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Case Report

Egg-sploring the unusual: ICSI in Klippel-Trenaunay-Weber syndrome

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ABSTRACT

Klippel-Trenaunay-Weber syndrome (KTWS) is a rare congenital vascular disorder characterized by capillary malformations, venous and lymphatic anomalies, and soft tissue or bone overgrowth. Patients with KTWS face unique challenges in assisted reproductive technology (ART) due to their hypercoagulable state and the presence of extensive vascular malformations. Pregnancy can exacerbate these vascular complications, increasing maternal morbidity and mortality. In vitro fertilization (IVF) with gestational surrogacy offers a safer reproductive option. A 34-year-old woman with KTWS, a history of intermittent rectal bleeding, and extensive vascular malformations presented with primary infertility. Clinical and diagnostic evaluation revealed a reasonable ovarian reserve (AMH: 1.08 ng/ml) but significant vascular abnormalities in the mesenteric, splenic, hepatic, and colonic vasculature. A multidisciplinary approach was undertaken to minimize the risks associated with ovarian stimulation and oocyte retrieval. A GnRH antagonist protocol was chosen, with a dual trigger (Decapeptyl 200 mcg and hCG 10,000 IU) and careful anticoagulation management using low molecular weight heparin (LMWH). Nine mature oocytes were retrieved and cryopreserved without complications, and the patient was advised to proceed with gestational surrogacy. This case highlights the complexities of fertility management in patients with KTWS. The successful oocyte retrieval in a high-risk vascular patient demonstrates that, with meticulous planning and individualized care, ART can be safely performed. A multidisciplinary strategy, including anticoagulation adjustments and perioperative monitoring, is crucial in achieving favourable reproductive outcomes while minimizing risks. This case adds to the limited literature on ART in KTWS, reinforcing the feasibility of fertility preservation through a well-planned, multidisciplinary approach.

Keywords: Egg-sploring, Klippel-Trenaunay-Weber syndrome, Assisted reproductive technology

INTRODUCTION

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular disorder characterized by a classical triad of capillary malformations (port-wine stains), venous varicosities, and soft tissue or bony hypertrophy involving one or more limbs. First described by Klippel and Trenaunay in 1900, the condition represents a spectrum of combined vascular malformations, ranging from localized cutaneous lesions to extensive visceral and skeletal involvement.[1] The clinical expression of KTS is highly variable, with some patients exhibiting mild cosmetic deformities, while others experience significant vascular and orthopedic complications that can profoundly affect quality of life.[1,2]

The exact pathogenesis of KTS has remained uncertain for decades, but recent molecular insights have identified somatic mutations in the PIK3CA gene as a key etiological factor. These mutations result in hyperactivation of the PI3K–AKT–mTOR pathway, leading to abnormal cellular proliferation, angiogenesis, and vascular remodeling. The syndrome is now recognized as part of the PIK3CA-related overgrowth spectrum (PROS) disorders, which includes conditions such as CLOVES (congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal/spinal anomalies) and isolated

macrodactyly.[3] This genetic understanding not only refines the diagnostic framework but also opens potential avenues for targeted therapy, such as mTOR inhibitors, although clinical use in reproductive settings remains largely experimental.

Clinically, KTS is associated with chronic venous insufficiency, thromboembolic events, and consumptive coagulopathy due to aberrant venous architecture and stasis. The incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE) is significantly elevated in these patients, often due to impaired venous drainage and the presence of extensive varicosities.[4]

In addition, platelet sequestration and local activation of the coagulation cascade within vascular malformations can lead to localized intravascular coagulopathy or even disseminated intravascular coagulation (DIC) in severe cases. These hematologic disturbances make surgical or interventional procedures—including those related to reproductive medicine—particularly high-risk.[4]

Pregnancy further compounds the thromboembolic risk in KTS patients. Physiological hypercoagulability, increased venous capacitance, and elevated estrogen levels contribute to a heightened risk of DVT and PE during gestation.[4] Moreover, expanding uterine and pelvic venous networks may worsen pre-existing venous malformations, potentially leading to catastrophic hemorrhage, venous rupture, or progressive tissue hypertrophy. Consequently, the management of pregnancy in women with KTS requires multidisciplinary coordination involving obstetricians, hematologists, and vascular specialists. In many cases, conception is discouraged due to maternal risks, prompting consideration of alternative reproductive strategies.[5]

Assisted reproductive technology (ART) has revolutionized fertility management in women with complex medical conditions, including KTS. With the advent of controlled ovarian stimulation (COS), *in vitro* fertilization (IVF), and cryopreservation techniques, it is now possible to achieve biological parenthood without exposing the patient to the systemic risks of pregnancy.[6]

However, ART procedures must be meticulously tailored. High-dose gonadotropin stimulation can lead to supraphysiologic estrogen levels, further aggravating the hypercoagulable state and predisposing to thrombotic complication. For such patients, GnRH antagonist protocols are preferred due to their shorter duration, lower estrogen exposure, and reduced risk of ovarian hyperstimulation syndrome (OHSS). The use of a dual trigger—combining a GnRH agonist (e.g., Decapeptyl) with low-dose hCG—balances the need for optimal oocyte maturation with safety against excessive hormonal stimulation.[7]

Furthermore, the option of gestational surrogacy offers a safer and more practical alternative for women with KTS who wish to achieve parenthood while avoiding the physical risks associated with pregnancy. Surrogacy allows the use of the patient's own gametes while transferring the embryo to a healthy gestational carrier, thereby mitigating maternal vascular and obstetric complications.[6]

This case report describes a 34-year-old woman with KTS who successfully underwent IVF and oocyte retrieval, leading to embryo cryopreservation and a planned gestational surrogacy. The report highlights the complexity of reproductive management in KTS, emphasizing the need for individualized treatment, strict anticoagulation control, and interdisciplinary collaboration among reproductive endocrinologists, hematologists, anesthesiologists, and vascular surgeons. This case not only demonstrates the feasibility of ART in KTS but also contributes to the growing evidence supporting safe fertility preservation strategies in patients with congenital vascular malformations.

CASE REPORT

A 34-year-old woman with Klippel-Trenaunay–Weber syndrome (KTWS) presented for fertility consultation with a desire for genetic parenthood. She had regular menstrual cycles (25–28 days) and normal baseline endocrine parameters. Her significant clinical history included lifelong vascular malformations involving the lower limb and gastrointestinal tract, manifested by intermittent rectal bleeding since childhood.

She had bony and soft-tissue hypertrophy of the left foot, complicated by episodic bleeding, for which she underwent percutaneous sclerotherapy at age 25. On gynecologic examination, a large, compressible venous malformation occupying the left labia majora was observed, raising concern for procedural safety during transvaginal oocyte retrieval.

Her ovarian reserve was acceptable (AMH 1.08 ng/ml). MRI demonstrated extensive hemangiomatosis involving the mesenteric, splenic, and hepatic vessels, along with diffuse colonic vascular malformations. Such widespread visceral involvement is an uncommon but clinically significant manifestation that markedly elevates the risk of catastrophic hemorrhage or thrombosis during pregnancy, as recently highlighted in contemporary reviews.

A vascular surgery consultation concluded that the patient faced substantial risk from both pregnancy and oocyte retrieval, recommending prophylactic anticoagulation and gestational surrogacy as the safest route to parenthood.

Management strategy

Rationale for ovarian stimulation approach

Given her hypercoagulable baseline and extensive venous malformations, stimulation was planned with the primary goals of: minimizing estradiol exposure, preventing

venous stasis-induced thrombosis, and ensuring procedural safety.

A GnRH antagonist protocol was selected to maintain lower peak estradiol levels and reduce the likelihood of OHSS an approach supported by recent evidence in high-thrombotic-risk patients.

Stimulation protocol

Gonadotropins: initiated with careful dose titration

Final oocyte maturation: dual trigger using Decapeptyl 200 mcg (to generate an endogenous LH surge) hCG 10,000 IU (to optimize oocyte competence). Prophylactic LMWH (40 mg SC daily) was started at the beginning of stimulation, reflecting the practice adopted for individuals with congenital vascular malformations prone to thrombosis.

Perioperative anticoagulation and retrieval

To balance bleeding and thrombosis risk: LMWH was withheld 12 hours prior to retrieval. Oocyte retrieval took place 35 hours post-trigger, with gentle transvaginal ultrasound guidance to avoid the labial venous malformation. LMWH was resumed 10–12 hours post-procedure, and the patient was monitored in an inpatient setting for early detection of occult hemorrhage. Anticoagulation was continued for one month postpartum to counteract post-stimulation hypercoagulability.

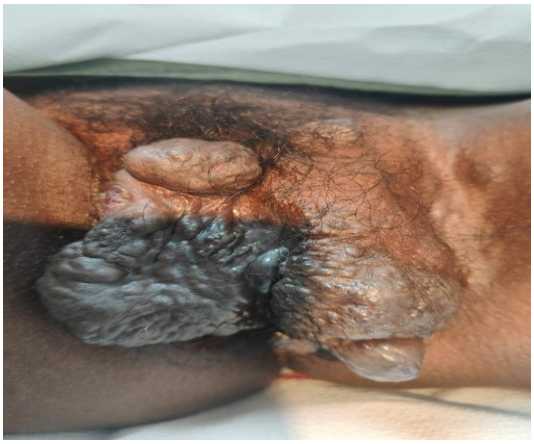

Figure 1: Vulval venous malformation.

Outcome

The patient completed stimulation and retrieval without hemorrhagic or thromboembolic complications. The procedure yielded viable oocytes for fertilization. Given the extensive visceral vascular involvement and the heightened maternal risks documented in recent KTWS literature including venous rupture, pulmonary embolism, and uncontrolled gastrointestinal bleeding she was strongly counselled to proceed with gestational surrogacy. This approach allowed her to pursue biological parenthood while avoiding the substantial risks that pregnancy would pose.

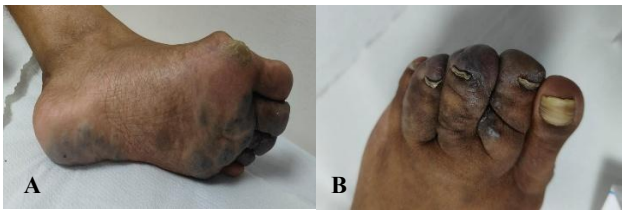

Figure 2 (A and B): Venous malformation of left foot with bony and soft tissue hypertrophy.

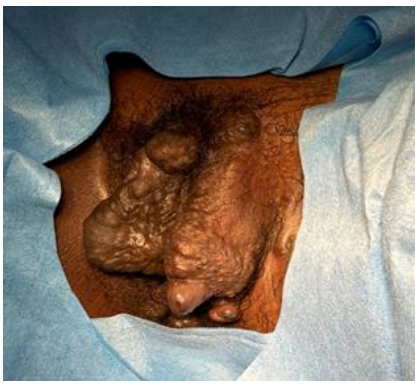

Figure 3: Venous malformation of labia majora.

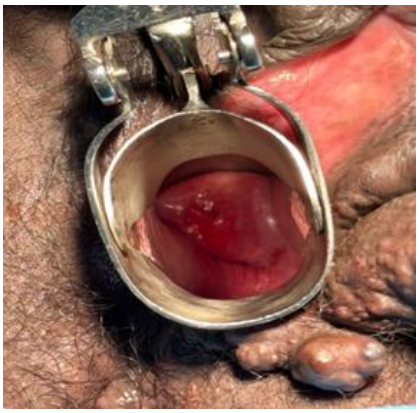

Figure 4: Normal cervix.

Figure 5: Normal vagina.

Table 1: Gonadotropins: initiated with careful dose titration.

Day of GT	Gonal F IU	IVF M IU	Setrosil mg	E2 pg/ml	LH mIU/ml	Right ovary	Left ovary	ET
1	225			47.4	2.77	AFC 7	AFC 8	Thin
2	225							
3	225							
4	225							
5	225		0.25	633	2.5	14,9,7,4	11,11,9,9,7,7,5	7.5 mm TL
6	225		0.25		2.56		9,9,8,7	
7	225		0.25					
8		300	0.25	622.1	0.7	16.7,14.1,10.3	15.2,14.3, 14, 13.9 (2),10 (2)	10.2 TL+
9		300	0.25					
10		300	0.25	1775.1	0.55	21.1, 13.5, 12.1, 10.2	20.7, 17.4, 16.2, 15.5, 14.4,11	9 mm
11		225	0.25	2620	0.35	24,16.3,12.4,11.3	19.1,17.9(2),17.4,16.8,16.1,13.2	9 mm, TL+
12		225	0.25			24.5,16.3,15,14	23.3,22.3,20.7,18.7,18.4,17.9,13.9	10 mm

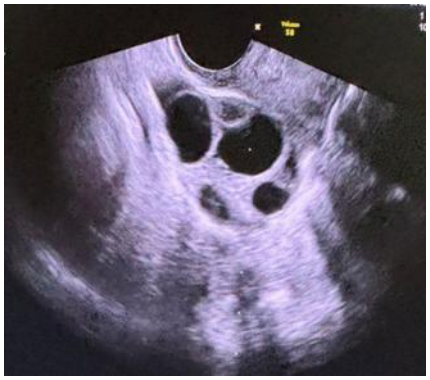

Figure 6: Ultrasound image of ovaries during egg collection.

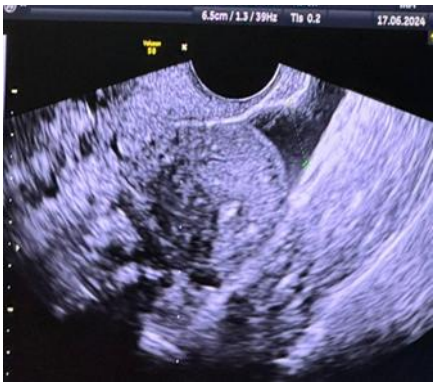

Figure 7: Free fluid in POD seen on USG.

DISCUSSION

The present case demonstrates that ART, particularly IVF with gestational surrogacy, can be safely and successfully performed in a patient with Klippel-Trenaunay-Weber Syndrome (KTWS) when managed through a multidisciplinary, individualized approach. Despite the traditionally high morbidity associated with this vascular disorder, the outcome of this case successful oocyte retrieval and cryopreservation without bleeding or thrombotic complications supports the feasibility of ART in carefully selected KTWS patients under controlled conditions.

Interpretation of present results

In this case, nine mature oocytes were retrieved following a GnRH antagonist stimulation protocol and dual trigger (Decapeptyl + low-dose hCG), under continuous hematologic and anesthetic supervision. The patient remained hemodynamically stable with no evidence of excessive bleeding, venous thrombosis, or local hematoma formation. This outcome highlights several important observations.

First, the antagonist protocol successfully achieved adequate follicular response while limiting serum estradiol levels, thereby minimizing the estrogen-related thrombotic burden. Second, the dual-trigger approach effectively supported final oocyte maturation without provoking ovarian hyperstimulation syndrome (OHSS), which is critical because OHSS can cause hemoconcentration and endothelial dysfunction that further heighten thromboembolic risk. Third, prophylactic anticoagulation with LMWH before and after retrieval balanced both hemorrhagic and thrombotic risks. Finally, the decision to cryopreserve oocytes and utilize a gestational surrogate effectively separated the patient's vascular risk from pregnancy-related hemodynamic stress. Collectively, these findings reinforce that fertility preservation and ART are possible in KTWS when there is multidisciplinary coordination between reproductive endocrinology, vascular surgery, hematology, and anesthesiology teams.

Comparison with previous reports

Few published reports have explored reproductive management in KTWS, and even fewer have documented

outcomes following ART. Previous case series and reviews indicate that pregnancy in KTWS is associated with substantial maternal risk. With DVT, pulmonary embolism (PE), and severe venous insufficiency as major contributors to morbidity and mortality.[8] Similarly, JR Matin et al reported that venous stasis and structural anomalies predispose these patients to chronic thrombosis and pulmonary embolism, with a 10-fold higher postoperative embolic risk compared to non-affected women.[6,8] Pregnancy exacerbates these vascular complications. Physiological hypercoagulability and increased estrogen levels during gestation can amplify thrombotic tendencies, occasionally resulting in disseminated intravascular coagulation (DIC) or massive postpartum hemorrhage. These findings parallel the concerns in the current case—where pregnancy was deemed unsafe—and justify the use of gestational surrogacy.[9] There are cases which have also reported worsening varicosities and bleeding complications during pregnancy in KTWS, supporting the avoidance of direct conception in high-risk cases.[10]

The present result contrasts favorably with earlier experiences of pregnancy in KTWS, which were often complicated by hemorrhage or thromboembolism. By employing ART and surrogacy, the patient in this report avoided the hemodynamic stresses that would have likely aggravated her extensive pelvic and visceral venous malformations. This strategy aligns with recommendations that advocated multidisciplinary pre-conceptual counseling and alternative reproductive planning for women with severe pelvic vascular involvement.[11]

COS and thrombosis

One of the main challenges in ART for KTWS is COS. Elevated estradiol levels are known to increase hepatic production of clotting factors and suppress fibrinolysis, producing a prothrombotic environment. The decision to employ a GnRH antagonist protocol was based on its safety profile in hypercoagulable women.[12] Studies in non-KTWS cohorts show that antagonist cycles result in lower peak estradiol levels and shorter stimulation durations compared with agonist regimens, while maintaining comparable oocyte yield and pregnancy rates. In the context of KTWS, these pharmacologic advantages directly translate into a reduced risk of thrombosis and vascular congestion.[12]

This finding is consistent with the reports by Miller VM, who emphasized minimizing estrogen exposure in patients with underlying vascular pathology.[13] Similarly, antagonist protocols have been recommended in women with a history of venous thromboembolism, as they avoid the high estrogen surges associated with agonist downregulation.[6] In our case, the use of the antagonist regimen allowed safe follicular recruitment with adequate oocyte yield and prevented escalation of estradiol beyond 3000 pg/ml—a level often linked with thrombotic complications.

Triggering final oocyte maturation

The choice of trigger in ART is another determinant of safety. Human chorionic gonadotropin (hCG) alone has traditionally been used to induce final oocyte maturation; however, it prolongs luteotrophic stimulation and increases vascular permeability, which can precipitate OHSS—a condition associated with hemoconcentration, ascites, and thrombosis.[14] In this case, a dual trigger (GnRH agonist + low-dose hCG) was employed to strike a balance between oocyte maturity and safety. The GnRH agonist component induces a physiologic LH surge, while the limited hCG dose supports luteal function without excessive vascular stimulation.[14] This approach aligns with recent reproductive endocrinology data demonstrating that dual triggers can achieve equivalent oocyte maturity rates to conventional hCG triggers but with significantly reduced OHSS risk.[15]

Similar strategies have been described in other high-risk populations, such as women with polycystic ovary syndrome (PCOS) and thrombophilic disorders, but reports in KTWS are rare. The successful use of this regimen in the present case expands its applicability to congenital vascular malformations, offering a safer option for final oocyte maturation in future cases.

Perioperative anticoagulation and risk mitigation

Anticoagulation forms the cornerstone of peri-ART management in KTWS.[16] The hypercoagulability in these patients arises from venous stasis, endothelial dysfunction, and, in some cases, inherited thrombophilias such as Factor V Leiden or MTHFR mutations. LMWH provides predictable anticoagulant activity with a lower risk of bleeding compared to vitamin K antagonists and is the preferred prophylactic agent. In our case, LMWH was initiated before stimulation, withheld 12 hours before retrieval, and resumed 10–12 hours afterward once bleeding was ruled out. This regimen parallels protocols proposed for high-risk ART patients in the literature and was critical to achieving a complication-free procedure.[6]

Previous reports emphasize similar strategies. McBane et al noted that peri-procedural anticoagulation reduces thrombotic complications in vascular malformation syndromes. In contrast, inadequate anticoagulation or abrupt discontinuation can lead to catastrophic outcomes, including fatal PE. The continued LMWH prophylaxis for one month post-retrieval in this case reflects an evidence-based approach to cover the residual hypercoagulable phase following ovarian stimulation.[17]

Gestational surrogacy and comparative outcomes

Despite advances in ART, the hemodynamic stress and hormonal milieu of pregnancy remain dangerous for KTWS patients. The physiological increase in cardiac output, blood volume, and venous distensibility during gestation can aggravate pre-existing vascular

malformations, leading to thrombosis, bleeding, or rupture. Reports by Xue W et al have documented cases of catastrophic hemorrhage and disseminated coagulopathy in KTWS pregnancies.[18] Consequently, gestational surrogacy is advocated as the safest option for achieving biological parenthood.[6]

In the present case, choosing surrogacy avoided maternal risk while achieving reproductive success through the patient's own oocytes. This approach parallels recommendations in recent reproductive literature suggesting that surrogacy offers a safer, ethical, and medically sound alternative for women with severe vascular malformations. The positive outcome in this case further validates surrogacy as a definitive solution for fertility in KTWS, reinforcing the shift from risk-laden pregnancy attempts to safer, surrogate-based reproduction.

Clinical implications and future directions

This case contributes meaningful insights to the limited pool of literature on ART in KTWS. It underscores that fertility preservation and parenthood are achievable when individualized stimulation protocols, vigilant perioperative monitoring, and multidisciplinary expertise are applied. The results also highlight the necessity of maintaining a delicate balance between anticoagulation and procedural safety.[18]

Future studies should aim to develop standardized guidelines for ART in vascular malformation syndromes. Prospective registries and multicenter collaborations could help define optimal stimulation thresholds, anticoagulation durations, and long-term outcomes for both patients and gestational carriers. Additionally, molecular studies exploring the impact of PIK3CA mutations on ovarian and endometrial function could elucidate whether KTWS affects reproductive potential beyond vascular considerations. [19]

In summary, the present study demonstrates that successful oocyte retrieval in KTWS is feasible using a GnRH antagonist protocol, dual trigger, and carefully titrated LMWH prophylaxis. The absence of procedural complications, together with favorable oocyte yield, supports the safety of this individualized ART approach. Compared with earlier reports of poor obstetric outcomes, this case provides encouraging evidence that modern ART, combined with gestational surrogacy, offers a viable and safe path to biological parenthood in women with KTWS, while aligning with prior literature advocating risk mitigation and multidisciplinary care.[6,19]

CONCLUSION

This case highlights the feasibility ART in patients with KTWS when managed with meticulous planning and a multidisciplinary approach. Despite the inherent challenges posed by extensive vascular malformations and an increased thromboembolic risk, successful oocyte retrieval and embryo transfer were achieved without major complications. The use of a GnRH antagonist protocol played a crucial role in minimizing estradiol levels, thereby reducing the risk of venous congestion and thrombosi. Additionally, the incorporation of a dual trigger (Decapeptyl' hCG) ensured optimal follicular maturation while lowering the likelihood of ovarian hyperstimulation syndrome (OHSS), a critical concern in hypercoagulable patients. A carefully tailored anticoagulation strategy, Including peri-procedural anticoagulation and post-retrieval hospitalization, further enhanced patient safety. The extension of anticoagulation therapy beyond the immediate post-procedure period significantly mitigated the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), which are major concerns in KTWS. This case adds valuable insights to the limited literature on ART in KTWS patients, underscoring the importance of individualized treatment strategies to optimize reproductive outcomes while safeguarding maternal health. Future research is essential to establish standardized guidelines for ART in patients with extensive vascular malformations, ensuring safer and more effective reproductive care for this high-risk population.

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