal cancer: Three case reports  
*Gu GL, Duan FX, Zhang Z, Wei XM, Cui L, Zhang B*
- 798 Mesenteric phleboscrosis with amyloidosis in association with the long-term use of medicinal liquor: A case report  
*Hu YB, Hu ML, Ding J, Wang QY, Yang XY*
- 806 Using Materialise's interactive medical image control system to reconstruct a model of a patient with rectal cancer and situs inversus totalis: A case report  
*Chen T, Que YT, Zhang YH, Long FY, Li Y, Huang X, Wang YN, Hu YF, Yu J, Li GX*
- 815 Delayed right coronary ostial obstruction after J-valve deployment in transcatheter aortic valve implantation: A case report  
*Xu Z, Yu H, Liang P*
- 820 Diverticulum of the buccal mucosa: A case report  
*Zhang Y, Wang L, Liu K*
- 825 Borderline form of empty follicle syndrome treated with a novel dual trigger method combined with delayed oocyte retrieval: A case report  
*Cao XL, Sun ZG*
- 831 Ligament augmentation reconstruction system artificial ligaments in patellar tendon reconstruction - a chronic patellar tendon rupture after multiple operations: A case report  
*Yang F, Wang GD, Huang R, Ma H, Zhao XW*

- 838** Thyroid metastasis from breast cancer presenting with enlarged lateral cervical lymph nodes: A case report  
*Zhang YY, Xue S, Wang ZM, Jin MS, Chen ZP, Chen G, Zhang Q*
- 848** Rescue treatment and follow-up intervention of a left main acute myocardial infarction with typical carina shift under 3D optical coherence tomography: A case report  
*Du BB, Tong YL, Wang XT, Liu GH, Liu K, Yang P, He YQ*

**ABOUT COVER**

Editor-in-Chief of *World Journal of Clinical Cases*, Sandro Vento, MD, Dean, Full Professor, Faculty of Medicine, University of Puthisastra, Phnom Penh, Cambodia

**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 PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2019 Edition of Journal Citation Reports cites the 2018 impact factor for WJCC as 1.153 (5-year impact factor: N/A), ranking WJCC as 99 among 160 journals in Medicine, General and Internal (quartile in category Q3).

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Responsible Electronic Editor: Ji-Hong Liu

Proofing Production Department Director: Xiang Li

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Semimonthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Bao-Gan Peng, Sandro Vento

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**EDITORIAL OFFICE**

Jin-Lei Wang, Director

**PUBLICATION DATE**

February 26, 2020

**COPYRIGHT**

© 2020 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

# Borderline form of empty follicle syndrome treated with a novel dual trigger method combined with delayed oocyte retrieval: A case report

Xian-Ling Cao, Zhen-Gao Sun

**ORCID number:** Xian-Ling Cao (0000-0001-9544-7419); Zhen-Gao Sun (0000-0002-9723-1213).

**Author contributions:** Cao XL reviewed the literature and contributed to manuscript drafting; Sun ZG was responsible for revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

**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.

**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 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: <http://creativecommons.org/licenses/by-nc/4.0/>

**Xian-Ling Cao**, College of Traditional Chinese Medicine, Shandong University of Traditional Chinese Medicine, Jinan 250011, Shandong Province, China

**Xian-Ling Cao, Zhen-Gao Sun**, Integrative Medicine Research Centre of Reproduction and Heredity, the Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan 250011, Shandong Province, China

**Corresponding author:** Zhen-Gao Sun, PhD, Doctor, Division of Reproductive Medicine, Shandong Traditional Chinese Medicine University, No. 42 Wen Hua Xi Road, Jinan 250011, Shandong Province, China. [sunzhengao77@126.com](mailto:sunzhengao77@126.com)

## Abstract

### BACKGROUND

Borderline form of empty follicle syndrome is a condition in which only a few mature or immature oocytes are recovered after meticulous follicular aspiration, despite adequate ovarian response to stimulation. It is a rare phenomenon with an unclear cause. Currently, the condition still lacks effective treatment.

### CASE SUMMARY

A patient with secondary infertility who had undergone three cycles of assisted reproductive technique (ART) is described. With regard to good follicular response, two oocytes were obtained in the first two ART cycles, but no embryo was formed. In the third ART cycle, which is the subject of this study, ovulation was induced by dual trigger of a supranormal dose of human chorionic gonadotropin (HCG) combined with a delayed oocyte retrieval approach. The method involved administration of gonadotropin-releasing hormone agonist, recombinant HCG, and urinary HCG 39 h before ovum pick-up. Ten oocytes were recovered, two out of three mature eggs were fertilized after intracytoplasmic sperm injection, resulting in two embryos that were subsequently cryopreserved. The case report guidelines have been used herein to present the first case of this novel dual trigger method.

### CONCLUSION

This approach provides a new treatment option for patients with a similar condition in the future. This study can also inspire further investigation on the effects of various  $\beta$ -HCG serum levels 36 h after intramuscular HCG administration.

ses/by-nc/4.0/

**Manuscript source:** Unsolicited manuscript**Received:** November 26, 2019**Peer-review started:** December 10, 2019**First decision:** January 7, 2020**Revised:** January 10, 2020**Accepted:** January 15, 2020**Article in press:** January 15, 2020**Published online:** February 26, 2020**P-Reviewer:** Exbrayat JM**S-Editor:** Zhang L**L-Editor:** Webster JR**E-Editor:** Qi LL**Key words:** Empty follicle syndrome; Dual trigger; Delayed oocyte retrieval;  $\beta$ -HCG threshold; Case report

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Although there is still a dispute regarding the existence of a borderline form of empty follicle syndrome, it is undeniable that this phenomenon does exist. Our case study reports a new ovulation triggering approach that involves a dual trigger of a supernormal dose of human chorionic gonadotropin combined with delayed oocyte retrieval. Our study provides a new technique for the treatment of borderline empty follicle syndrome.

**Citation:** Cao XL, Sun ZG. Borderline form of empty follicle syndrome treated with a novel dual trigger method combined with delayed oocyte retrieval: A case report. *World J Clin Cases* 2020; 8(4): 825-830

**URL:** <https://www.wjnet.com/2307-8960/full/v8/i4/825.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v8.i4.825>

## INTRODUCTION

Empty follicle syndrome (EFS) was first described by Coulam *et al*<sup>[1]</sup>. It refers to a condition in which no oocytes are recovered after meticulous follicular aspiration, despite normal follicular development. Failure to recover oocytes from dominant follicles is a rare phenomenon, and the incidence is estimated to be between 0.045% and 3.5%<sup>[2]</sup>. The condition is divided into two types, that is, “genuine” EFS and “false” EFS. The genuine form is a situation in which aspiration produces no oocytes despite a satisfactory ovarian response, whereas the false form can be described as a failure to recover oocytes due to low levels of beta-human chorionic gonadotropin ( $\beta$ -HCG). Low serum  $\beta$ -HCG levels may occur as a result of its erroneous administration or decreased bioavailability<sup>[3]</sup>.

A borderline form of EFS has been described in cases in which only a few mature or immature oocytes are recovered from several mature follicles. The condition was initially thought to be caused by the poor quality of  $\beta$ -HCG or its improper administration<sup>[4-6]</sup>. Until now, the underlying causes of the condition remain a mystery. Also, the optimum threshold level of circulating serum  $\beta$ -HCG is still disputed (reports vary from 5–160 IU/L of exogenous HCG administration after about 36 h)<sup>[7]</sup>. The main reason for these conflicting findings could be because of limited knowledge regarding the pathophysiology of EFS, which has resulted in a lack of practical solutions for the management of these conditions. Currently, it is thought that changing the trigger strategy could be a feasible approach to improve the egg acquisition in EFS patients<sup>[7]</sup>.

## CASE PRESENTATION

### Chief complaints

A couple with six years of secondary infertility visited a reproductive and genetic center in 2019.

### History of present illness

The 38-year-old patient had experienced irregular menses since menarche (which occurred at the age of 14), with maximal amenorrhea periods of 90 d. Her body mass index was 22.04 kg/m<sup>2</sup>.

### History of past illness

She had undergone induced abortion in 2006 after 40 d of pregnancy (because of an unplanned pregnancy) and had no other pregnancy history. In 2015, she received drug-induced ovulation treatment for three months (clomiphene/letrozole/urinary gonadotropins). Subsequently, she was able to produce dominant follicles monthly and could ovulate naturally; however, she was unable to conceive. In December 2015, she underwent laparoscopic removal of bilateral ovarian endometriosis cysts followed



by hysteroscopic resection of an endometrial polyp, which was conducted in Qilu Hospital based on strict surgical indications. Other than that, she had no surgical or disease history.

### Physical examination

Her physical examination results were generally normal. Her husband was a 40-year-old civil servant without a history of smoking or drinking. No apparent abnormalities were found during his physical examination.

### Laboratory examinations

The serum concentrations of the following hormones were examined in the laboratory on the third day of her menstrual cycle on May 2019, and the early follicular phase hormone profile was: Follicle-stimulating hormone (FSH) 5.64 U/L; luteinizing hormone (LH) 3.06 U/L; estradiol (E2) 42.13 pg/mL; prolactin (PRL) 10.64 ng/mL; testosterone (T) 0.14 ng/mL. Due to her long-term infertility, her chromosome status was analyzed using peripheral blood. Her chromosomal examination results displayed a 46, XX, 1qh+ karyotype.

Her husband's semen test results revealed oligo-asthenozoospermia (12 mol/mL, 35% motility), which was diagnosed following the 5<sup>th</sup> World Health Organization semen parameter standard and his chromosome karyotype was 46, XY.

### Imaging examinations

Hysterosalpingography indicated bilateral obstruction of her fallopian tubes, but the cause could not be determined. Pelvic sonography revealed normal pelvic conditions with a 1.04 mm regular endometrium and 1.6 mm ovarian follicle.

## FINAL DIAGNOSIS

The previous definition of the borderline form of EFS which has been described in cases in which only a few mature or immature oocytes are recovered from several mature follicles. In combination with the history of this case, in her first two *in vitro* fertilization (IVF) cycles, her target number of mature follicles was both more than 10, but only one oocyte was obtained each time. Thus, we have reason to believe that she meets the definition of a borderline form of EFS and was therefore diagnosed as having a borderline form of EFS.

## TREATMENT

In December 2016, IVF was performed in Qilu Hospital using the GnRH-antagonist protocol<sup>[8]</sup> to assist her in conception. Twelve follicles  $\geq 14$  mm, and one M1 egg was obtained; however, embryo formation failed to occur. In March 2017, another IVF was performed in Shandong University using a short protocol<sup>[9]</sup>. Fourteen follicles  $\geq 14$  mm, and one egg was obtained, fertilization of one egg occurred, but embryo formation failed. Unfortunately, the quantitative  $\beta$ -HCG level was not examined at the time. The specific trigger method and medication protocol are described in Table 1.

On June 7, 2019, a third IVF cycle was conducted in our reproductive and genetic center using a flexible luteal phase ovarian stimulation protocol<sup>[9]</sup>. Ovulation was maintained at high progesterone (P) levels by oral administration of dihydroxyprogesterone. On the 24<sup>th</sup> d of her menstrual cycle, a B-ultrasound and serological hormone test was performed. The hormone profile showed that E2 was 64 pg/mL, LH was 1.79 IU/L, and P was 0.82 ng/L. Pelvic sonography revealed normal pelvic conditions (with a 12.1 mm endometrium and 6.5 mm, 6 mm two ovarian follicles, and ten antral follicles). The medication strategy was changed in this study based on her previous two IVF failures.

Subsequently, from the 24<sup>th</sup> to 29<sup>th</sup> d of her menstrual cycle, she was administered a daily dose of 75U of urinary gonadotropin (HMG, Zhu hai Li zhu group Libao Biochemical Pharmaceutical Co., Ltd., Zhuhai, China, specification: 75 u/PC), 200U of recombinant human FSH (rFSH, Merck Serono SA Aubonne Branch, specification: 75 u/PC), 75U recombinant LH (rLH, Merck Serono S.A, 75 u/PC) and 40 mg of dydrogesterone. Administration of the gonadotropin (Gn) continued for three days (from 29<sup>th</sup> to 32<sup>nd</sup>) depending on growth of the follicles. After nine days of medication, the serum E2 level was 2357 pg/mL, LH was 1.42 IU/L, and P was 0.78 ng/L. B-ultrasound indicated normal follicle growth. To obtain more eggs, the dose of HMG was doubled to 300U a day for the next three days while maintaining the dosage of



**Table 1** Assisted reproductive technique cycle description

Date	Gonadotrophin	Daily dosage	Total	GnRH analog	Ovulation trigger	Protocol	Estrogen level (pg/mL)	Oocyte no
December, 2016	HMG	225U	2475U	GnRH-ant (0.25 mg)	HCG 1000U	Antagonist, fixed	3101	M I × 1
March, 2017	rFSH + HMG	75U+225U	900U + 2700U	GnRH-a (0.1 mg)	HCG 2000U + rHCG 250U	Agonist, short	4870	M I × 1
June, 2019	rFSH + HMG + rLH	200U+75U+75U	2200U + 825U + 825U	GnRH-a (0.05 mg)	GnRH (0.2 mg) rHCG + HCG 10000U	Agonist, long	3623	M I × 2 M II × 3

GnRH-a: Gonadotropin-releasing hormone agonist; GnRH-ant: Gonadotropin-releasing hormone antagonist; HCG: Human-chorionic gonadotropin; HMG: Human menopausal gonadotropin; rFSH: Recombinant human follicle stimulating hormone; rHCG: Recombinant human chorionic gonadotropin.

other medications. The treatment lasted for 11 d with a total dosage of rFSH, HMG, and rLH of 2200U, 825U, and 825U, respectively. On the 12<sup>th</sup> d of Gn administration, which was the 35<sup>th</sup> d of her menstruation, all the drugs were stopped. The serum E2 level was 3623 pg/mL, LH was 1.03 IU/L, and P was 1.48 ng/L at this time. To avoid the recurrence of a borderline form of EFS, her trigger protocol was carefully evaluated and administration of 10000U of HCG, 250 µg of recombinant HCG (rHCG) (Choriogonadotropin alfa, Ovitrelle 250 µg, Serono), and 0.2 mg of GnRH-antagonist (Ipsen Pharma Biotech, diphereline, Triptorelin acetate, decapeptyl 0.1 mg × 2) was finally decided upon. At this point, ten follicles were greater than 1.4 mm. Oocyte pick-up (OPU) was delayed for 3 h due to her situation. Eventually, five oocytes (M I × 2, M II × 3) were obtained, two of them were fertilized and later formed two embryos (embryo rating, 6C II × 1, 9C II × 1). To prevent ovarian hyperstimulation syndrome, embryo cryopreservation was performed in this cycle. At present, she is undergoing preparation for frozen embryo transfer. A detailed record is provided in [Table 2](#).

## OUTCOME AND FOLLOW-UP

Eventually, three mature oocytes were obtained in this study, which later formed two embryos after intracytoplasmic sperm injection. The patient decided to rest for a few months before undergoing frozen thawed embryo transfer.

## DISCUSSION

Despite the low incidence of a borderline form of EFS, the condition causes a great burden to patients and doctors who spend a lot of time and other resources on these patients. Predisposing factors for the condition include ovarian dysfunction and factors related to dosage, time of administration, bioavailability, and metabolism of HCG<sup>[10]</sup>. Presently, the main treatment to ensure final oocyte maturation involves administration of HCG 10000 IU (most common), rHCG 250 µg<sup>[11]</sup> and a double-trigger GnRH-a (0.2 mg) + rHCG (250 µg) + HCG 2000 IU<sup>[12]</sup>. In addition, prolonging the interval between ovulation is effective<sup>[10]</sup>.

Triggering and inappropriate OPU could be a contributory factor in some cases of EFS, because it may affect the number or quality of oocytes<sup>[13,14]</sup>. Most studies on EFS are limited in sample size, and this casts doubt on the reliability of their findings.

Indeed, the existence of EFS remains controversial<sup>[10]</sup>. The condition can still occur in cases in which correct administration and high bioavailability of HCG have been achieved. Also, EFS could be caused by the low availability of HCG in the ovary, and this condition has been described as “pharmaceutical industry syndrome”<sup>[15]</sup>. In the present study, a trigger method that involved a dual trigger of a supernormal dose of HCG combined with delayed oocyte retrieval prevented HCG-related faults and ensured adequate HCG action time and a relative increase in HCG concentration in the ovary. However, this study had some limitations: (1) The dosage of HCG used was higher than the conventional dosage, and this might increase the risk of ovarian hyperstimulation syndrome; (2) Oocyte retrieval was performed 39 h post HCG injection which might lead to excessive maturation of oocytes or spontaneous ovulation; and (3) This study did not determine whether increased dose of HCG and delayed oocyte retrieval affected the fundamental aspects of oocyte or embryo quality.

**Table 2** Introduction to the third *in vitro* fertilization

Date	June 7, 2019	June 12, 2019	June 15, 2019	June 17, 2019	June 18, 2019	June 20, 2019
D (Gn)	24 (1)	29 (6)	32 (9)	34 (11)	35 (12)	
E2 (pg/mL)	64	1120	2357	4146	3623	
LH (IU/L)	1.79	2.19	1.42	1.49	1.03	
P (ng/L)	0.82	1.01	0.78	1.28	1.48	
RF (cm)	0.65, 0.2 × 10	1.2, 1.1 × 3, 1.0, 0.9 × 3	1.35 × 2, 1.25 × 3, 1.2 × 4, 0.95 × 3	1.7, 1.65, 1.55, 1.3 × 3, 1.15 × 3, 1.05 × 3, 0.9	1.9, 1.7 × 2, 1.6, 1.45, 1.4, 1.35, 1.3, 1.25 × 3, 1.15, 1.0	Total 10, ≥ 1.4
LF (cm)	0.6, 0.2 × 10	1.25, 1.15, 1.1, 0.8 × 2, 0.75 × 2, 0.6	1.65, 1.45, 1.25, 1.05, 0.95 × 2, 0.9, 0.85, 0.75, 0.6	1.7, 1.55, 1.5, 1.15 × 3, 0.95, 0.9, 0.7 × 2	1.75 × 2, 1.7, 1.4, 1.35, 1.2 × 3, 1.0 × 2	
EM (cm)	1.21A-B	1.2B	1.38B	1.29B	1.13B	
HMG	75U × 5	75U × 3	150U × 2	150U × 1		
rFSH	200U × 5	200U × 3	200U × 2	200U × 1		
rLH	75U × 5	75U × 3	75U × 2	75U × 1		
Dydrogesterone	20 mg Bid	20 mg Bid	20 mg Bid	20 mg Bid		
Ovulation trigger					rHCG 250U + GnRH-a 0.2 mg + HCG 10000U	39 h oocyte retrieval

Gn: Gonadotropin; RF: Right follicle; LF: Left follicle; EM: Endometrium; HCG: Human chorionic gonadotropin; HMG: Human menopausal gonadotropin; rFSH: Recombinant human follicle-stimulating hormone; rHCG: Recombinant human chorionic gonadotropin; rLH: Recombinant luteinizing hormone; P: Progesterone, E2: Estradiol.

In the present study, the serum  $\beta$ -HCG level was 389.47 U/L, 3 h before OPU, which was higher than the  $\beta$ -HCG threshold previously mentioned in borderline forms of EFS<sup>[16]</sup>. Therefore, a standardized  $\beta$ -HCG threshold level and time of its detection in serum is still needed for EFS diagnosis<sup>[17]</sup>. The results of this study suggested that patients who have been diagnosed with EFS multiple times should have a more rigorous final oocyte maturation approach in the next IVF cycle to avoid the recurrence of EFS.

## CONCLUSION

The patient in the present study received three cycles of ART in three different reproductive centers, and the oocytes collected in the first two cycles were of poor quality, despite adequate ovarian response. In the third cycle, a high *P* level controlled the ovarian hyperstimulation protocol, and was applied to obtain more oocytes. A dual trigger of a supernormal dose of HCG combined with a delayed oocyte retrieval approach was selected after careful evaluation of the patient's medical history. Dual trigger involves using a single bolus of GnRH agonist combined with a reduced or standard dosage of HCG to trigger ovulation<sup>[18]</sup>. Eventually, three mature oocytes were obtained in this study, which later formed two embryos after intracytoplasmic sperm injection.

This case study reports a new ovulation triggering approach that involves a dual trigger of a supernormal dose of HCG combined with delayed oocyte retrieval. The method can be applied in the treatment of a borderline form of EFS.

## ACKNOWLEDGEMENTS

The authors wish to thank the patient for supporting this study and Zhen-Gao Sun for assisting in manuscript preparation.

## REFERENCES

1. **Coulam CB**, Bustillo M, Schulman JD. Empty follicle syndrome. *Fertil Steril* 1986; **46**: 1153-1155 [PMID: 3781029 DOI: 10.1016/s0015-0282(16)49898-5]
2. **Beck-Fruchter R**, Weiss A, Lavee M, Geslevich Y, Shalev E. Empty follicle syndrome: successful treatment in a recurrent case and review of the literature. *Hum Reprod* 2012; **27**: 1357-1367 [PMID: 22511111 DOI: 10.1093/humrep/des311]

- 22357773 DOI: [10.1093/humrep/des037](https://doi.org/10.1093/humrep/des037)]
- 3 **Stevenson TL**, Lashen H. Empty follicle syndrome: the reality of a controversial syndrome, a systematic review. *Fertil Steril* 2008; **90**: 691-698 [PMID: [18023430](https://pubmed.ncbi.nlm.nih.gov/18023430/) DOI: [10.1016/j.fertnstert.2007.07.1312](https://doi.org/10.1016/j.fertnstert.2007.07.1312)]
  - 4 **Isik AZ**, Vicdan K. Borderline form of empty follicle syndrome: is it really an entity? *Eur J Obstet Gynecol Reprod Biol* 2000; **88**: 213-215 [PMID: [10690684](https://pubmed.ncbi.nlm.nih.gov/10690684/) DOI: [10.1016/s0301-2115\(99\)00152-9](https://doi.org/10.1016/s0301-2115(99)00152-9)]
  - 5 **Desai N**, Austin C, AbdelHafez F, Goldfarb J, Falcone T. Evidence of 'genuine empty follicles' in follicular aspirate: a case report. *Hum Reprod* 2009; **24**: 1171-1175 [PMID: [19174447](https://pubmed.ncbi.nlm.nih.gov/19174447/) DOI: [10.1093/humrep/den497](https://doi.org/10.1093/humrep/den497)]
  - 6 **Nikolettos N**, Asimakopoulos B, Simopoulou M, Al-Hasani S. A borderline form of empty follicle syndrome. Case report. *Clin Exp Obstet Gynecol* 2004; **31**: 79-80 [PMID: [14998197](https://pubmed.ncbi.nlm.nih.gov/14998197/)]
  - 7 **Revelli A**, Carosso A, Grassi G, Gennarelli G, Canosa S, Benedetto C. Empty follicle syndrome revisited: definition, incidence, aetiology, early diagnosis and treatment. *Reprod Biomed Online* 2017; **35**: 132-138 [PMID: [28596003](https://pubmed.ncbi.nlm.nih.gov/28596003/) DOI: [10.1016/j.rbmo.2017.04.012](https://doi.org/10.1016/j.rbmo.2017.04.012)]
  - 8 **Al-Inany HG**, Youssef MA, Ayeleke RO, Brown J, Lam WS, Broekmans FJ. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. *Cochrane Database Syst Rev* 2016; **4**: CD001750 [PMID: [27126581](https://pubmed.ncbi.nlm.nih.gov/27126581/) DOI: [10.1002/14651858.CD001750.pub4](https://doi.org/10.1002/14651858.CD001750.pub4)]
  - 9 **Qin N**, Chen Q, Hong Q, Cai R, Gao H, Wang Y, Sun L, Zhang S, Guo H, Fu Y, Ai A, Tian H, Lyu Q, Daya S, Kuang Y. Flexibility in starting ovarian stimulation at different phases of the menstrual cycle for treatment of infertile women with the use of in vitro fertilization or intracytoplasmic sperm injection. *Fertil Steril* 2016; **106**: 334-341.e1 [PMID: [27114329](https://pubmed.ncbi.nlm.nih.gov/27114329/) DOI: [10.1016/j.fertnstert.2016.04.006](https://doi.org/10.1016/j.fertnstert.2016.04.006)]
  - 10 **Bustillo M**. Unsuccessful oocyte retrieval: technical artefact or genuine 'empty follicle syndrome'? *Reprod Biomed Online* 2004; **8**: 59-67 [PMID: [14759289](https://pubmed.ncbi.nlm.nih.gov/14759289/) DOI: [10.1016/s1472-6483\(10\)60498-1](https://doi.org/10.1016/s1472-6483(10)60498-1)]
  - 11 **Duru NK**, Cincik M, Dede M, Hasimi A, Baser I. Retrieval of zona-free immature oocytes in a woman with recurrent empty follicle syndrome: a case report. *J Reprod Med* 2007; **52**: 858-863 [PMID: [17939607](https://pubmed.ncbi.nlm.nih.gov/17939607/)]
  - 12 **Song J**, Sun Z. A borderline form of empty follicle syndrome treated with a double-trigger of gonadotropin-releasing hormone agonist and human chorionic gonadotropin: A case report. *Medicine (Baltimore)* 2019; **98**: e16213 [PMID: [31277129](https://pubmed.ncbi.nlm.nih.gov/31277129/) DOI: [10.1097/MD.00000000000016213](https://doi.org/10.1097/MD.00000000000016213)]
  - 13 **Thornton SJ**, Pantos C, Speirs A, Johnston I. Human chorionic gonadotropin to oocyte retrieval interval in in vitro fertilization--how critical is it? *Fertil Steril* 1990; **53**: 177-179 [PMID: [2295341](https://pubmed.ncbi.nlm.nih.gov/2295341/) DOI: [10.1016/s0015-0282\(16\)53239-7](https://doi.org/10.1016/s0015-0282(16)53239-7)]
  - 14 **Bjercke S**, Tanbo T, Dale PO, Abyholm T. Comparison between two hCG-to-oocyte aspiration intervals on the outcome of in vitro fertilization. *J Assist Reprod Genet* 2000; **17**: 319-322 [PMID: [11042828](https://pubmed.ncbi.nlm.nih.gov/11042828/) DOI: [10.1023/a:1009401027251](https://doi.org/10.1023/a:1009401027251)]
  - 15 **Zegers-Hochschild F**, Fernández E, Mackenna A, Fabres C, Altieri E, Lopez T. The empty follicle syndrome: a pharmaceutical industry syndrome. *Hum Reprod* 1995; **10**: 2262-2265 [PMID: [8530648](https://pubmed.ncbi.nlm.nih.gov/8530648/) DOI: [10.1093/oxfordjournals.humrep.a136281](https://doi.org/10.1093/oxfordjournals.humrep.a136281)]
  - 16 **Kourtis A**, Rouso D, Panidis D. The empty follicle syndrome. *J Endocrinol Invest* 2004; **27**: 187-191 [PMID: [15129817](https://pubmed.ncbi.nlm.nih.gov/15129817/) DOI: [10.1007/BF03346267](https://doi.org/10.1007/BF03346267)]
  - 17 **Ndukwe G**, Thornton S, Fishel S, Dowell K, Aloum M, Green S. 'Curing' empty follicle syndrome. *Hum Reprod* 1997; **12**: 21-23 [PMID: [9043895](https://pubmed.ncbi.nlm.nih.gov/9043895/) DOI: [10.1093/humrep/12.1.21](https://doi.org/10.1093/humrep/12.1.21)]
  - 18 **Kasum M**, Kurdija K, Orešković S, Čehić E, Pavičić-Baldani D, Škrnatić L. Combined ovulation triggering with GnRH agonist and hCG in IVF patients. *Gynecol Endocrinol* 2016; **32**: 861-865 [PMID: [27275861](https://pubmed.ncbi.nlm.nih.gov/27275861/) DOI: [10.1080/09513590.2016.1193141](https://doi.org/10.1080/09513590.2016.1193141)]



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](mailto:bpgoffice@wjgnet.com)  
Help Desk: <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

