Impact of oocytes exhibiting smooth endoplasmic reticulum cluster (SERC) on fertilization: A case report

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Abstract

Introduction: The presence of smooth endoplasmic reticulum in oocytes (SERC) has been linked to various cellular functions and is proposed as a potential marker of oocyte quality.
Case description: A couple underwent two cycles of IVF treatment The 15 oocytes retrieved were inseminated by conventional IVF (cIVF). Seven oocytes fertilized normally, while 4 displayed smooth endoplasmic reticulum cluster (SERC) and 3 were immature. None of the SERC positive oocytes fertilized successfully. Only 3 fertilized oocytes developed into quality embryos by day 3 but necessitated cryopreservation due to the patient's mild ovarian hyperstimulation syndrome (OHSS) condition. Subsequently, frozen embryo transfer (FET) on day 3 did not result in pregnancy. A year later, the couple returned for another IVF cycle, 22 oocytes were retrieved, 6 appeared normal, 3 were immature, and 13 exhibited SERC. Both cIVF and Intracytoplasmic Sperm Injection (ICSI) were employed. Thirteen SERC-positive oocytes underwent ICSI, while the remaining 9, including the immature ones, underwent conventional IVF. Only 6 out of the 13 oocytes treated with ICSI displayed normal fertilization, none of the oocytes treated by cIVF fertilized. Three of 6 SERC oocytes fertilized by ICSI and progressed to the cleavage stage and developed into good-quality embryos by day 3 of embryo culture, demonstrating their developmental competence. Due to OHSS the embryos were cryopreserved for future transfer. During subsequent FET one of the SERC-cryopreserved embryos did not survive the thawing process. The FET proceeded with a single embryo transfer from a non-SERC-cryopreserved embryo, but unfortunately, it did not result in pregnancy.
Discussion and Conclusion: The presence of SERC in certain ICSI-treated oocytes did not preclude successful fertilization and subsequent embryo development. These findings underscore the complexity of oocyte quality assessment and the need for further research to elucidate the precise role of SERC in determining fertility outcomes in ART procedures.

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Introduction

Seven distinct cytoplasmic phenotypes described by Van Blerkom and Henry (1992) have been identified in human oocytes, including dark granular appearance, clustered organelles accumulation of Smooth endoplasmic reticulum (SER), vesiculated morphology, presence of necrotic regions, polarized cortical depletion of organelles, and vacuolated structure. Smooth endoplasmic reticulum cluster (SERC) in oocytes has been identified as a potential indicator of oocyte quality and developmental competence. The SERC is a membrane-bound organelle present in oocytes and is believed to play a crucial role in the maturation of oocytes (Figure 1.1). SER is an organelle that is abundant in the ooplasm. It is a network of sacs or tubes enclosed by membranes. The most significant role of SER in oocyte physiology is to

store and redistribute calcium, which is responsible for cell activation in the course of fertilization (Ebner et al., 2006). The SERC is an intracytoplasmic dimorphism that has been suggested to interfere with calcium stores and oscillations during fertilization and may harm embryo development and implantation (Mateizel et al., 2013).

Previous studies have demonstrated that oocytes exhibiting smooth endoplasmic reticulum cluster (SERC) may lead to compromised fertilization rates, embryo development, pregnancy outcomes, and obstetric and neonatal outcomes (Sa et al., 2011). In response, the Alpha Scientists in Reproductive Medicine and the European Society of Human Reproduction and Embryology (ESHRE) Special Interest Group of Embryology advised against inseminating oocytes presenting with SERC due to potential risks of abnormal outcomes (Alpha Scientists in Reproductive Medicine and ESHRE, 2011). However, more recent findings by Mateizal et al. (2013) suggested that healthy babies could still be obtained from oocytes displaying SERC. Consequently, the clinical significance of SERC-positive oocytes remains a topic of debate, with limited and conflicting information available.

This case study aims to investigate the association between the presence of SERC in oocytes and the fertilization rate in both conventional In Vitro Fertilization (cIVF) and Intracytoplasmic Sperm Injection (ICSI) procedures. We hope the present case report can shed light on the factors affecting fertilization in oocytes with SERC.

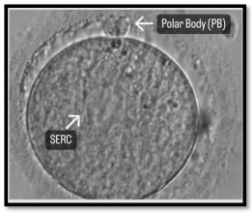

Figure 1.1 Mature oocyte with SERC. Adaptation from https://www.sciencedirect.com/science/article/pii/S0015028216627966

Materials and methods

Case Presentation

A Chinese couple, aged 38 and 39, underwent two cycles of IVF treatment at the University of Malaya Medical Centre (UMMC) Fertility Unit. They had been experiencing primary infertility for four years. The wife was diagnosed with mild polycystic ovary syndrome (PCOS), while the husband's sperm analysis revealed normal results. Both individuals are employed in the Information Technology Department. The results of fertilization rates and embryo development during both their treatment cycles were determined and analyzed with reference to the presence of SERC.

Results

First treatment cycle: 25th July 2022

Fifteen oocytes were retrieved during the ovarian stimulation cycle, and all oocytes subjected to cIVF, according to the post-washed spermatozoa count were normal (91 x 106 ml; 90% motile; 5% normal morphology). After fertilization checking, only 7 oocytes were fertilized normally, characterized by the presence of two pronuclei (2PN) and two polar bodies (2PB) (Figure 1.2), 4 oocytes displayed SERC and 3 oocytes were immature. All SERC-oocytes were not fertilized. 3 out of 7 fertilized oocytes, only 3 oocytes can develop to good quality on day 3 and proceed to freeze. This cycle was planned to freeze all on Day 3 and transfer them in frozen embryo transfer (FET) due to the condition of the patient with mild ovarian hyperstimulation syndrome (OHSS). The patient came back to do FET but did not become pregnant on day 3 FET.

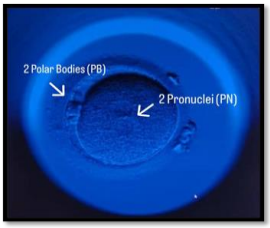

Figure 1.2 Fertilized Oocyte (2PN;2PB). Adaptation from Embryo Timelapse UMFertility.

Second treatment cycle: 11th August 2023

After one year, this couple came back to do a second cycle of IVF treatment. A total of 22 oocytes were retrieved during the ovarian stimulation cycle. Among these, 6 oocytes exhibited optimal characteristics with healthy cumulus, while 3 were found to be immature. Intriguingly, 13 oocytes displayed the presence of SERC, indicating a potential deviation in oocyte quality. As planned by the doctors, this patient will do both procedures of insemination to get a better fertilization outcome although the post-washed spermatozoa count was normal (122 x 10^6/ml; 92% motile; 4% normal morphology). In line with standard protocols, 13 oocytes were designated for ICSI, while the remaining 9 oocytes, including the immature ones, underwent conventional cIVF. Notably, upon denuding, 8 out of the 13 ICSI oocytes showed the presence of SERC in the ooplasm, while 5 out of 9 cIVF-denuded oocytes exhibited SERC.

Upon assessment following fertilization, only 6 out of the 13 ICSI-treated oocytes displayed normal fertilization with 2PN's and 2PB's. None of the cIVF-treated oocytes showed signs of fertilization. Further analysis revealed that 3 of the 6 fertilized oocytes from the ICSI group displayed SERC. All three oocytes progressed to the cleavage stage and developed into good-quality embryos (graded as 1 and 2) by day 3 of embryo culture, demonstrating their developmental competence. All 6 embryos that reached the cleavage stage were subsequently cryopreserved for future use due to the patient's condition of OHSS, which precluded fresh embryo transfer (Figure 1.3). However, during the subsequent frozen embryo transfer (FET) on day 3, one of the SERC cryopreserved embryos did not survive the thawing process a result, the FET proceeded with a single embryo transfer from a non-SERC-cryopreserved embryo, but unfortunately, it did not result in pregnancy.

Discussion

Emerging evidence suggests that SERC may serve as a potential indicator of oocyte quality, with implications for fertility treatment outcomes. The presence of SERC in oocytes has been linked to compromised fertilization rates, as evidenced by the absence of fertilization in SERC positive oocytes during the first IVF cycle

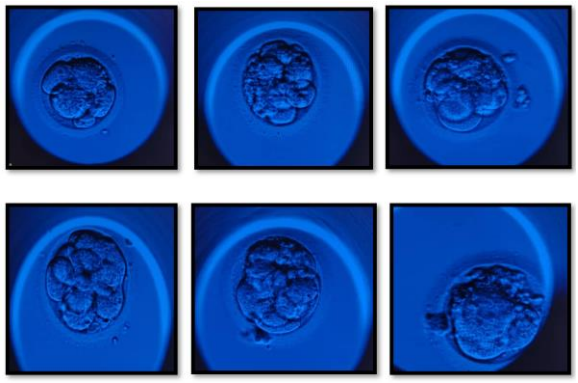

Figure 1.3 Embryos frozen on Day 3. Adaptation from Embryo Timelapse UMFertility

and reduced fertilization rates in the subsequent cycle. Recent studies (Setti et al., 2016), have highlighted the negative impact of SERC on embryo implantation potential. This suggests that SERC may adversely affect oocyte quality, leading to lower fertilization rates and potentially affecting the success of IVF cycles.

The presence of SERC in oocytes has been consistently linked to lower fertilization and implantation rates in both cIVF and ICSI procedures (Hattori, 2014; Setti, 2016). In the present case, ICSI showed better success rates in terms of fertilization compared to cIVF. Moreover, the direct injection of sperm into the oocyte cytoplasm appear to overcome challenges related to both sperm and oocyte quality. This could be attributed to the bypassing of potential barriers posed by oocytes containing SERC. By directly injecting sperm into the oocyte cytoplasm, ICSI circumvents potential obstacles associated with the oocyte's cytoplasmic environment, potentially enhancing fertilization success rates despite the presence of SERC. ICSI appear to offer advantages in overcoming the challenges posed by SERC-positive oocytes (Vishwakarma et al., 2024).

Specifically, the occurrence of SERC during the metaphase II (MII) stage of oocyte development has been associated with decreased rates of oocyte maturation and fertilization, as well as the production of lower-quality embryos, ultimately leading to reduced chances of successful implantation and pregnancy (Sa et al., 2011; Oudshoorn-Roessen

et al., 2015; Restelli et al., 2015; Otsuki et al., 2004).

Moreover, the presence of SERC has been linked to suboptimal ovarian stimulation, further diminishing the reproductive potential of oocytes (Massarotti, 2021). Despite these findings, the reproductive outcomes of oocytes with SERC are not significantly impaired, with similar clinical pregnancy, implantation, and live birth rates compared to oocytes without SERC, according to Wang et al., 2021.

SERC-positive oocytes have been associated with higher rates of miscarriage (Ebner et al., 2008). Furthermore, morphological abnormalities in oocytes, including the presence of SERC, play a crucial role in determining their developmental fate and may be influenced by controlled ovarian stimulation protocols and ovarian response (Figueira, 2010). However, the impact on post-implantation development and neonatal outcomes is minimal (Hattori 2014).

In conclusion, understanding the impact of SERC on fertilization rates and treatment outcomes is crucial in optimizing success rates in ART. ICSI insemination result in better fertilization in SERC-positive oocytes.

Conclusion

This case study underscores the potential significance of SERC as a predictive marker for fertilization outcomes in IVF and ICSI procedures. Understanding the role of SERC in oocyte quality assessment may contribute to improving ART success rates and optimizing patient management strategies in assisted reproduction. The presence of SERC may be associated with lowered chances of successful fertilization and implantation. Careful oocyte observation that considers the presence of SERC should be part of the strategy for the procedure of oocyte insemination and embryo selection for transfer.

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