

Early-Onset Preeclampsia and Ovarian Hyperstimulation Syndrome following ovulation induction in a woman with Polyendocrine Metabolic Ovarian Syndrome: A Case Report.

Abstract:

Ovarian Hyperstimulation Syndrome (OHSS) and preeclampsia are well-documented complications of Assisted Reproductive Technology (ART) and ovulation induction. In patients with Polyendocrine Metabolic Ovarian Syndrome (PMOS) undergoing fertility treatment, these conditions may present together or sequentially. Their simultaneous occurrence after letrozole ovulation induction, a medication with low OHSS risk, is rarely documented. This report details a rare case of OHSS and preeclampsia after letrozole induction in a woman with Polyendocrine Metabolic Ovarian Syndrome.

Case summary

A 25-year-old woman with Polyendocrine Metabolic Ovarian Syndrome conceived following letrozole ovulation induction. She presented as an emergency at 30 weeks of gestation with abdominal pain, persistent headache, elevated blood pressures, ascites and significant bilateral ovarian enlargement. She was diagnosed with moderate OHSS and severe early-onset preeclampsia. Management included hospital admission, close fluid balance monitoring, prophylactic anticoagulation, and antihypertensive therapy. Ultimately, she underwent caesarean delivery at 34 weeks.

Conclusion

Although rare, OHSS and early-onset preeclampsia can occur together after letrozole ovulation induction. Close monitoring, supportive care, and timely delivery are essential for optimal outcomes.

Keywords: PMOS, OHSS, preeclampsia, letrozole, ovulation, case report

Background

Polyendocrine Metabolic Ovarian Syndrome is the leading cause of anovulatory infertility in reproductive-age women(1). Ovulation induction increases the risk of Ovarian Hyperstimulation Syndrome(2). PMOS also predisposes patients to hypertensive disorders of pregnancy due to insulin resistance and vascular endothelial dysfunction(3). The coexistence of OHSS and preeclampsia is rare and challenging to manage because of this overlapping pathophysiology and clinical features(4).

Letrozole ovulation induction has a low risk of OHSS(5)(6). However, in women with PMOS, combining letrozole with gonadotropins or HCG can increase this risk(7)(8). Patient factors including prior OHSS, high antral follicle count (AFC), elevated anti-Müllerian hormone (AMH), young age, and black ethnicity further increase susceptibility(9). On rare occasions, OHSS can also develop spontaneously, either during a natural conception cycle and even in the absence of pregnancy(10)(11).

Letrozole is the preferred first-line agent for ovulation induction in some women with PMOS. However, rare hyper-responses do occur. Cases regarding the simultaneous development of OHSS and severe preeclampsia after letrozole is remarkably scarce. We detail a rare clinical case where moderate OHSS and severe preeclampsia manifested concurrently in a pregnant patient with underlying PMOS after a letrozole monotherapy cycle.

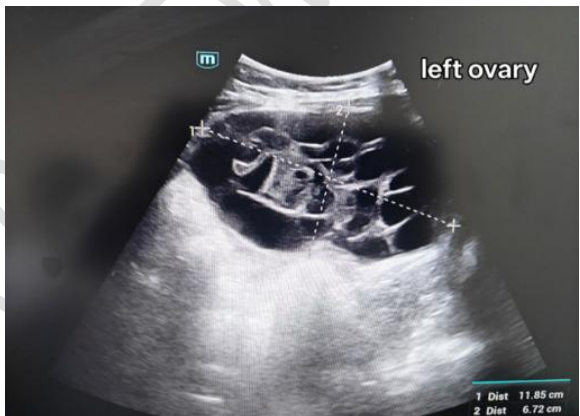
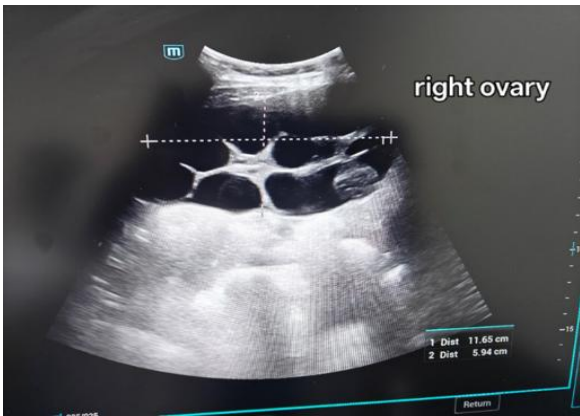
Patient history

A 25-year-old woman with Polyendocrine Metabolic Ovarian Syndrome presented in 2023 with secondary amenorrhea and two years of primary infertility. Ovulation induction with clomiphene citrate in April 2025 was unsuccessful. Letrozole induction in August 2025 resulted in a missed abortion at 7 weeks. A further letrozole cycle in December 2025 resulted in pregnancy. Pre-induction ultrasound showed bilaterally enlarged, cystic ovaries measuring 4.2 on the left and 5.6cm on the right. Unfortunately, she missed early antenatal visits.

She presented at 30 weeks and 2 days with flank abdominal pain, persistent headache, and abdominal fullness. Her blood pressure was 172/112 mmHg, the pulse was 93bpm, and a weight of 74 kg.

She had deep abdominal tenderness, guarding at the flanks without rebound tenderness. She had ascites, 2+ pitting oedema, severe hirsutism, and acne. Pulmonary and cardiac examinations were unremarkable.

There was a singleton pregnancy at 30 weeks and 4 days with an estimated fetal weight was 1520g. The umbilical Doppler PI was on the 99th percentile. Notably, both ovaries were markedly enlarged with multiple cysts (right: 11.65 cm, left: 11.85 cm) (figure 1 and 2) Furthermore, moderate ascites was



present.

Figure 1: Right Ovary

Figure 2: Left Ovary

The haemoglobin was

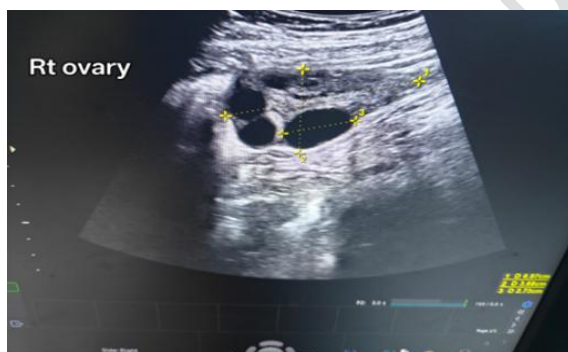
14.8 g/dL, and haematocrit was 47. The serum creatinine was 59.3 mmol/l, while AST and ALT were elevated at 78 U/L and 85 U/L, respectively. Urinary proteinuria was +++, and random glycaemia was 7.6 mmol/L.

Diagnosis and management

She was diagnosed with concurrent moderate Ovarian Hyperstimulation Syndrome and severe early-onset pre-eclampsia. We admitted her to the high-risk ward for close hemodynamic and fluid balance monitoring aiming for delivery at 34 weeks. Fluid replacement was administered orally and guided by the patient's thirst. Magnesium sulphate was administered for seizure prophylaxis, starting with a 14 g loading dose followed by 5 g intramuscularly every 4 hours for 24 hours. Blood pressure was initially controlled with intravenous hydralazine 5mg then oral nifedipine 40mg twice daily targeting blood pressures below 150/90 mmHg.

Given the high thromboembolic risk, enoxaparin 40mg subcutaneously once daily was initiated. Dexamethasone 6 mg twice daily for 48 hours promoted fetal lung maturation, while intravenous paracetamol 1 g provided abdominal pain relief. Urine output, vital signs, body weight, and fetal wellbeing (biophysical profile, Doppler) were closely done once a week. Fluid intake and output were recorded daily. Laboratory investigations were repeated after 48 hours and on day 7. Ovarian pelvic ultrasounds were performed weekly.

Over the next three weeks, haematocrit normalized, liver enzymes decreased, and urine output remained good. Blood pressure was variable, necessitating an adjustment of nifedipine to 40 mg three times daily and the addition of methyldopa 500 mg three times daily to maintain target blood pressure. Ovarian size was unchanged, but ascites resolved. Abdominal pain persisted. She required intermittent intravenous paracetamol 1g per rising need to control the symptoms. She was hospitalized for an additional week up



to 34 weeks when fetal growth restriction was diagnosed. The Dopplers and BPP were normal.

Labour was induced with oxytocin after cervical ripening with misoprostol. Due to a non-reassuring fetal heart rate, caesarean section was performed, resulting in delivery of a 1980 g neonate. Large bilateral ovarian cysts were identified intraoperatively. The patient was discharged on day five post caesarean section.

Postpartum follow up

At the three-week postpartum follow-up, the patient was asymptomatic with well-controlled blood pressure on nifedipine. Abdominal/pelvic ultrasound still showed bilaterally enlarged, multicystic ovaries, each about half their pregnancy size but larger than at ovulation induction (right: 6.9 cm, left: 7.2 cm). (Figure 3 and figure 4). Ascites had completely resolved.

Discussion

Ovarian Hyperstimulation Syndrome (OHSS) and preeclampsia are recognised complications of assisted reproductive technology (ART) and ovulation induction (12). Although distinct, both share a common mechanism involving systemic endothelial dysfunction and abnormal vascular permeability(13).The coexistence of OHSS and preeclampsia is a diagnostic and management challengesince both may manifest with oedema, ascites, excessive weight gain, oliguria, and abnormal liver or renal function tests(14).

The core existence of OHSS and preeclampsia is a rareinteraction between pro-angiogenic and anti-angiogenic pathways. OHSS is mediated by excess angiogenic VEGF and vasoactive cytokines(15). Early-onset preeclampsia involves systemic release of anti-angiogenic factors, especially soluble fms-like tyrosine kinase-1 (sFlt-1(16)(17).

In this patient, the clinical picture demonstrated thattwodistinct angiogenic pathways can operate simultaneously in separate vascular compartments. Her underlying Polyendocrine Metabolic Ovarian Syndrome provided a baseline predisposition to both complications.

The main challenge in this dual diagnosis is balancing two opposing fluid management strategies. Moderate OHSS is manged with fluids intravascular volume expansion and renal perfusion (18). On the contrary, severe preeclampsia is managed by restricting fluid to prevent volume overload.

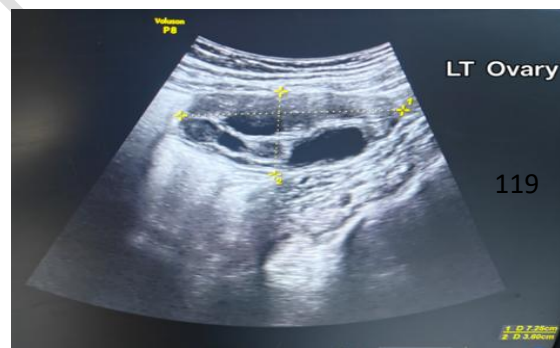


Figure 4: left ovary

Figure 3: Right ovary

In this case, we addressed this balance by implementing an oral-hydration-first strategy as the patient was hemodynamically stable. We were therefore able to avoid aggressive intravenous fluid expansion and at the same time stabilised the intravascular volume without risk to the patient.

Severe preeclampsia must be managed in hospital due to risk of rapid complications. Moderate ovarian hyperstimulation syndrome (OHSS) on the other hand can be managed as outpatient if hemodynamic

stability, oral intake, and followup are ensured(19)(20).In this case, inpatient management was preferred because of the severe preeclampsia,and some OHSS outpatient management criteria were not met.

OHSS induces a prothrombotic state through haemoconcentration and endothelial dysfunction (21) .The incidence of thrombosis has been estimated by other studies to be between 0.7% and 10% of OHSS (22).The additive hypercoagulable risks from pregnancy, severe preeclampsia made Enoxaparin administration crucial to prevent thromboembolic complications in this patient.

The severe hypertensionwas managed with slow-infusion IV hydralazine due to the unavailabilityof labetalol in our setting. Long-term control was achieved with oralnifedipine and methyldopa as per guidelines(23).Expectant management continued until 34 weeks, consistent with international protocols for stable preeclampsia with severe features(24).

The elevated umbilical artery Doppler pulsatility index (PI) at the 99th percentile indicated severe placental insufficiency. This was directly associated with a birth weight of 1980g and features of IUGR observed in the foetus.

The persistence of enlarged, multicystic ovaries throughout pregnancy, at caesarean section, and into the postpartum period suggests that the resolution of late-onset OHSS is a prolonged process, corroborating findings reported in previous studies(25)(26).

Conclusions and Recommendations

Ovarian hyperstimulation syndrome may persist or present in the late third trimester. Coexistence with early-onset preeclampsia though rare may occurin patients with metabolic disorders like PMOS. While letrozole is generally safe for ovulation induction, some individuals may experience a hyper-response.

Clinicians should suspect this dual pathology in patients with abdominal pain, hypertension, and enlarged ovaries and or ascites after ovulation induction. Effective management requires individualized inpatient monitoring, strict fluid balance, tailored antihypertensive therapy, aggressive thromboembolic prophylaxis, and timely delivery.

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Consent for PublicationWritten informed consent for publication of this case report and accompanying images were obtained from the patient.

Author Contributions

Handsome Dube: Manuscript conception, data collection, manuscriptpreparation,analysis,drafting, revision, proof reading and submission.

Daniel Niyomufasha: Data collection, Analysis, proof reading

All authors gave final approval of the version to be published.

Disclosure

The authors declare that there is no competing interest.

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