Massive pulmonary embolism in Klippel-Trenaunay syndrome after leg raising

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Abstract

BACKGROUND

Klippel-Trenaunay syndrome (KTS) is a rare congenital disorder characterized by a combination of capillary malformations, soft-tissue or bone hypertrophy, and varicose veins or venous malformations. The syndrome predisposes patients to hypercoagulable states, including venous thromboembolism and pulmonary embolism (PE).

CASE SUMMARY

A 12-year-old girl with KTS was scheduled 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. After induction, the surgeon elevated the patient’s leg for sterilization, whereupon she experienced a massive PE and refractory cardiac arrest. Extracorporeal membrane oxygenation (ECMO) was performed after prolonged resuscitation, and she had a return of spontaneous circulation. After this episode, the patient was discharged without any neurologic complications.

CONCLUSION

The mechanism of PE, a lethal disease, involves a preexisting deep vein thrombosis that is mechanically dislodged by compression or changing positions and travels to the pulmonary artery. Therefore, patients predisposed to PE should be prescribed prophylactic anticoagulants. If the patient has unstable vital signs, resuscitation should
be started immediately, and extracorporeal cardiopulmonary resuscitation (ECPR) should be considered in settings with existing ECMO protocols, expertise, and equipment. Awareness of PE in patients with KTS while leg raising for sterilization is critical.

**INTRODUCTION**

Klippel-Trenaunay syndrome (KTS) is a rare congenital disorder and 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. Vascular malformations involve the lower limbs, gastrointestinal tract, and genitourinary tract. The incidence has been estimated at two to five per 100,000. KTS predisposes patients to hypercoagulable states, including venous thromboembolism (VTE) and pulmonary embolism (PE). Dislodgement of the clots from pre-existing thrombosed veins upon movements and subsequent migration to pulmonary circulation can lead to massive pulmonary embolism. 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.

**CASE PRESENTATION**

*Chief complaints*

A 12-year-old girl with KTS (height, 124 cm; weight, 20 kg) was referred to our hospital for recurrent left lower limb lymphangioma since the age of eight years.

*History of present illness*

She presented with clitoral hypertrophy, hemihypertrophy in the left lower limb along with varicose veins and multiple lipomas, and gastrointestinal bleeding.

*History of past illness*
Four years ago, she had undergone extensive resection of the vascular malformations in the left lower limb, including amputation of the lateral fourth toe on her left foot (Figure 1). There was no record of difficulty in intubation. 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.

**Personal and family history**

There was no specific personal or family history.

**Physical examination**

Physical examination presented with clitoral hypertrophy, hemihypertrophy in the left lower limb

**Laboratory examinations**

Preoperative laboratory data showed anemia (hemoglobin: 9.2g/dL, mean corpuscular volume: 66.9fl) no thrombocytopenia or coagulopathy (platelet count, 379,000/μL; prothrombin time, 11.1 s; international normalized ratio, 1.07; and partial thromboplastin time, 27.9 s), liver and renal function were within normal limit, C-reactive protein: 7.43mg/L.

**Imaging examinations**

The preoperative CT revealed angiomatosis extending from the left pelvis to the left foot, pelvic hemangiomas involving the rectum, a splenic lymphangioma, and engorged epidural vessels on the left side of the sacral canal. There is no obvious DVT on the preoperative CT.

**FINAL DIAGNOSIS**

Klippel-Trenaunay syndrome presented with hemihypertrophy in the left lower limb along with varicose veins and multiple lipomas and angiomatosis extending from the
left pelvis to the left foot, pelvic hemangiomas involving the rectum, a splenic lymphangioma, and engorged epidural vessels on the left side of the sacral canal

**TREATMENT**
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

**OUTCOME AND FOLLOW-UP**
The patient was discharged without any neurologic complications

**DISCUSSION**
KTS was first described by two French doctors, Klippel and Trenaunay (1900). KTS is a congenital vascular disorder characterized by a triad of main symptoms affecting one or more limbs, namely cutaneous hemangiomas, varicose veins, and bone and soft tissue hypertrophy. Approximately 95% of patients have lower limb malformations. If capillary malformations are sufficiently large, the cutaneous lesions may sequester platelets. In addition, large varicose veins may cause localized intravascular coagulation, and many patients have hematologic evidence of coagulopathy, defined by elevated D-dimer and soluble fibrin complex levels, decreased fibrinogen levels, and elevated prothrombin times, with normal to moderately low platelet counts. Therefore, patients with KTS have a known significantly increased risk for PE.

PE while leg raising for sterilization before surgery is rare. 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. Patients can be stratified before surgery based on the clinical prediction scoring system, the Modified Well’s criteria (Table 1) recommended by the European Society of Cardiology (ESC) and the American College of Chest Physicians (ACCP), which standardizes the diagnosis and management of acute PEs. 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.\cite{6} Patients with KTS are at high risk and require a series of examinations, such as ultrasonography, CT, or magnetic resonance imaging (MRI). In some case reports,\cite{7,9} the thrombi can dislodge from the vein by leg massage, probe compression, and application of sterile elastic exsanguination tourniquets. If thromboembolism is suspected, prevention using anticoagulants and IVC filters might be indicated. However, prophylactic anticoagulants are not prescribed in some Asian regions, and studies have reported a lower incidence of VTE in the Asian population than in Caucasians.\cite{10,11} Although data on pediatric thromboembolism prophylaxis are limited, a systemic review demonstrated that low-molecular-weight heparin is safe and effective in children.\cite{12} The IVC filter is ineffective in KTS because of an anomalous venous connection between the lower extremities and the IVC, effectively bypassing the filter.\cite{13} Considering the risk of lower limb thrombophlebitis associated with venous anomalies, femoral cannulation is better avoided.\cite{14}

If PE is suspected intraoperatively, supportive care should be started in unstable patients, including ventilation with 100% O₂, use of positive end-expiratory pressure, resuscitation of the circulating fluid volume, and administration of inotropic drugs as early as possible. In addition, invasive monitors should be placed for diagnosis and management, including arterial and central venous lines, transthoracic echocardiography, and TEE, which is generally considered the primary diagnostic technique for identifying intraoperative PE because of its high safety, availability, and utility in the operating room and its lack of interference with resuscitation efforts.\cite{15} If vital signs are profoundly unstable, CPCR should be performed, and a cardiac surgeon should be consulted for cardiopulmonary bypass or venoarterial ECMO. Extracorporeal life support is an effective therapy for unstable patients, offering acceptable outcomes; however, these studies lacked pediatric patients. The American Heart Association guidelines, updated for pediatric advanced life support in 2019,\cite{16} recommend ECPR
for pediatric patients with cardiac diagnoses and an in-hospital cardiac arrest in settings with existing ECMO protocols, expertise, and equipment. For infants and children who remain comatose after out-of-hospital or in-hospital cardiac arrest, either target temperature management (TTM) from 32°C to 34°C followed by TTM of 36°C to 37.5°C or TTM of 36°C to 37.5°C can be used. There were no significant differences in the outcomes between the two TTM groups in the Therapeutic Hypothermia after Pediatric Cardiac Arrest (THAPCA) trials.[17]

Postoperatively, the patient should be admitted to the ICU, and CT pulmonary angiography (CTPA) should be performed. If there is no major bleeding, anticoagulant treatment should be started as soon as possible, and experts should be consulted for systemic or catheter-directed thrombolysis.

In current standard therapy, if the patient has no major active bleeding, the ACCP recommends immediate initiation of parenteral anticoagulation using low-molecular-weight heparin and fondaparinux, as they are superior to intravenous unfractionated heparin, owing to a lower risk of adverse bleeding events and the absence of need for serial laboratory monitoring. However, there are no guidelines or group consensus for therapies for intraoperative PE. Therefore, the authors organized a reference algorithm for intraoperative PE management (Figure 6).

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 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.\cite{14,18,19}

CONCLUSION

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 h 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.

Bradley S. Marino, Sarah Tabbutt, Graeme MacLaren, Mary Fran Hazinski et al. "Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease: A Scientific Statement From the American Heart Association", Circulation, 2018

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