Case Report / Olgu Sunumu

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Pulmonary Embolism in a Child with Klippel-Trenaunay Syndrome: A Case Report and Review of Current Guidelines

Klippel-Trenaunay Sendromu Tanılı Çocukta Pulmoner Emboli: Olgu Sunumu ve Güncel Kılavuzların İncelenmesi

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Abstract

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular disorder associated with an increased risk of thromboembolic complications, including potentially life-threatening pulmonary embolism (PE). We report a case of an 8-year-old boy with KTS who was receiving sirolimus therapy and developed fatigue, tachypnea, and hypoxemia. Echocardiography demonstrated right heart strain, and computed tomography pulmonary angiography confirmed bilateral PE. The patient was hemodynamically stable and was classified as intermediate-risk PE. Treatment with intravenous unfractionated heparin and supportive intensive care was initiated. On day 4, anticoagulation was transitioned to subcutaneous enoxaparin, with near-complete regression of right ventricular dilatation on follow-up echocardiography. He was discharged on rivaroxaban for long-term thromboprophylaxis. This case highlights the role of early echocardiography in risk stratification, the importance of conservative anticoagulation in complex vascular disorders, and individualized long-term management of pediatric patients with KTS.

Keywords: Pulmonary embolism, Klippel-Trenaunay syndrome, sirolimus, echocardiography, risk assessment

Öz

Klippel-Trenaunay sendromu (KTS), potansiyel olarak yaşamı tehdit eden pulmoner emboli (PE) dahil olmak üzere tromboembolik komplikasyon riskinin arttığı nadir bir konjenital vasküler bozukluktur. Bu yazıda, sirolimus tedavisi almakta olan KTS tanılı 8 yaşında bir erkek çocukta gelişen PE olgusu sunulmaktadır. Hastada halsizlik, taşipne ve hipoksemi gelişmiş olup ekokardiyografide sağ kalp yüklenmesi saptanmıştır. Bilgisayarlı tomografi pulmoner anjiyografi ile bilateral PE tanısı doğrulanmıştır. Hemodinamik olarak stabil olan hasta, orta riskli PE olarak sınıflandırılmıştır. Damar içi fraksiyone olmayan heparin ve destekleyici yoğun bakım tedavisi başlanmıştır. Dördüncü günde antikoagülasyon deri altı enoksaparine geçilmiş ve izlem ekokardiyografisinde sağ ventrikül dilatasyonunda belirgin gerileme gözlenmiştir. Hasta, uzun dönem tromboprofilaksi amacıyla rivaroksaban tedavisi ile taburcu edilmiştir. Bu olgu, erken dönemde ekokardiyografinin risk sınıflandırmasındaki rolünü, kompleks vasküler bozukluklarda konservatif antikoagülasyon yaklaşımının önemini ve KTS tanılı çocuk hastalarda bireyselleştirilmiş uzun dönem yönetimin gerekliliğini vurgulamaktadır.

Anahtar Kelimeler: Pulmoner emboli, Klippel-Trenaunay sendromu, sirolimus, ekokardiyografi, risk değerlendirmesi

Introduction

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular disorder characterised by the triad of capillary malformations, venous malformations, and limb hypertrophy.[1] Its most serious complications include thromboembolic events, which occur due to venous stasis, abnormal vascular structure, and localized intravascular coagulopathy. Pulmonary embolism (PE), although rare, represents a potentially life-threatening

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complication in patients with KTS and may lead to pulmonary hypertension and right ventricular failure if not promptly recognized and treated.[2] In the pediatric population, PE is uncommon and often presents with non-specific symptoms like fatigue, tachypnea, or pallor.[3] In this setting, echocardiography can serve as a valuable bedside tool for early identification of right ventricular function and pulmonary hypertension prior to confirmatory imaging.[4]

We present a case of bilateral PE in a child with KTS who was receiving sirolimus therapy, highlighting the importance of early echocardiography for diagnosis, risk-stratified management in the intensive care setting, and the long-term challenges of anticoagulation in pediatric patients with complex vascular malformations.

Case Report

An 8-year-old boy with KTS, diagnosed in infancy based on extensive port-wine stains and limb asymmetry, presented with a one-week history of increasing pallor, fatigue, and tachypnea. His medical history included multiple hospitalisations for complications associated with vascular malformations. He had been on sirolimus therapy for four years to control refractory cutaneous vascular malformations, with a good clinical response.

On initial presentation, the patient exhibited tachycardia (150 beats/min), tachypnea (40 breaths/min), and hypoxemia with an oxygen saturation of 88% on room air and remained afebrile and normotensive. Physical examination was notable for bilateral coarse breath sounds, decreased in intensity over the right hemithorax. In addition, diffuse cutaneous capillary malformations were observed over the anterior and lateral aspects of the left leg (Figure 1a, b). Abdominal examination revealed localized tenderness in the right upper quadrant.

Chest radiography showed blunting of the right costophrenic angle and a basal opacity, while thoracic ultrasonography confirmed a moderate pleural effusion with atelectasis of the right lower lobe. Abdominal ultrasound revealed gallbladder wall edema, minimal ascites, and venolymphatic malformations suggestive of venous stasis or thrombosis.

Given the clinical context of KTS and pleural effusion, PE was suspected. Initial blood gas analysis demonstrated a mixed metabolic acidosis with mild respiratory compensation (pH 7.31, pCO_2 36.2 mmHg, HCO_3- 17.9 mmol/L) and an elevated lactate level (3.3 mmol/L). Cardiac biomarkers were elevated, with a high-sensitivity troponin T level of 31.3 ng/L and an N-terminal pro-B-type natriuretic peptide level of 4176 ng/L, indicating right ventricular strain. D-dimer was markedly elevated to 20.260 µg/L, strongly supporting the diagnosis of acute PE. Transthoracic echocardiography demonstrated right ventricular dilation, moderate tricuspid regurgitation, and elevated right ventricular systolic pressure (30 mmHg), consistent with right heart strain (Figure 2a, b). Computed tomography pulmonary angiography (CTPA) confirmed bilateral massive pulmonary emboli, with thrombus extending into segmental branches, and associated pulmonary infarction, right heart chamber enlargement, and right-sided pleural effusion (Figure 2c, d). Lower extremity Doppler ultrasound identified venolymphatic malformations but no deep vein thrombosis (DVT).

The patient was admitted to the pediatric intensive care unit and was initiated on intravenous unfractionated heparin (UFH) with a bolus of 50 U/kg, followed by a continuous infusion at 20 U/kg/h. Anticoagulation was monitored using both activated partial thromboplastin time and anti-factor Xa levels. Supportive management included high-flow nasal oxygen, intravenous hydration, continuous electrocardiography monitoring, and compression therapy. He remained hemodynamically stable with no indication for thrombolytic therapy. By day 4, UFH was transitioned to subcutaneous enoxaparin, with doses titrated to anti-Xa levels; the marked dilatation of the right heart chambers had

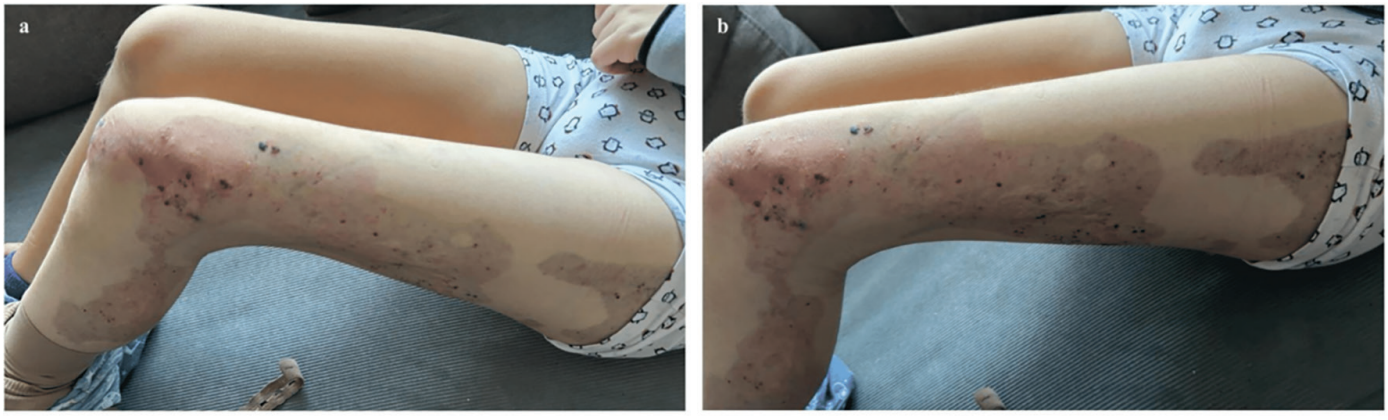

Figure 1. (a, b) Diffuse cutaneous capillary malformations on the left thigh and leg, consistent with Klippel-Trenaunay syndrome

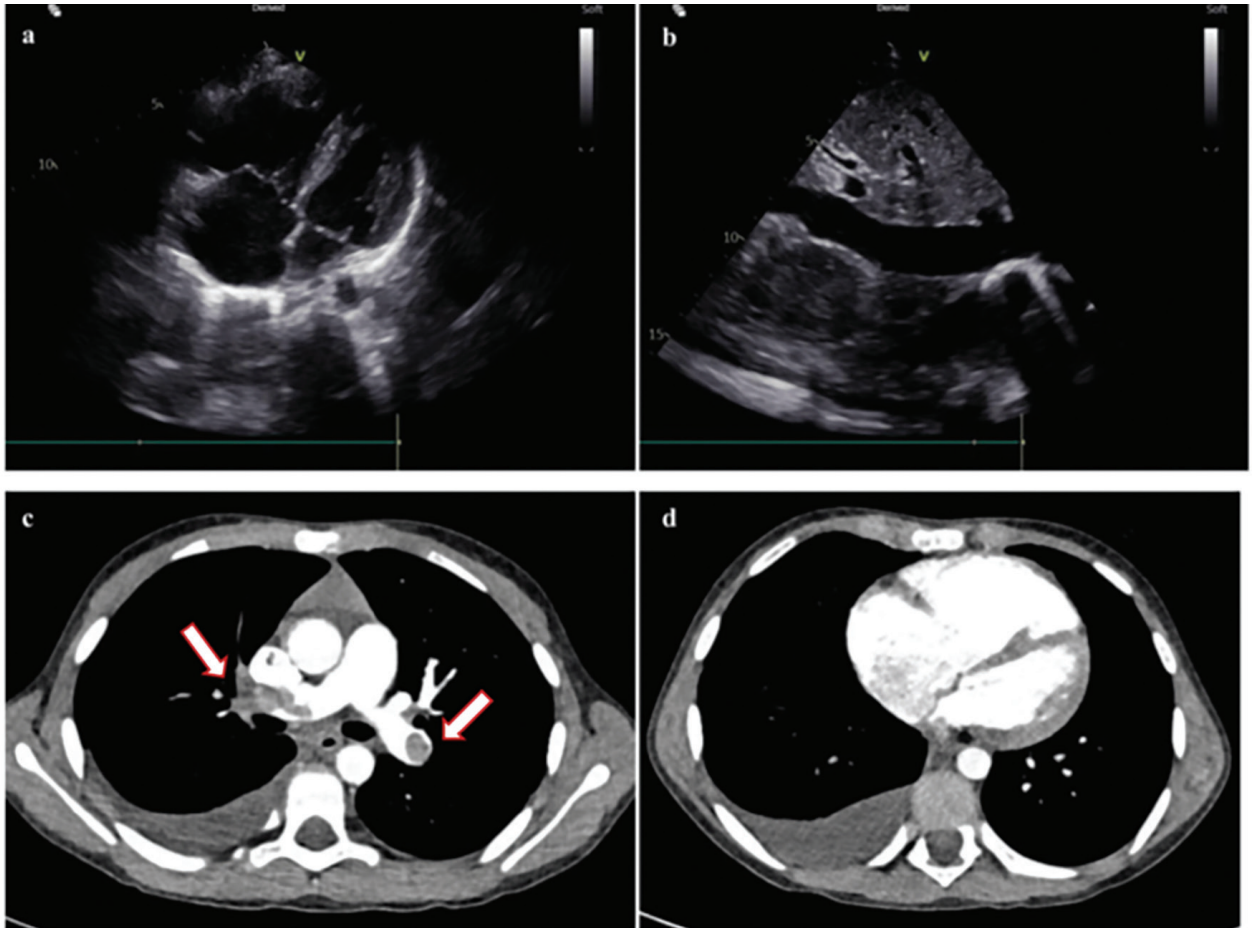

Figure 2. (a, b) Transthoracic echocardiography showing marked right ventricular dilatation and dilated inferior vena cava, consistent with right heart strain. (c, d) CT pulmonary angiography images demonstrating bilateral massive pulmonary emboli with thrombus extending into segmental branches (white arrows), enlargement of the right heart chambers, and right-sided pleural effusion
CT: Computed tomography

largely regressed to near-normal dimensions (Figure 3a, b).

The patient's respiratory status steadily improved, and he was weaned to room air by day 6. Follow-up echocardiography showed improved right ventricular function and repeat CT angiography on day 13 demonstrated significant thrombus regression and resolution of strain (Figure 3c, d). After 15 days of hospitalization, he was discharged on subcutaneous enoxaparin, with plans for long-term thromboprophylaxis with rivaroxaban. At 2-year follow-up, he remained clinically stable with no recurrence of thromboembolic events.

Written informed consent was obtained from the patient's parents for publication of this case report.

Discussion

Thromboembolic events remain a leading cause of morbidity and mortality in patients with KTS. In a large single-center retrospective series, nearly one-third of patients with KTS experienced venous thromboembolism (VTE), including both DVT and PE, highlighting the significant thrombotic burden in this population.[5] When PE is not promptly identified and treated, it may progress to pulmonary hypertension and right ventricular failure.[2] Pediatric case reports further document fatal outcomes in the absence of timely anticoagulation.[6,7] Although PE is relatively rare in children, occurring in approximately 0.14-0.9 per 100.000 in the general pediatric population, the incidence rises considerably in hospitalized settings.[8,9] Diagnostic delays are common due to the non-specific nature of presenting symptoms. Retrospective pediatric series report a median time to diagnosis exceeding seven days.[3] Our patient's presentation was consistent with these findings; symptoms had persisted for nearly a week before the diagnosis of PE.

Sirolimus, a mammalian target of rapamycin (mTOR) inhibitor targeting the phosphoinositide 3-kinase/protein kinase B/mTOR pathway, has emerged as a promising therapeutic option for refractory vascular malformations, including KTS, with reports of improved symptoms and lesion control in pediatric cohorts.[10] Recent case series have described extensive VTE occurring shortly after sirolimus initiation,

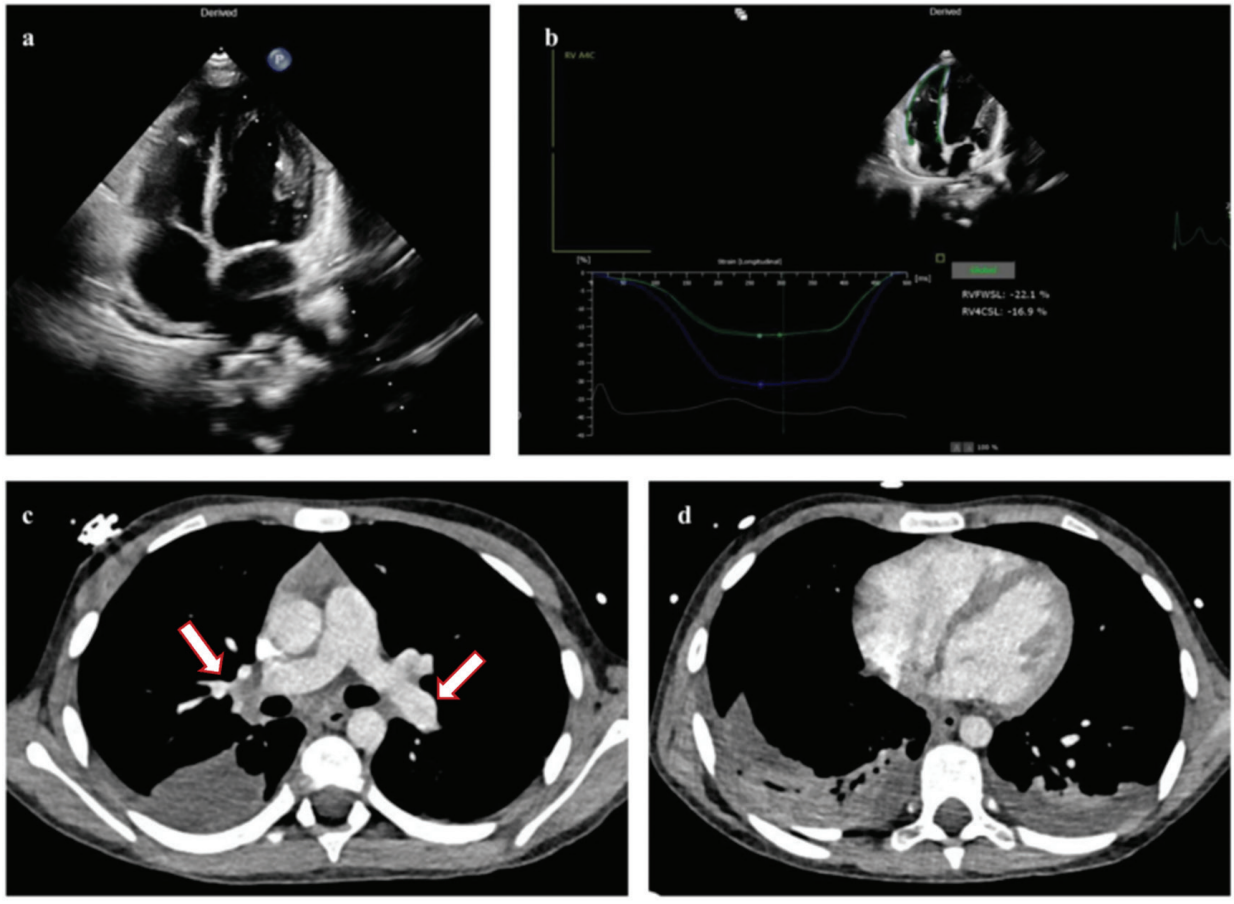

Figure 3. (a) Echocardiography showing regression of right heart chamber dilatation. (b) Improvement in right ventricular strain on follow-up imaging. (c, d) CT pulmonary angiography demonstrating a marked regression of bilateral massive pulmonary emboli extending into segmental branches (white arrows) and a reduction in right heart chamber size

CT: Computed tomography

including cases despite concurrent anticoagulation.[11] Similarly, in our patient, sirolimus therapy was associated with clinical improvement in vascular malformation-related symptoms; however, the patient developed a significant thrombotic event. Although several reports have suggested a potential association between sirolimus and thrombosis, the available evidence remains insufficient to establish a definitive causal relationship, particularly in patients with KTS.[11,12] In this population, the inherent prothrombotic state remains the primary risk factor for VTE.[1,2] Nonetheless, these observations underscore the need for vigilant thrombotic monitoring in KTS patients receiving sirolimus.

Current pediatric guidelines recommend transthoracic echocardiography as a first-line modality for initial risk stratification in suspected PE, while CTPA remains the gold standard for definitive diagnosis.[4,9] Risk stratification is clinically essential, as treatment decisions are primarily guided by the patient's hemodynamic profile. High-risk PE is defined by the presence of hypotension, shock, or cardiac arrest, whereas intermediate-risk PE refers to hemodynamically stable patients with evidence of right ventricular dysfunction or elevated cardiac biomarkers.[4] In our patient, the absence of both systemic hypotension and circulatory collapse excluded high-risk PE. However, the presence of right ventricular dysfunction on echocardiography and elevated biomarkers supported a diagnosis of intermediate-risk PE.

In intermediate-risk pediatric PE, as in our case, systemic thrombolysis or surgical thrombectomy is generally not indicated. Instead, intravenous UFH remains the first-line therapy due to its rapid onset, ease of titration, reversibility, and suitability for use in the intensive care setting. Current protocols recommend an initial bolus of 50-100 U/kg, followed by continuous infusion at 20 U/kg/h, with dose adjustments based on anti-factor Xa levels, targeting a therapeutic range of 0.35-0.7 U/mL.[4,13,14] In our patient, a lower bolus of 50 U/kg was chosen considering the underlying vascular malformation and potential bleeding risk in KTS.[1,2] This conservative anticoagulation strategy, combined with

serial echocardiography and close hemodynamic monitoring, resulted in clinical stabilization and recovery. Importantly, it avoided the potential complications associated with advanced interventions such as thrombolysis or surgical embolectomy.

Long-term secondary prophylaxis is essential in KTS due to the high risk of recurrent thromboembolic events.[5,6,15] Fatal outcomes have been reported in pediatric patients who did not receive extended anticoagulation following a first event[6] and recurrent PE has occurred despite prior thrombotic episodes.[15] Traditionally, vitamin K antagonists and low molecular weight heparin (LMWH) have been used for extended prophylaxis. However, recent studies and randomized trials have demonstrated the safety and efficacy of direct oral anticoagulants, such as rivaroxaban and dabigatran, in the pediatric population with VTE.[13] In the KTS cohort reported by Saleem et al.[5] rivaroxaban was commonly prescribed for long-term prophylaxis, supporting its role in this high-risk group. Transition from UFH to LMWH was guided by clinical stability, improvement in hemodynamics, absence of bleeding, and early echocardiographic improvement in right ventricular strain. Rivaroxaban was selected for long-term anticoagulation over vitamin K antagonists, given reports of recurrent thrombotic events in KTS and the well-recognized difficulty of maintaining stable warfarin levels in pediatric patients.[13,14] The switch occurred after clinical stabilization. This individualized, stepwise approach led to favorable outcomes, with no thromboembolic recurrence over two years.

This case highlights several key considerations in the management of pediatric patients with KTS. First, in this population, PE may present with non-specific symptoms that contribute to diagnostic delays; therefore, early echocardiography and confirmatory CTPA are essential for timely recognition and risk stratification. Second, while sirolimus therapy can improve symptoms of vascular malformations, it may increase the underlying thrombotic risk in KTS, necessitating close monitoring. Third, intermediate-risk PE can often be managed effectively with conservative, risk-guided therapy using intravenous UFH, avoiding the complications of thrombolysis or surgical intervention. Finally, long-term secondary prophylaxis remains a cornerstone of care.

Conclusion

This case emphasizes the need for heightened clinical vigilance, timely diagnostic evaluation, and risk-guided management in pediatric patients with KTS who develop PE. Careful monitoring of thrombotic risk, particularly in the setting of sirolimus therapy, and the judicious use of conservative anticoagulation strategies are central to achieving favorable outcomes.

Ethics

Informed Consent: Written informed consent was obtained from the patient's parents for publication of this case report.

Footnotes

This case was presented as an oral presentation in the Young Academy Session at the 22nd National Pediatric Cardiology and Pediatric Cardiovascular Surgery Congress, March 7-10, 2024, Antalya, Türkiye.

Authorship Contributions

Surgical and Medical Practices: M.T., Ö.Ö., M.H.K., Concept: M.H.K., Design: M.H.K., Data Collection or Processing: B.B., Analysis or Interpretation: M.T., M.H.K., B.O.S., E.Ö., Literature Search: B.B., Writing: B.B., M.T., Ö.Ö., M.H.K., B.O.S., E.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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