Pregnancy in women with Klippel-Trenaunay syndrome: Report of three pregnancies in a single patient and review of literature

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Abstract

Klippel-Trenaunay syndrome is characterised by vascular abnormality which increases the risk of thromboembolism and haemorrhage. Physiological changes in pregnancy pose an increased risk to these complications. Being an uncommon disorder, there is limited literature about the management of women with pregnancy and Klippel-Trenaunay syndrome. We report in detail two of three pregnancies in a woman with Klippel-Trenaunay syndrome who had repeated episodes of haematochezia leading to anaemia, managed with Argon laser Photo-Coagulation in pregnancy and also reviewed the complications and the management of pregnant women with Klippel-Trenaunay syndrome.

Keywords

Klippel-Trenaunay syndrome, argon laser photocoagulation, thromboembolism, pregnancy

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Introduction

Klippel-Trenaunay syndrome (KTS), also called 'Naevus vasculosus osteohypertrophicus', is a rare congenital disorder characterised by a triad of cutaneous haemangioma, venous varicosities and soft tissue/bone hypertrophy affecting extremities.¹ Morbidity from this disease is mainly due to vascular abnormalities which may result in venous insufficiency, thromboembolism or haemorrhage.² Normal physiological changes during pregnancy such as increased venous return, venous stasis and increased cardiac output may be associated with exacerbations of complications such as haemorrhage and thromboembolism in these women.³

Being a rare disease, there are only case reports and case series available in peer-reviewed literature regarding pregnancy outcomes in women with KTS. There is no consensus in the literature regarding the management of pregnancy in women with KTS. Here, we report three pregnancies in a woman with KTS complicated by gastrointestinal vascular malformation. We also systematically reviewed the available English language peer-reviewed literature from 1989 till 2016 for pregnancy outcomes and complications in such cases.

Case report

A 24-year-old female presented to the surgery department with bleeding per rectum on and off since 2001. She had a history of dilated veins over the right lower limb since childhood with associated pain and swelling (Figure 1). She underwent sclerotherapy in 2010 for haemorrhoids. She was evaluated for multiple varicosities over the lower limb, limb length discrepancy and port-wine stain in the right lower limb and was diagnosed with KTS in 2012. Doppler ultrasonography and angiography showed multiple dilated veins along the short saphenous venous system with sapheno-femoral incompetence and perforator incompetence of the right leg and ectatic vessels in the rectum and recto-sigmoid colon. She had recurrent episodes of haematochezia for which Argon Plasma Coagulation (APC) was performed twice.

Pregnancy 1 (2013)

She underwent medical termination of pregnancy at nine weeks as she was undergoing evaluation and treatment for KTS.

Pregnancy 2

Two years later, she presented to the obstetric emergency department with haematochezia and severe anaemia (Hb = 3.7 g/dL) at 14 weeks of gestation. Local examination revealed vulval varicosities. Colonoscopy showed scarring of the upper rectum with vascular ectasia from 8 to 25 cm. She received two units of packed red blood cell (PRBC) transfusion and APC was performed. She was discharged after 11 days, and APC was done again at week 23 for bleeding per rectum. She was regularly monitored and serial ultrasounds for fetal growth were normal. Her haemoglobin concentration remained between 7.8 and 9 g/dL. She was admitted at 34 weeks in view of anaemia (Hb = 7.8 g/dL) and KTS. At 35⁺ weeks of gestation, she had spontaneous pre-labour rupture of membranes. After augmentation of labour with oxytocin and parenteral analgesia with opioids, she delivered vaginally a preterm, small for gestational age female baby of 1.83 kg with APGAR score of 8 and 9 at 1 and 5 min. The baby was observed in the Neonatal Intensive Care Unit (NICU) in view of

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Figure 1. (a) and (b) The right lower limb hypertrophy with port-wine stain and varicosities. (c) The vulval varicosities especially on the right labia.

prematurity for 6 h and both mother and baby were subsequently discharged three days after delivery. Her postnatal review at six weeks was uneventful with no complaints.

Pregnancy 3

Fifteen months later, she again presented with bleeding per rectum and severe anaemia (Hb – 3.4 g/dL) at 24 weeks of gestation. During her hospital stay of 24 days, she had recurrent episodes of bleeding per rectum and was transfused a total of four units of PRBC. She underwent APC twice in the antenatal period for the same symptoms at 24 and 30 weeks. Antenatal imaging (ultrasonography (USG) and magnetic resonance imaging (MRI)) showed multiple vascular spaces in the entire uterine wall, right gluteal region extending to right parametrium and perirectal region. Fetal growth monitoring was done by serial ultrasound, without any evidence of growth restriction. She delivered vaginally at 35+6 weeks of gestation a male baby weighing 2.2 kg with APGAR score of 7 and 8 at 1 and 5 min. She received parental opioids for labour analgesia. Her postnatal period was uneventful. She opted for permanent sterilisation, and bilateral tubectomy was done six weeks later. She was planned for APC two weeks after the surgery and follow-up thereafter has been uneventful.

Discussion

KTS has an incidence of 3–5/1,00,000 births and was described as early as 1900 by French physicians Maurice Klippel and Paul Trenaunay.^{1,4} KTS is a disease of sporadic origin with only 1% reported to be hereditary.^{5,6} Diagnosis of KTS is usually made in childhood with the early onset of symptoms and signs.⁷ Vascular abnormalities which are the hallmark of the disease become more pronounced during pregnancy secondary to the physiological changes in the cardiovascular system and the increase in intraabdominal pressure and compression of the inferior vena cava due to the enlarging uterus. Vulvo-vaginal and cervical varicosities must be observed with caution during pregnancy, for they may cause massive blood loss following laceration or trauma.⁸ Vascular abnormalities at the neuro-axial level can complicate the anaesthetic management of the patient.³

Systematic review of the literature

There are few case reports and series reported in the literature on pregnancy outcomes in women with KTS. We performed a literature

search in MEDLINE, Google Scholar, Scopus databases for case reports and case series published in English language from 1989 to 2016 using the keywords 'Klippel Trenaunay syndrome', 'Naevus vasculosus osteohypertrophicus', 'pregnancy outcome' and 'varicosities' (Figure 2). Titles and abstracts of the search results were screened in duplicates by three authors (AK, KK and AK). Full texts of those articles that passed through the first stage were screened in duplicate by AK and KK. Disagreements were resolved through discussion and consensus building between the three searchers with the help of DKM. Finally, we included 26 case reports/series of pregnancy outcome in women with KTS reporting 33 pregnancies and also included the three pregnancies of our case. Table 1 contains the included studies and their key characteristics.

Diagnosis, manifestations and pre-pregnancy management

Among 33 cases that were reported, the classical triad of KTS was noticed in 25 (75%) during childhood, of which six cases were diagnosed early in the neonatal period. Seven cases were diagnosed during pregnancy and puerperium. Most women presented with thrombotic complications with few having haemorrhagic complications. Other rare presentations included focal seizures and lymphedema. Nine cases (25%) had multiple episodes of thrombosis or thromboembolism involving vessels of the lower limb and pulmonary artery during pregnancy or prior to pregnancy. Four cases (12.12%) presented with bleeding manifestations which included chronic haematochezia, haemarthroses and postpartum haemorrhage (PPH). Index case had multiple episodes of haematochezia leading to anaemia.

Imaging studies demonstrated the absence of deep venous system in the lower limbs in two cases. Skeletal deformities were noted in 24.2% of the cases; scoliosis and limb shortening being the most common abnormality (9% each). Other skeletal deformities were hemi-hypertrophy, fixed flexion deformity of the lower limb and foot deformity (3% each). Instances of orthostatic hypotension were also reported occasionally in patients with KTS.

Surgical interventions were performed in 10 women (30.3%) in the pre-pregnancy period. Eight of them underwent surgeries for varicosities of the lower limb; of which one had varicectomy performed seven times but without success. One patient underwent lymphatic mass excision and another patient had left leg amputation, splenectomy and pelvic vein embolisation performed for splenic arterio-venous malformation (AVM) and multiple episodes of thromboembolism. Irradiation was done in two patients for cutaneous AVM.

Figure 2. The search strategy for systematic review.

Medical complications during pregnancy

Pulmonary embolism occurred in one patient during the antenatal period and was treated with heparin and Greenfield inferior vena cava (IVC) filter placement. Anticoagulation and elastic stocking were advised in one-third of the pregnancies, and aspirin prophylaxis was advised in a few. Paraplegia developed at 30 weeks' gestation in a patient due to an expanding spinal AVM and AV fistula. She underwent caesarean section at term under general anaesthesia in view of her paraplegia. Spontaneous recovery of the lower limb strength occurred gradually from the seventh postoperative day. Imaging showed dilated epidural venous plexus in another patient who had an uneventful spontaneous vaginal delivery. The case reported had repeated episodes of rectal bleeding leading to severe anaemia during both pregnancies which was managed with APC and multiple blood transfusions.

Obstetric complications and pregnancy outcome

The mean age of patients during pregnancy was 27 years (24–30 years). The most common problem encountered during pregnancy was pain

and swelling of the limbs, which even required treatment with opioid analgesia. Significant increase in the size of vulvo-vaginal varices was noted in 27% of patients. Prenatal imaging showed uterine/cervical varicosities and haemangiomas in eight (22.2%) of the reported pregnancies. Two cases with cervical haemangioma presented with vaginal bleeding in the first and second trimester with one requiring haemostatic suture ligation of the haemangioma. Intrauterine growth restriction (11.1%) and fetal malpresentation (11.1%) were the most commonly noted obstetric complications, rates being similar to the background rates in the general population. Pre-eclampsia was reported in two pregnancies and one had gestational diabetes mellitus. Prenatal ultrasound in one woman showed suspected KTS in the fetus, and this patient underwent termination of pregnancy as the previous male child also had KTS.

Of the 36 pregnancies, three underwent termination of pregnancy (unwanted pregnancy – 2, suspected fetal KTS – 1). Among the remaining 33 pregnancies, the mean gestational age at delivery was 37.4 weeks (36–39 weeks). Preterm deliveries occurred in 27.3% as noted in two of the pregnancies in our patient. Of the 33 deliveries, 23 underwent caesarean section. Caesarean section was performed for non-obstetric indications in 11 cases (vulvovaginal varices – 8, large

Table 1. Key characteristics of the included case report or series.

S. no	Author	Case no.	Medical complication	Obstetric complication	
				Antepartum	Postpartum
1.	Samonakis et al. ⁹	1. G3	Portal vein thrombosis		
2.	Rebarber et al. ¹⁰	1. G1	Pulmonary embolism	IUGR	Puerperal pyrexia
		2. G6A5	Multiple episodes of thromboembolism		
		3. G1	Multiple episodes of thromboembolism		Superficial caesarean wound gape
3.	Tanaka et al. ¹¹	1. G1			
4.	Gündoğan et al. ³	1. G1		Dilatation of epidural venous plexus	
		2. G1			Acute Phlegmasia Alba Dolen requiring thrombectomy
5.	González-Mesa et al. ¹²	2.G1			
6.	Kemfarg et al. ¹³	1. G2A1	Varicectomy – 7 times (without success)		
7.	Yara et al. ¹⁴	1. G1	Focal left sided seizures, Talipes equinus of both lower limbs, Limb dystonia		Six unit packed red cell transfusion
8.	Hidalgo et al. ¹⁵	1. G1	Pulmonary thromboembolism, Orthostatic hypotension	Fetal malposition	
9.	Dobbs et al. ¹⁶	1. G1P0	Multiple episodes of thromboembolism		
10.	De et al. ¹⁷	1. G1P0		Gestational diabetes mellitus	
11.	Gupta et al. ⁴	1. G1			
12.	Watermeyer et al. ⁸	1. G1		Oligohydramnios, oblique lie	Two unit packed red cell transfusion
13.	Sivaprakasam and Dolak ¹⁸	1. G1		Pre-eclampsia, Breech presentation	
14.	Fait et al. ¹⁹	1.Preg1: G1		IUGR	
		Preg 2: G2L1		IUGR at 35 weeks	
15.	Bouchard-Fortier et al. ²⁰	1. multi gravida		Breech presentation	
16.	Atis et al. ²¹	1. G2A1		Premature contractions at 33 weeks requiring tocolysis	
17.	Stein et al. ²²	1. G4P1L1A2			
		2. G1			
		3. G1	chronic haematochezia, chronic anaemia, multiple blood transfusions	Vaginal bleeding in first trimester	Traumatic PPH and two additional surgeries – four packed red cell transfused
		4. G1		Vaginal bleeding at 28-4/7 weeks secondary to cervical haemangioma, oligohydramnios	
18.	Verheijen et al. ²³	1.G1	Thrombosis in AVM in right popliteal artery	IUGR at 34 weeks	Anaemia – blood transfusion
19.	Jorgenson et al. ²⁴	1. G2L1		Suspected fetal KTS	
20.	Pollack et al. ²⁵	1. G1	Superficial thrombophlebitis		
21.	Gaiser et al. ²⁶	1. G1	Orthostatic hypotension		Atonic PPH, low-grade disseminated intravascular coagulation, postoperative wound exploration and evacuation
22.	Andreasen et al. ²⁷	1. G1			Traumatic PPH
23.	Hergesell et al. ²⁸	1. G1	Deep vein thrombosis		

(continued)

Table 1. Continued

S. no	Author	Case no.	Medical complication	Obstetric complication	
				Antepartum	Postpartum
24.	Neubert et al. ²⁹	I. GI			Postoperative wound haematoma, diagnosed with Kasabach-Merritt syndrome
25.	Richards and Cruz ³⁰	I. GI			
26.	Demir et al. ³¹	I. GI	Acute paraplegia of lower limb due to spinal AVM		

AVM: arterio-venous malformation; PPH: postpartum haemorrhage; KTS: Klippel Trenaunay syndrome; IUGR: intrauterine growth restriction

multiple uterine myomas – 1, severe dystonia – 1, paraplegia – 1). Of these 11 cases, three were elective classical caesarean sections done for AVM or increased vascularity of the lower uterine segment which were detected by ultrasound showing multiple dilated vessels in the lower uterine segment. Obstetric indications for caesarean section included malpresentation, fetal distress, premature rupture of membranes with soft tissue hypertrophy, contracted pelvis, failed induction, IUGR with previous caesarean section, oligohydramnios and cephalo-pelvic disproportion. There were no maternal or neonatal deaths reported.

Of the 10 vaginal deliveries, information regarding labour analgesia was available for six deliveries. Epidural analgesia was provided in three, while parenteral analgesia with opioids was given in three deliveries including two deliveries in our case. Of the 23 caesarean deliveries, only 11 of them reported the type of anaesthesia used for the surgery. Five cases were done under general anaesthesia, while epidural and spinal anaesthesia were given in three cases each.

PPH was reported in four cases (12.1%), of which three were traumatic and one was atonic. Among three cases of traumatic PPH, one was due to left-sided vaginal laceration with bleeding from suspected vaginal AV malformation following vaginal delivery. The other two cases were due to increased blood loss from varicosities in the lower uterine segment during caesarean section. Six patients (18.2%) received transfusion for anaemia/increased bleeding with three requiring massive transfusions. There were four cases (12.1%) of wound dehiscence, requiring repair. Three of these women had wound haematoma leading to dehiscence. Kasabach Meritt syndrome (KMS), i.e. haemangioma with thrombocytopenia was diagnosed in a patient who developed wound haematoma in the post-operative period, requiring two explorative laparotomies, wound haematoma evacuation, multiple red cell and blood products transfusion. Occurrence of KMS may be secondary to platelet trapping in the large and extensive haemangiomas in the vulval and right lower abdominal wall. One patient underwent thrombectomy in the immediate postpartum for phlegmasia alba dolens with complete thrombosis of superficial veins of right leg. About two-thirds of the patients received prophylactic anticoagulation, with heparin and/or mechanical compression stocking in the postpartum. Complications such as endomyometritis (n = 1), deep vein thrombosis (n = 1) and disseminated intravascular coagulation (n = 1) were reported which were managed conservatively.

Conclusion

Favourable obstetric outcome can be achieved in such women when managed by a multidisciplinary team of obstetricians, anaesthetists, surgeons, radiologists, haematologists and paediatricians. The incidence of obstetric complication is noted to be similar to those women without KTS. Pregnant women with KTS are at increased risk for thromboembolism and haemorrhage, and hence thromboprophylaxis may be considered in the peri-partum period. Mode of delivery can be based on obstetric indications and screening for AV

malformation over the anterior surface of the uterus by imaging (USG/MRI) might help in planning uterine incision for caesarean section. Consultation with obstetric anaesthetist in the third trimester will also aid in planning the labour analgesia/anaesthesia for women with KTS.

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AK.

Contributorship

AnK, KK and ArK conceived the idea and performed the search. AnK and KK wrote the first draft. AnK, ArK and DKM reviewed and revised the final draft. KD and SS reviewed and commented on the final draft.

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