Successful Pulmonary Thromboendarterectomy in a Patient With Klippel-Trenaunay Syndrome*

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Klippel-Trenaunay syndrome (KTS) is a rare congenital disorder that consists of a triad of cutaneous vascular nevi, soft tissue or bony hypertrophy, and varicose veins or venous malformations involving one or more extremities. In addition to these main features, a wide range of associated conditions and complications involving the skeletal system, soft tissues, and cardiovascular system have been described. Among these complications is a propensity to thromboembolic events that, in a subset of patients, may lead to chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is a well-described entity; recognition of CTEPH is important because its natural history includes a high mortality rate and because it is potentially amenable to surgical intervention. This case report outlines the clinical history and management of a patient with CTEPH associated with KTS to underscore that evaluation for pulmonary thromboendarterectomy (PTE), a potentially curative procedure, should be considered in patients with KTS suffering from pulmonary hypertension.

Case Report
A 24-year-old man with KTS was referred to University of California, San Diego Medical Center for evaluation of his pulmonary hypertension. The patient experienced a pulmonary embolic event 2.5 years prior to admission following a surgical procedure. There was no evidence of lower extremity venous thrombosis by duplex ultrasonography, although the examination was reported to be incomplete. He was treated with heparin, then warfarin for 4 months. He presented again 14 months later with dyspnea, chest tightness, and syncope. Ventilation/perfusion (V/Q) scan demonstrated multiple, segmental mismatched defects. Anticoagulation was restarted, and an inferior vena caval filter was placed. Three months later, a repeat V/Q scan was unchanging. CT confirmed the presence of intraluminal thrombus. Echocardiography revealed right atrial and right ventricular enlargement, with an estimated pulmonary artery systolic pressure of 75 mm Hg. He remained dyspneic with exertion (New York Heart Association class II), and was referred to University of California, San Diego Medical Center for further evaluation.

Physical examination was notable for a widely split S2 and a prominent pulmonic closure sound. Examination of the lower extremities revealed typical capillary malformations and hypertrophy of the left leg and right foot.

A V/Q scan revealed a global decrease in perfusion to the left lung, with additional defects involving the right upper and middle lobes; ventilation scan was normal. Echocardiography demonstrated moderate right atrial and right ventricular enlargement. The peak velocity of the tricuspid regurgitant envelope was 4.0 m/s, suggesting a peak pulmonary artery systolic pressure of approximately 75 mm Hg. The left popliteal to mid-superficial femoral veins could not be visualized by duplex ultrasonography. The remainder of the deep venous system of the lower extremities was potentially amenable to surgical intervention. The patient was referred for evaluation of chronic thromboembolic pulmonary hypertension.

The patient underwent a successful pulmonary thromboendarterectomy for CTEPH. Three months following surgery, the patient was asymptomatic and returned to full activity. The patient was discharged with oral warfarin 1 mg daily and was followed in the outpatient clinic.

Key words: Klippel-Trenaunay syndrome; pulmonary embolism; pulmonary hypertension; thromboendarterectomy; venous thromboembolism

Abbreviations: CTEPH = chronic thromboembolic pulmonary hypertension; KTS = Klippel-Trenaunay syndrome; PTE = pulmonary thromboendarterectomy; V/Q = ventilation-perfusion

References
increased to 7,500 U subcutaneously every 8 hours on the first postoperative day. The heparin dose was unfractionated heparin administered subcutaneously every 12 hours. Postoperative hemodynamics included a pulmonary artery pressure of 29/13 mm Hg with a cardiac output of 6.5 L/min. Anticoagulation with 7,500 U of unfractionated heparin administered subcutaneously every 12 hours was initiated on the evening of surgery. The heparin dose was increased to 7,500 U subcutaneously every 8 hours on the first postoperative day, and warfarin therapy was initiated. This dose of heparin was continued until the international normalized ratio had reached a therapeutic range for 2 consecutive days. The patient was discharged in excellent condition on the seventh postoperative day, and warfarin therapy was continued until the international normalized ratio in a 2.5 to 3.5 range, was recommended.

Functional status at follow-up 7 months after surgery had returned to New York Heart Association class I. Echocardiography performed at that time estimated the pulmonary artery systolic pressure to be 30 mm Hg.

**DISCUSSION**

The literature suggests that venous thromboembolism is common among patients with KTS, with a frequency in larger series ranging from 8 to 22%. However, the precise mechanism for this increased thromboembolic risk remains unclear. One study, utilizing both venography and impedance plethysmography, did not demonstrate anatomic difference to explain the increased incidence of venous thromboembolism in a subgroup of KTS patients with thromboembolism compared to KTS patients without thromboembolism. Only limited data regarding inherited thromboembolic states in KTS are available. Baskerville found normal levels of protein C and antithrombin III in 11 patients with KTS with and without venous thromboembolism. The same study also reported elevated levels of fibrinopeptide A in the same 11 patients. However, this finding is nonspecific and does not allow conclusions as to the underlying pathophysiological predisposition to thromboembolism. In our patient, an inherited thromophilic tendency was not present.

More than 20 patients with pulmonary embolism associated with KTS have been reported. In uncomplicated pulmonary embolism, conservative management with anticoagulation appears to be successful. In other patients, placement of an inferior vena caval filter has been utilized as an additional prophylactic measure.

Recurrent or unresolved pulmonary embolism can lead to the development of CTEPH in patients with KTS. One patient with KTS and CTEPH who underwent an attempted PTE has been reported. This patient died 10 days postoperatively as a result of a massive embolic event originating from an upper-extremity venous plexus. The authors did not state whether or not a vena caval filter was placed. Another report describes a patient with KTS, recurrent thromboembolic events, and subsequent death from right ventricular failure in whom thromboendarterectomy was not attempted.

It has been well established that PTE offers patients with CTEPH an opportunity for highly satisfactory improvement in their hemodynamic and functional status. The primary goal of PTE is to reduce right ventricular afterload by restoring normal pulmonary hemodynamics. Prevention of recurrent thromboembolism, however, represents an essential secondary objective. Since the overwhelming majority of embolic events arise from the deep veins of the lower extremities, placement of an inferior vena caval filter along with lifelong anticoagulation have been recommended in patients undergoing the procedure.

In patients with KTS, however, standard, infrarenal filter placement may not prove optimally effective. Recurrent pulmonary emboli may arise from upper extremity sites. Furthermore, recurrent pulmonary embolism despite placement of an inferior vena caval filter in a patient with lower-extremity KTS has been reported. The basis for thromboembolic recurrence was ascribed to a large hemangiomatous collateral vessel that circumvented the inferior vena caval filter. Whether concurrent anticoagulant therapy was administered, however, was not specified. Nevertheless, this report emphasizes the importance of considering venous anatomic variation as a basis for thromboembolic recurrence in patients with KTS.

Prior to consideration of thromboendarterectomy in a patient with KTS, it is essential that the source of the emboli be defined so effective pharmacologic and mechanical prophylactic interventions can be applied to...
minimize the possibility of short-term and long-term recurrence. In selected circumstances, specifically those involving an upper-extremity source of emboli, this may include the placement of a superior vena caval filter. Filter placement in the superior vena cava has been reported as a safe and effective means for preventing pulmonary embolism due to acute upper extremity venous thrombosis.\textsuperscript{12}

In summary, this initial report of a successful PTE in a patient with KTS confirms that this procedure is a potentially curative option in selected patients with this syndrome who develop CTEPH.

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