A 17-year-old Girl with Klippel-Weber Syndrome Complicated with a Pulmonary Thromboembolism and RV Thrombus

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Abstract

A 17-year-old girl with multiple areas of skin hemangiomas that had been present since birth was referred to our institution complaining of sudden onset of dyspnea. Enhanced CT demonstrated a pulmonary thromboembolism and transthoracic echocardiogram showed a thrombus-like echo in the right ventricle. CT further revealed thrombi in the inferior vena cava (IVC) and peripheral vein. The thrombi, especially those in the RV, were highly life-threatening; therefore, immediate thrombectomy was performed and an IVC filter was placed. Because no major complications occurred, the patient was discharged 34 days after admission. In such young women, carefully using anticoagulation therapy and planning pregnancy are recommended.

Key words: Klippel-Weber syndrome (KWS), pulmonary thromboembolism (PTE), inferior vena cava (IVC) filter, anticoagulation, pregnancy


Introduction

Klippel-Weber syndrome (KWS) is a congenital disorder characterized by cutaneous vascular nevi and a combination of capillary, venous and lymphatic malformations and localized disturbed growth of bone and/or soft tissue. The clinical presentation varies from asymptomatic to the development of potentially life-threatening complications, such as venous thromboembolism (VTE) and recurrent bleeding. Due to the continuous formation of thrombi, lifelong anticoagulation therapy is recommended. In cases in which the administration of anticoagulation therapy is impossible, placement of an IVC filter is useful. We herein present a case of KWS complicated with a pulmonary thromboembolism and an RV thrombus in a 17-year-old girl. The clinical issues regarding the use of anticoagulation therapy and IVC filter placement in young women with KWS are also discussed.

Case Report

A 17-year-old girl visited a general physician due to the sudden onset of shortness of breath and dyspnea. A high D-dimer level (3.0 μg/mL) and transthoracic echocardiogram (TTE) revealed findings suggestive of pulmonary hypertension; therefore, the patient was promptly referred to our institution for a further examination.

The patient was alert. Her blood pressure was 122/56 mmHg, her pulse rate was 90 beats/min and her respiratory rate was 20 breaths/min. An arterial blood gas analysis on 2 L/min of O2 revealed a PaO2 of 86.5 mmHg, a PaCO2 of 31.2 mmHg, a pH of 7.458 and an SaO2 of 98.9%.

The patient’s palpebral conjunctivae were anemic, her respiratory sounds were clear and the pulmonary component of her second heart sound was increased in intensity. The left
lower extremity was edematous and swollen and multiple areas of grouped hemangiomas were seen in the left forehead, left upper perioral region, left lower back field and left lower extremity that had existed from birth (Fig. 1).

A hematological study disclosed microcytic hypochromic anemia with a hemoglobin value of 6.0 g/dL, a hematocrit value of 23.5% and a red blood cell count of 3.8 million units. There were no obvious findings of bleeding on the patient’s body; thus, the anemia was not related to bleeding caused by KWS. A diagnosis of typical anemia in adolescence was suggested. The D-dimer level was elevated as high as 17.9 μg/mL, the levels of antithrombin III, protein C activation and protein S antigens were within the normal limits and the patient was negative for anticardiolipin antibodies.

A chest X-ray showed enlargement of the right ventricle and pulmonary arteries (Fig. 2). An electrocardiogram demonstrated first degree A-V block, SI, QIII and inverted T waves in V1 and V2 (Fig. 3). TTE was significant for the small left ventricle due to right ventricular enlargement (the reverse Bernheim effect) and demonstrated a thrombus-like echo in the right ventricle (Fig. 4). An emergency CT scan revealed thrombi in both major branches of the pulmonary arteries, the inferior vena cava and left lower peripheral veins (Fig. 5).

Thrombectomy was performed and the thromboembolic materials were dissected from the right ventricle and pulmonary arteries. An IVC filter (Günther Tulip™ Vena Cava fil-
ter) was placed after thoracotomy. Unfractionated heparin administration was initiated and regulated to maintain the activated partial thromboplastin time (APTT) at approximately twice as high as the normal level at that time. Soon after unfractionated heparin was administered, warfarin therapy was initiated. A second CT scan performed two weeks after admission revealed disappearance of the thrombi in both pulmonary arteries and the RV; however, the thrombi in the IVC and left lower extremity veins remained. The inferior vena cava thrombus was large, with an estimated size of 5 by 3 cm; therefore, retrieval of the IVC filter was abandoned, and warfarin therapy was continued. The prothrombin time-international normalized ratio (PT-INR) at discharge was 2.16, and the D-dimer level decreased to 2.1 μg/mL.

Discussion

The triad of cutaneous nevi, varicose veins and hypertrophy of one or more limbs was identified by Klippel and Trénaunay in 1900 (1), and Parkes-Weber further described a similar condition with arteriovenous rather than venous malformations (2). Both syndromes form a part of a wider spectrum of vascular anomalies that result in limb enlargement and sometimes lead to cutaneous abnormalities. The manifestations of this syndrome begin at birth or shortly thereafter, with most patients displaying cutaneous hemangiomas of the portwine type. It has been reported that the activating mutation, E133K, in the angiogenic factor VEGF (formally named AGGF1), is closely linked to KWS; however, the exact cause of KWS remains to be elucidated (3).

Venous thromboembolism has been reported in 8% to 22% of patients with KWS (4, 5). The exact mechanism underlying the hypercoagulability observed in the vascular malformations remains unclear; however, the coagulation may be attributed to stagnation of blood within the disordered, enlarged venous blood vessels, which can lead to the continuous formation of thrombi, resulting in recurrent pulmonary thromboembolism (PTE) (6, 7). IVC filters have been proven effective for preventing recurrent PTE when anticoagulant therapy is contraindicated (8). Even when an IVC filter is placed, unless the cause of the continuous formation of thrombi is relieved, the patient will require continuous anticoagulation therapy due to complications, such as dysfunction of venous return. When the patient is a young woman, as in the present case, careful administration of anticoagulation therapy is necessary in anticipation of pregnancy and delivery. Furthermore, the administration of anticoagulation therapy in patients with KWS is critical for patient safety because, in addition to being in a hypercoagulable state, patients with KWS may have coagulation defects that predispose them to bleeding due to the consumption of coagulation factors in venous malformations (9).

During pregnancy, patients must quit warfarin ther-
apy (10) and begin anticoagulation with low-molecular-weight heparin (LMH). In Japan, the use of LMH is forbidden; however, outside of Japan, LMH is used worldwide as standard therapy. It is believed that heparin does not pass into the placenta (11). Planning pregnancy is therefore recommended. Concerning IVC filter placement during pregnancy, it was reported that, in eight pregnancies, IVC filters in situ inserted before conception did not lead to any obvious adverse maternal or fetal effects (9).

**Conclusion**

We treated a young girl with a sudden onset of PTE associated with KWS. The prognosis of KWS is dependent on the prevention and management of life-threatening complications, such as VTE and recurrent bleeding. Optimal IVC filter placement, along with the careful administration of anticoagulation therapy and planning for pregnancy, is therefore recommended.

The authors state that they have no Conflict of Interest (COI).

**References**


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