

Reviewer #1: Abstract: The inferior vena cava (IVC) filter might be ineffective in patients with KTS. This statement is not a direct observation of the current study and therefore may not be included in the abstract. Patient presentation: elaborately discussed Discussion: Are there any previously published articles on this subject. Kindly include Reasonably well written paper
Has been corrected.

Reviewer #2: The case report of "Massive pulmonary embolism in Klippel-Trenaunay syndrome after leg raising" is well presented; however, the manuscript needs the following corrections/additions before publication:

<ul style="list-style-type: none"> The authors mention that "A 12-year-old girl with KTS underwent excision of verrucous hyperkeratosis in the left foot and posterior aspect of the left leg and left thigh and excision of a cutaneous hemangioma in the right buttock." Did the patient undergo surgery after an episode of Pulmonary embolism? If so when? If not then change the sentence to: A 12-year-old girl was scheduled for excision of verrucous hyperkeratosis in the left foot and posterior aspect of left leg and left thigh as well as excision of cutaneous haemangioma in the right buttock. (line 65 to 67)
The patient had received the surgery 3 months later after the episode
<ul style="list-style-type: none"> Line 80 -82: should be written as: Diagnosis of KTS is established when two of the triad features, viz. capillary malformation (port wine stains), hypertrophy of soft tissue or bones and varicose veins, are present.
Has been corrected
<ul style="list-style-type: none"> Do mention how many cases in the world are reported in the literature till now.
<p>The incidence has been estimated at two to five per 100,000.</p> <p>Alwalid O, Makamure J, Cheng QG, Wu WJ, Yang C, Samran E, Han P, Liang HM. Radiological Aspect of Klippel-Trénaunay Syndrome: A Case Series With Review of Literature. Curr Med Sci. 2018 Oct;38(5):925-931.</p>
<ul style="list-style-type: none"> Line 84-85: kindly change as: Dislodgement of the clots from pre-existing thrombosed veins upon movements and subsequent migration to pulmonary circulation can lead to massive pulmonary embolism.
Has been corrected
<ul style="list-style-type: none"> Line 86: "There are few reports of patients with severe PEs after leg sterilization". Kindly give the references.
<p>There have been no reports of severe pulmonary embolisms occurring after leg sterilization, except in cases where a massage or ultrasound examination was being performed.</p> <p>Sufian S, Arnez A, Lakhanpal S. Case of the disappearing heat-induced thrombus causing pulmonary embolism during ultrasound evaluation. J Vasc Surg. 2012 Feb;55(2):529-31. doi: 10.1016/j.jvs.2011.07.070. Epub 2011 Sep 29. PMID: 21958568.</p> <p>Sutham K, Na-Nan S, Paiboonsithiwong S, Chaksuwat P, Tongsong T. Leg massage during pregnancy with unrecognized deep vein thrombosis could be life threatening: a case report. BMC Pregnancy Childbirth. 2020 Apr 22;20(1):237. doi: 10.1186/s12884-020-02924-w. PMID: 32321459; PMCID: PMC7178622.</p>
<ul style="list-style-type: none"> Line 91: authors mention that she had hemihypertrophy..... of what?

hemihypertrophy in the left lower limb along with varicose veins and multiple lipomas
<ul style="list-style-type: none"> Line 92-93: mention when the last surgery was performed.
4 years ago, for excision
<ul style="list-style-type: none"> Line 93-95: "On admission, she would receive excision of verrucous hyperkeratosis on the left foot and posterior aspect of the left leg and thigh and excision of a cutaneous hemangioma on the right buttock" Change it as "She was admitted for excision of verrucous hyperkeratosis on the left foot and posterior aspect of the left leg and thigh and excision of a cutaneous hemangioma on the right buttock."
Has been corrected
<ul style="list-style-type: none"> After line 97 do mention what other pre-operative investigations were done. Any relevant finding on pre-anesthetic examination whether there was any hypertrophy of soft tissue in the mouth and intubation was going to be easy or difficult.
There was no record of difficulty in intubation
<ul style="list-style-type: none"> To start with the procedure, the patient's heart rate was 111/minute. Was the cause for this tachycardia established pre-operatively? Any heart examination was done to rule out right ventricular failure was done? Since the surgery was on blood vessels, was pre-operative angiography or scans were done? If not then why or else it would have established pre-existing thrombosis in the lower limbs or DVT. This should be mentioned in the discussion if these investigations were not performed pre-operatively.
The patient was irritably crying in her father's arms at the time. Might related to that the patient is nervous and mild dehydration due to NPO.
<ul style="list-style-type: none"> Any DVT prophylaxis like LMWH was given to this patient at least 8 hours prior to the proposed surgery?
No. DVT prophylaxis is not routinely administered in our hospital.
<ul style="list-style-type: none"> What was the indication to perform arterial blood gas analysis (ABG) immediately after induction?
Every testing instrument has a certain degree of different normal values, so our hospital routinely performs ABG tests as baseline values immediately after induction.
<ul style="list-style-type: none"> Was the Hb 8.4 G% pre-operatively too as I find no reason for Hb to drop on induction of anesthesia? Did anyone try to correct that pre-operatively?
Pre-op CT showed splenomegaly, it might be the most possible cause of anemia.
<ul style="list-style-type: none"> What was done for 60 minutes after induction of anesthesia? Why did the surgeons take so long to prepare the limb for surgery?
Because the surgeon had an emergency situation in another area, the preparation for the surgery started later than usual. This is not a common occurrence.
<ul style="list-style-type: none"> Line 112: "The blood gas was redrawn" please replace with "The ABG analysis was repeated."
Has been corrected
<ul style="list-style-type: none"> Line 113: after 63 minutes CPR was started. Did the patient have a cardiac arrest at this stage. If so then clearly mention that.

Yes, the patient have a cardiac arrest.
<ul style="list-style-type: none"> Line 118-119: Right Femoral vein was cannulated. If the DVT was suspected as a cause for PE then is it wise to cannulate the femoral vein? It would be wiser to use the neck veins under ultrasound guidance for CVC. Kindly mention this in discussion why the femoral vein was used for CVC. If there was no particular reason then mention as an error on the part of the anesthesiologist who performed it.
<p>We proceeded with femoral CVC despite the absence of thrombus on ultrasound examination, as it was an emergency situation.</p> <p>Considering the risk of lower limb thrombophlebitis associated with venous anomalies, femoral cannulation is better avoided.</p> <p>George SE, Sreevidya A, Asokan A, Mahadevan V. Klippel Trenaunay syndrome and the anaesthesiologist. Indian J Anaesth. 2014;58(6):775-777. doi:10.4103/0019-5049.147161</p>
<ul style="list-style-type: none"> Line 117-118: CPR was started again after 83 minutes....did the patient have a second cardiac arrest? If yes, the mention that clearly.
Has been corrected
<ul style="list-style-type: none"> Was hypothermia induced intentionally? If not then mention in the discussion that incidental hypothermia protected patient's brain and helped in full recovery of the patient.
The cardiac surgeon started target temperature management (TTM) of 32°C to protect the patient's brain.
<ul style="list-style-type: none"> Line 154: was this 12-year-old girl patient stratified according to the Modified Well's criteria? If so then mention the score of the patient in the discussion.
<p>Our patient's score of the Modified Well's criteria is 1.5. However, the Modified Wells' criteria may not be applicable to patients with KTS, as the score may not accurately reflect the patient's high risk for pulmonary embolism.</p> <p>Ndzengue A, Rafal RB, Balmir S, Rai DB, Jaffe EA. Klippel-trenaunay syndrome: an often overlooked risk factor for venous thromboembolic disease. Int J Angiol. 2012;21(4):233-236. doi:10.1055/s-0032-1328969</p>
<ul style="list-style-type: none"> In discussion also list the anesthetic problems that are encountered during, before and after surgery in patients with KTS. (Difficult airway, potential neurovascular malformation leading to contraindication for neuraxial block, possibility of excessive bleeding intraoperatively, risk of PE, DIC etc)
<p>Despite the lack of established strategies for anesthetic management of KTS patients undergoing surgery, some preoperative evaluations have been recommended. Firstly, anesthesiologists should consider the potential difficulties in managing the airway due to soft tissue hypertrophy in the mouth, hypopharynx, and facial anomalies commonly observed in KTS patients. Secondly, neuraxial anesthesia should be avoided as it is contraindicated due to the possibility of neurovascular malformations in the spinal cord and surrounding structures. It must be noted that central regional blockade can be performed safely in KTS patients, provided that vascular malformations in the central nervous system have been ruled out through computed tomography/magnetic resonance imaging and that there are no cutaneous lesions at the site of needle insertion. Thirdly, the risk of excessive intraoperative blood loss should always be taken</p>

into consideration, even in minor surgeries, due to the presence of widespread varicosities and venous malformations. Fourthly, KTS patients have a relatively high risk of developing venous thrombosis and pulmonary thromboembolism. Chronic coagulopathy such as disseminated intravascular coagulation can also occur in these patients. Finally, intracerebral aneurysm is a potential complication in KTS patients, which can rupture during the perioperative period.

Lee JH, Chung HU, Lee MS. An anesthetic management of a patient with Klippel-Trenaunay syndrome. Korean J Anesthesiol. 2012;63(1):90-91. doi:10.4097/kjae.2012.63.1.90

Barbara DW, Wilson JL. Anesthesia for surgery related to Klippel-Trenaunay syndrome: a review of 136 anesthetics. Anesth Analg. 2011;113(1):98-102. doi:10.1213/ANE.0b013e31821a03c2

George SE, Sreevidya A, Asokan A, Mahadevan V. Klippel Trenaunay syndrome and the anaesthesiologist. Indian J Anaesth. 2014;58(6):775-777. doi:10.4103/0019-5049.147161

Line 156- 165 was it done for the reported patient? Computed tomographic angiography of the lower limbs should have been done for the reported patient.

The mechanism of PE is that a preexisting deep vein thrombosis is mechanically dislodged by compression or changing positions and travels to the pulmonary artery.

There have been no reports of severe pulmonary embolisms occurring after leg sterilization, except in cases where a massage or ultrasound examination was being performed.

Sufian S, Arnez A, Lakhanpal S. Case of the disappearing heat-induced thrombus causing pulmonary embolism during ultrasound evaluation. J Vasc Surg. 2012 Feb;55(2):529-31. doi: 10.1016/j.jvs.2011.07.070. Epub 2011 Sep 29. PMID: 21958568.

Sutham K, Na-Nan S, Paiboonsithiwong S, Chakswat P, Tongsong T. Leg massage during pregnancy with unrecognized deep vein thrombosis could be life threatening: a case report. BMC Pregnancy Childbirth. 2020 Apr 22;20(1):237. doi: 10.1186/s12884-020-02924-w. PMID: 32321459; PMCID: PMC7178622.

- Conclusion should also include: All patient having KTS should be evaluated of lower limb circulation and pre-existing DVT pre-operatively. Also, all patients with KTS should receive DVT prophylaxis at least 8 hours prior to surgery irrespective of the age.

Conclusion has been re-written.

KTS is a congenital vascular disorder that primarily affects the lower limbs and is characterized by cutaneous hemangiomas, varicose veins, and bone and soft tissue hypertrophy. Patients with KTS are at high risk for pulmonary embolism (PE). All patient having KTS should be evaluated of lower limb circulation and pre-existing DVT pre-operatively. Also, all patients with KTS should receive DVT prophylaxis at least 8 hours prior to surgery irrespective of the age. The Modified Wells' criteria may not be applicable to patients with KTS. Care should be taken to monitor for PE in patients with KTS while leg raising for sterilization. Intraoperative PE is lethal, and the management of hemodynamically unstable patients requires efficient CPR and early mechanical support. Anesthesiologists should consider potential difficulties in managing the airway and avoid neuraxial anesthesia. Central regional blockade can be performed safely in KTS patients if vascular malformations in the central nervous system have been ruled out.

- Clearly mention if the surgery was abandoned. If so then throughout the manuscript please mention

post-incident and not post-operatively where applicable.
The surgery was abandoned. Have been corrected