CASE REPORT

A case report of giant smooth endoplasmic reticulum clusters in oocytes, post-ICSI: Successful outcome leading to live birth

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Abstract

This particular case study examines the association between oocyte morphology and assisted reproductive technology (ART), particularly, the smooth endoplasmic reticulum clusters (sERCs). It describes an extraordinary case in which 80% of the mature oocytes had giant sERCs, which raised concerns about the oocyte quality and the resultant embryonic development and clinical prognosis It concerned a patient who underwent intracytoplasmic sperm injection (ICSI). Two embryos, derived from oocytes with sERCs, were transferred on day 3 following ICSI and sERCs became the focus. The results covered the entire continuum of fertilization, embryonic maturation, and clinical outcomes, the endpoint of which was a successful live birth. Such results demonstrate the complex background between the oocyte dysmorphia and reproductive performance, still, in ART, it is possible that considerable dysmorphia is not necessarily a negative prognostic factor. Further studies are needed to address the oocyte dysmorphia and ART's changes *(Afr J Reprod Health 2025; 29 [11]: 249-254).*

Keywords: Smooth Endoplasmic Reticulum Cluster, Fertilization Rate, Oocyte, Embryo Transfer, Live Birth,

Résumé

Cette étude de cas examine le lien entre la morphologie ovocytaire et les techniques de procréation médicalement assistée (PMA), notamment les amas de réticulum endoplasmique lisse (ACRs). Elle décrit un cas exceptionnel où 80 % des ovocytes matures présentaient des ACRs géants, ce qui a soulevé des inquiétudes quant à la qualité ovocytaire, au développement embryonnaire et au pronostic clinique. Il s'agissait d'une patiente ayant bénéficié d'une injection intracytoplasmique de spermatozoïdes (ICSI). À l'exception d'une morphologie ovocytaire inhabituelle, deux embryons ont été transférés au troisième jour suivant l'ICSI, et les ACRs ont été utilisés. Les résultats ont couvert l'ensemble du continuum de la fécondation, de la maturation embryonnaire et des résultats cliniques, dont le critère d'évaluation était une naissance vivante réussie. Ces résultats démontrent le contexte complexe entre la dysmorphie ovocytaire et la performance reproductive. Cependant, en PMA, il est possible qu'une dysmorphie importante ne soit pas nécessairement un facteur pronostique négatif. Des études complémentaires sont nécessaires pour traiter la dysmorphie ovocytaire et les modifications de l'ART. *(Afr J Reprod Health 2025; 29 [11]: 249-254).*

Mots-clés: Reticulum endoplasmique lisse, Taux de fécondation, Ovocyte, Transfert d'embryon, Naissance vivante

Introduction

The normal oocyte cytoplasm is characterized by its richness in mitochondria, smooth endoplasmic reticulum, small vesicles, and tubules. These minute organelles remain elusive when observed through an inverted microscope. However, during ovulation induction, some oocytes display conspicuous large smooth endoplasmic reticulum clusters (sERCs) at the center of their cytoplasm.[1] The sERC exhibits distinctive features, with large tubular sERCs aggregated by ring- and horseshoe-shaped mitochondria, along with small vesicles.[2] Despite this, there remains controversy regarding the impact of this sizable sERC on oocyte fertilization and embryonic development. To the best of our knowledge, this is the first documented instance where a significant percentage (80%) of large sERCs was found in mature oocytes and the consequence was a live birth, highlighting the therapeutic significance of this finding. Studies have shown both negative and neutral effects, raising doubts about the therapeutic significance of sERCs, despite the frequent reporting of general cytoplasmic abnormalities in oocytes.[3]

Methods

Case presentation

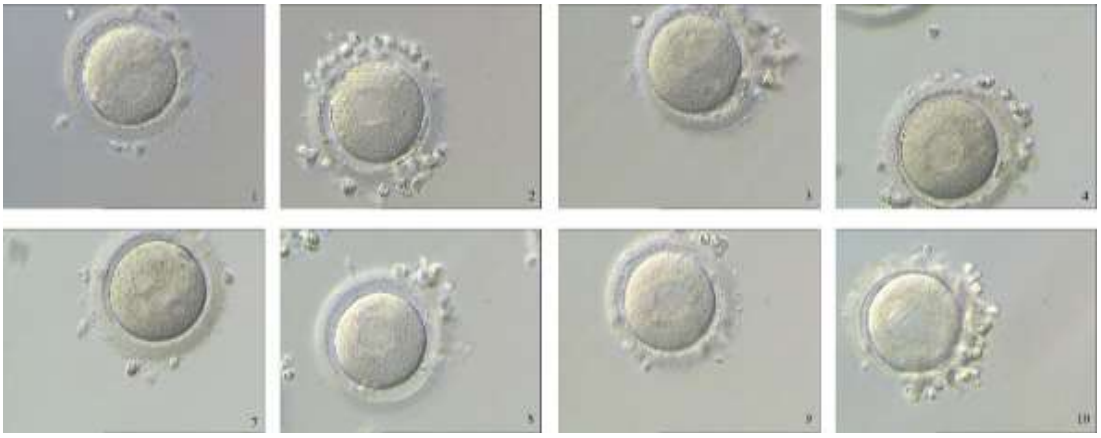
In May 2018, a couple sought help for primary infertility after trying to conceive for a year. Married for 4 years, they initially used condoms and later prepared for pregnancy for a year. The 30-year-old female partner had regular menstrual cycles and a normal sexual life. This was the patient's first IVF/ICSI attempt after surgical management for tubal obstruction and endometriosis. Her endocrine results showed: basal FSH 6.6 IU/L, LH 5.81 IU/L, estrogen 102.1 pmol/L, and AMH 6.58 ng/mL, with a BMI of 25.1 kg/m². A 2017 hysterosalpingogram revealed bilateral tubal obstruction, leading to laparoscopic excision of a right chocolate cyst and hysteroscopic endometrial polypectomy. The 29-year-old male partner's semen analysis showed: volume 2 mL, sperm concentration 111.33x10⁶/mL, motility 55.27%, progressive motility 44.41%, and normal morphology 2.5%. In May 2018, semen analysis indicated: volume 1 mL, concentration 55.25x10⁶/mL, motility 57.08%, progressive motility 48.07%, and normal morphology 2%.

Both analyses indicated teratozoospermia. Ovarian stimulation using the GnRH agonist protocol started in May 2018. The patient received GnRH agonist (Triptorelin acetate) for pituitary downregulation. Once downregulated, ovarian stimulation with recombinant human follitropin began, tailored to her age, follicle count, and BMI. After three or more follicles reached 18 mm, 250 μg of recombinant human choriogonadotropin (HCG) was administered for oocyte maturation. Transvaginal retrieval 36 hours later collected 13 oocytes. Of these, 10 were mature (metaphase II) and 3 were malformed. Most mature oocytes (80%) had centrally located sERCs (Figure 1). The sERCs ratio in oocytes was calculated using Photoshop CS6 (Figure 2 and Table 1a,1b).

All 10 mature oocytes were injected with spermatozoa and exhibited 100% normal fertilization (Table 1a). Embryo quality was assessed at the cleavage stage (Table 2) and blastocyst stage using the Gardner scoring system[3] (Table 1b). Ten embryos were cultured to day 3, resulting in seven high-quality and three non-high-quality embryos. With consent, two high-quality embryos were transferred, four were cryopreserved, and the rest were cultured to the blastocyst stage, resulting in two non-transferable blastocysts. Following day 3 embryo transfer, luteal phase supports were administered. Fourteen days later, blood hCG was 375.4 IU/L. An ultrasound at 28 days confirmed a singleton pregnancy. A baby girl, weighing 4,100 g with a neonatal score of 10, was delivered *via* cesarean section at 41+3 weeks

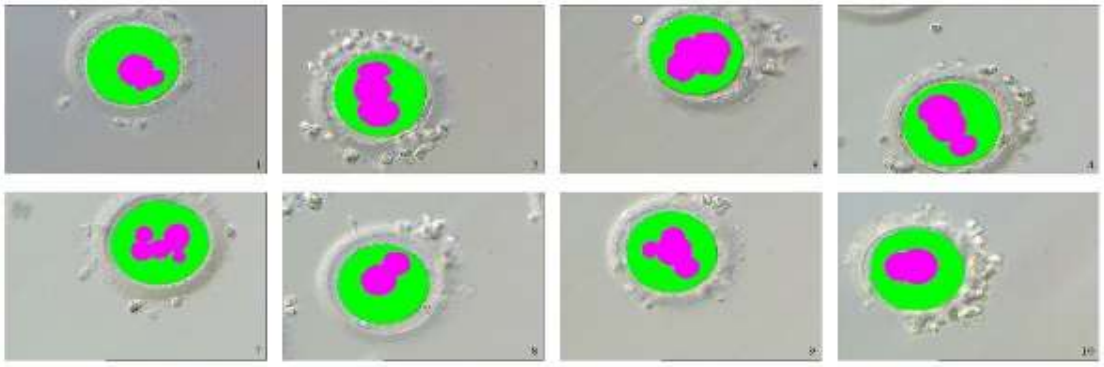
Discussion

The morphology of oocytes is crucial for fertilization and embryo development. Approximately 60-70% of oocytes exhibit morphological abnormalities, including both cytoplasmic and extra-cytoplasmic traits such as ovoid shape, cytoplasmic irregularities, fragmented first polar bodies, enlarged perivitelline spaces, and thick or dark zona pellucida.[4] These abnormalities, particularly those affecting the meiotic spindle and cytoskeleton, can impair normal fertilization and embryonic development.[5] sERCs (smooth endoplasmic reticulum clusters) are common cytoplasmic abnormalities in oocytes during IVF-ET, with incidence rates ranging from 5.4% to 23.1%.[6] Ebner *et al*. reported sERCs in 3.9% of oocytes, with varying quantities of single, double, and multiple sERCs.[7] Normally, the smooth endoplasmic reticulum in oocytes, along with mitochondria, serves as a calcium storage depot, crucial for post-fertilization calcium waves essential for embryonic development.[8] Morphological abnormalities with large sERCs can disrupt the calcium storage and oscillations, impacting oocyte fertilization, embryo development, and implantation.[9] Studies have shown that sERCs can reduce fertilization rates, compromise embryonic development, delay blastocyst formation, and lower embryo implantation rates.[2,10] Clinical studies also link sERCs to decreased pregnancy rates in IVF-ET, higher miscarriage risks, and suggest avoiding embryos from sERC-containing oocytes.[10] A systematic analysis by Bartolacci *et al*. confirmed the negative correlation between sERCs and IVF outcomes, highlighting increased perinatal complications, birth defects, and imprinting disorders associated with sERCs.[11]



Note: Oocyte 1-4, 7-10 pictures showing the percentage of sERCs in cytoplasm

Figure 1: Method of sERC quantification.



Note: Images acquired with inverted microscope at ×4200 magnification.

Figure 2: Representative micrographs of mature oocytes with giant sERCs in the cytoplasm.

Table 1a: Oocyte morphology and fertilization outcomes

Oocyte	Morphology check day 0	Fertilization (2PN2pb)
1	19.84% sERC	2PN2pb
2	36.33% sERC	2PN2pb
3	40.86% sERC	2PN2pb
4	33.11% sERC	2PN2pb
5	/	2PN2pb
6	/	2PN2pb
7	24.40% sERC	2PN2pb
8	23.66% sERC	2PN2pb
9	28.56% sERC	2PN2pb
10	24.84% sERC	2PN2pb
11	Malformed oocyte	
12	Malformed oocyte	
13	Malformed oocyte	

Table 1b: Embryo development and clinical outcomes

Oocyte	Morphology day 2	Morphology outcome	Fate
1	4C/I (1/4 sERC)	8C/I	ET
2	4C/I (1/4 sERC)	8C/I	ET
3	5C/II (2/5 sERC)	7C/II (1/7 sERC)	NO
4	4C/I (2/4 sERC)	8C/I	F
5	5C/II	7C/II	NO
6	4C/I	8C/I+	F
7	4C/I (2/4 sERC)	8C/I	F
8	4C/I (1/4 sERC)	8C/II	NO
9	4C/I (2/4 sERC)	8C/II (1/8 sERC)	NO
10	4C/I (2/4 sERC)	8C/I+ (1/8 sERC)	F
11			D/C
12			D/C
13			D/C

Note: D/C = discarded, ET = Embryo transferred, F=frozen on day3, NO = Embryo was cultured up to blastocyst stage, no transferable embryo was available, finally was discarded

Table 2: Embryo grading system on day 3

Rank	Classification description
Grade I	Blastomeres with even shape and size, without vacuole in cytoplasm, ≤5% fragmentation
Grade I+	Blastomeres with even shape and size, without vacuole in cytoplasm, >5% ~ ≤10% fragmentation
Grade II	Blastomeres with slightly uneven shape and size, with very few vacuoles in cytoplasm, >10% ~ ≤15% fragmentation
Grade II+	Blastomeres with moderate uneven shape and size, with a small amount of vacuoles in cytoplasm, >15% ~ ≤20% fragmentation
Grade III	Blastomeres with moderate uneven shape and size, with more vacuoles in cytoplasm, >20% ~ ≤40% fragmentation
Grade IV	Blastomeres with significant uneven shape and size, with lots of vacuoles in cytoplasm, >40% fragmentation

Otsuki *et al*. found higher failure rates in mitotic and meiotic division in sERC-containing oocytes.[7] Conversely, a retrospective cohort study and Shaw-Jackson's report suggested sERCs do not affect implantation rates, clinical pregnancy, live birth rates, or birth defects in ICSI cycles.[12,13]

In this case, 80% of mature oocytes exhibited multiple large sERCs. Following ICSI fertilization, 80% of embryos on day 3 were of high quality. Transferring two cleavage embryos resulted in a successful singleton pregnancy and a healthy baby girl delivered by cesarean section. Despite the high 80% incidence of sERCs in mature oocytes, the presence of multiple sERCs did not impede fertilization or embryonic development, resulting in a clinical pregnancy and live birth. Further calculations determined that the proportion of sERCs in oocytes ranged from 19.84% to 40.86%, seemingly not affecting embryonic development. However, Wallbutton et al. found that only two out of five oocytes with large sERCs had normal fertilization, and no usable embryos were obtained by day 3. One oocyte with moderate sERC developed into a 6-cell embryo but failed to achieve pregnancy post-transplantation, suggesting large sERCs reduce fertilization rates and adversely affect development.[14,15] Discrepancies in the impact of sERCs on oocytes in IVF-ET may stem from variations in their occurrence, location, size, and quantity. The limited number of cases and lack of large-scale studies may introduce statistical bias, limiting definitive conclusions. Extensive research with large-scale samples and multi-center studies is needed to comprehensively understand the

relationship between sERCs and IVF-ET clinical outcomes. This article highlights that rather than being immediately thrown away, embryos from oocytes carrying sERC should be carefully studied.

Conclusions

In conclusion, the couple faced primary infertility despite a year of dedicated efforts to conceive. The female partner, with normal endocrine results but a history of tubal obstruction and ovarian cysts, and the male partner, with consistent teratozoospermia, underwent successful ovarian stimulation and ICSI treatment. This resulted in the retrieval of 13 oocytes, of which 10 were mature and successfully fertilized. Two high-quality embryos transferred resulted in a singleton pregnancy and the birth of a healthy baby girl, highlighting the efficacy of tailored fertility treatments. This case demonstrates that viable embryos and live birth are possible even in cases where gigantic sERCs are prevalent. Consequently, it is not appropriate to immediately discard embryos produced from these oocytes, and more extensive research is necessary to improve clinical judgment.

Author contributions

Conceptualization, Yuhua Zhang, Wenjie Zhao; Data curation, Wenjie Zhao; Formal analysis, Yuhua Zhang; Investigation, Kunkun Liu; Methodology, Pingping Sun; Software, Dan Wang, Jinguang Wang; Writing – original draft, Yuhua Zhang, Wenjie Zhao; Writing – review & editing, Yuhua Zhang, Wenjie Zhao.

Ethics approval

This study was reviewed and approved by the local ethics committee of Weifang People's Hospital (Approval NO.202310). Informed written consent was obtained from the patient for the publication of this case report and the accompanying images.

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