Pulmonary embolism in a patient with Klippel-Trenaunay-Weber syndrome

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ÖZET

Klippel-Trenaunay-Weber sendromlu bir hastada pulmoner emboli


SUMMARY

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Klippel-Trenaunay-Weber syndrome (KTWS) is a rare, congenital disorder that is described in 1900’s. This syndrome consists of venous and lymphatic anomalies, cutaneous capillary malformations; hypertrophy of soft tissue and bone mostly on extremities which have increased vascularity and arteriovenous fistula. Deep venous thrombosis can be seen as a complication in this syndrome. It is important to note that despite a higher incidence of deep venous thrombosis in patients with KTWS, pulmonary embolism is a rare event (1).

This case report outlines the clinical history of a patient with KTWS who had a pulmonary embolism attack after having many surgical operations.

CASE REPORT

A 25 year old man with KTWS was referred to our state hospital with a history of sudden, bilateral chest pain, shortness of breath, and hemoptysis for one time at the beginning of pain. He had loss of power and pain on lower extremities. He suffered from urinary and anal incontinence. On own history; he was taken to an university hospital when 27 days old because of fever, cough and swelling on left lower extremity and had medical treatment with the diagnosis of bronchopneumonia. He was referred to orthopedic and cardiovascular surgery departments because of congenital hemihypertrophy of left leg. After examined on these departments he was diagnosed as KTWS when six months old. When five years old, he was hospitalized and treated for acute lymphangitis. Between 5 and 21 years old the patient was on the control of a university hospital. When 21 years old he had acute lymphangitis attack again and took medical treatment. He was hospitalized in a university hospital with acute abdomen findings when he was 22 years old. On evaluation; lumbar puncture and cranial computerized tomography (CT) findings were normal. Abdomen ultrasonography (USG) revealed multiple acoustic shining areas on spleen. Abdomen CT revealed splenomegaly with multiple hypodense lesions on parenchyma, multiple mesenteric and paraaortic lymphadenopathies, lytic areas on vertebra corpuses (Figure 1). On bilateral leg magnetic resonance imaging (MRI) there were enlarged vascular structures in subcutaneous, intramuscular tissue and femur medulla compartment of left leg (Figure 2). On thorax CT there were bilaterally multiple nodular infiltrative areas. With these findings he dispatched to medical oncology department with the suspicion of lymphoma. But the patient admitted to a special doctor outside the hospital and was taken six cures of cyclophosphamide, doxorubicin, vincristine and pred-

Figure 1. Abdomen CT of the patient showing multiple hypodense lesions on parenchyma of spleen.
nisone (CHOP) regimen chemotherapy with the prediagnosis of non-Hodgkin’s lymphoma without biopsy. After chemotherapy, radiotherapy had planned by the same doctor but the patient didn’t accept and admitted to a university hospital. Then the patient was hospitalized for 45 days, the laparotomy operation was made in this hospital and on surgery there was no lymphadenopathy. Splenectomy was made, and liver biopsy was taken. On histopathological examination; multiple cystic lymphatic and vascular dilatation areas which have thrombosis were found on spleen, there were no neoplastic changes. With these results the clinical findings of patient was found to be related with KTWS. On spinal MRI there were cystic lesions on vertebra corpuses between T12-L2 segments (Figure 3) and these were suggested to be related to intramedullar spinal arteriovenous malformations. Then the patient had loss of power and sensation on both lower extremities, and he had his first operation at 23. When he was 25 he had two more operations in neurosurgical department. In these operations; the branch of arteriovenous malformation feeding was closed by silver clip and coagulation; and then arteriovenous malformation and T11-L3 spinal vertebrae were excised totally. After these operations prophylactic anticoagulation therapy with 8000 iu of enoxaparin sodium was administered subcutaneously every 24 hours. Ten days after these operations the chest pain started.

On examination he had a blood pressure of 120/70 mmHg, a pulse of 86 beats/min and a respiratory rate of 21 breaths/minute On auscultation of lungs there were rare inspiratory rales on right basal area. There were operation incision scars on abdomen at median line, on back at lumbar-lower thoracic vertebrae level. The left leg was larger in diameter and taller than the right one. There was reticular hyperpigmentous lesions and nonpitting edema on the left leg (Figure 4). Patient had paraplegia, urinary and anal incontinence.

On laboratory examination, the patient had microscopic hematuria. Serum d-dimer (933 ng/mL) and fibrin degradation proteins (> 500) levels were high. An arterial blood gas analysis revealed a PaO2 of 68 mmHg, a PaCO2 of 35.2 mmHg and a pH of 7.48. On chest X-ray there were bilateral discoid atelectasis at basal areas (Figure 5). Lower extremity venous doppler ultrasound revealed intraluminal ecogenous thrombosis material in left posterotibial vein, spontaneous reflux blood flow on both left and right main femoral veins. A ventilation perfusion (V/Q) scan revealed a decrease in perfusion at right lung upper lobe apical segment as segmentary and right lung upper lobe posterior segment as subsegmentary and at left lung lingula segment as subsegmentary defects, ventilation scan was normal. There was high probability of pulmonary embolism.

After the diagnosis of pulmonary embolism anticoagulation with 60 mg of enoxaparin sodium (6000 IU) administered subcutaneously every 12 hour, and then at fifth day the warfarin therapy was initiated in the dose of 10 mg/day. Enoxaparin sodium was continued until the in-
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Figure 3. Spinal MRI showing cystic lesions on vertebra corpus between T_{12}-L_{2} segments (related to intramedullar spinal arteriovenous malformations).

Figure 4. The left leg of the patient is larger and taller than the right one.

Figure 5. Chest X-ray of the patient showing bilateral discoid atelectasis at lower zones.
International normalized ratio (INR) had reached to the therapeutic range of 2.5-3 in seven days. Then we decreased the dose of warfarin to 7.5 mg/day and then to 5 mg. We did not plan to place inferior vena cava filter, because there was only one thromboembolism source and the patient had only one attack. With improved clinical and laboratory findings we discharged our patient from the hospital. At least one year anticoagulation with warfarin at the dose of 5 mg/day, maintaining the INR in a 2.5 to 3 range was recommended.

DISCUSSION

Klippel-Trenaunay syndrome (KTS) was first described by two French doctors, Klippel and Trenaunay in 1900. This congenital vascular disorder is described by three main symptoms, known as triad affecting one or more limbs. The triad consists of cutaneous hemangioma, varicose veins and bone and soft tissue hypertrophy. In 1907, Parkes and Weber described a disorder with the same symptoms involved in KTS with the addition of arteriovenous fistula. This derivative of KTS was called Klippel-Trenaunay-Weber syndrome (2-5).

Although the cause of KTWS is still unknown, there are some theories that have been argued by the medical community. These theories are:

a. KTWS is a mesodermal abnormality that causes vascular and soft tissue malformations during fetal development (Baskerville, 1985) (4),

b. KTWS is caused by gene mutation (5q or 11p deletion, balanced translocations involving chromosomes 8q 22,3 and 14q 13) (6),

c. KTWS is caused as a result of intrauterine injury to the sympathetic ganglia or intermediolateral tract resulting in dilatation of microscopic arteriovenous anastomosis (Bliznak and Staple) (2).

d. IGF 2 overexpression is involved in the etiology of tissue hypertrophy (7).

As incidence there are nearly less than 1000 cases worldwide. Males and females are affected equally. There is no racial predilection (1,3).

KTWS can be diagnosed by clinical observations; laboratory findings, dermoscan, and radiological examination of the bones of the limbs, doppler USG, photoplethysmography, venoscan and bone isotope scan (8). Recently in a study which made in King Edward Hospital a case of prenatal KTWS was presented with a description of the sonographically observed disease progression in uterus (9). Especially CT and ultrasound can demonstrate multiple low attenuation areas in the abdominal organs like liver, adrenal glands, kidneys and spleen (10). This finding can result in misdiagnosis, as in our case that was prediagnosed as lymphoma and administered chemotherapy of CHOP regimen.

KTWS presents at birth or during early infancy or childhood. Although there are reports of multiple affected limbs, KTWS generally affects a single extremity. The leg is the most common site followed by the arms, trunk and rarely the head and neck. Most patients demonstrate all four major signs of the clinical syndrome (1,5,8,11) (Table 1).

In a series of 252 patients with KTS at Mayo Clinic; 63% of patients had all features of port wine stain, varicosities and limb hypertrophy. Portwine stain was seen in 98% of patients, varicosities in 72% and limb hypertrophy in 67% (2). Our patient had these characteristic features of this syndrome; one leg involvement with bone and soft tissue hypertrophy, dermatological findings with reticular pigmentous lesions and varicose veins, arteriovenous malformations in spleen and spinal column.

KTWS patients demonstrate some of minor findings (2,10) (Table 1). The patient we reported had lymphedema, thrombophlebitis attacks, microscopic hematuria, splenomegaly, spinal arteriovenous fistulas.

There is no known cure for KTWS. Conservative treatment of symptoms seems to be most effective without significant side effects. The nonoperative management includes external compression with graduated compression bandages or elastic stockings. Patients with recurrent attacks of cellulites may benefit from prophylactic antibiotic therapy. Orthotic device using for leg length differences is also possible. In general operation should be done to improve cosmesis.
at the expense of function. A reason for operative treatment is a leg length discrepancy of more than 2 cm (epiphysiodesis). Laser therapy is useful in some patients for decreasing the intensity of capillary malformations. Surgical intervention in the treatment of varicosities and venous malformations is controversial. One might consider surgery for either significant cosmetic deformity or the symptoms of pain, heaviness of the leg, bleeding or infectious complications. Venous legation, stripping, excision or sclerotherapy are contraindicated unless the surgery is directed to the superficial system. The deep system must be normal or demonstrate only mild to moderate reflux (2-4). As a result management in most patients with KTWS should be nonoperative. May be in our patient it would be better if multiple surgical operations are not executed for curative purposes. Also it is important in the management of KTWS to develop an optimal doctor-patient relationship to provide adequate social support (5).

The pulmonary abnormalities associated with KTWS include:

- Pulmonary lymphatic obstruction, lymphatic hyperplasia, aplasia and hypoplasia,
- Pulmonary vein varicosities,
- Cavernous hemangiomas of the pleura leading to hemathorax,
- Thromboembolic phenomenon (1,11-13).

It is important to note that, although deep venous thrombosis seems in higher incidence, pulmonary embolism appears to be a rare complication in patients with KTWS. In a small group of patients with KTWS (49 patients) Baskerville et al. estimated the incidence of pulmonary embolism to be %14 to %22 (14). Although nearly 1000 KTWS cases have been reported to date only 10 cases of pulmonary embolism in KTWS patients have been published (1,4,15). In some cases pulmonary embolism was recurrent leading to chronic thromboembolic pulmonary
hypertension and subsequent death (15). Our patient had pulmonary embolism attack 10 days after surgical operations while he was taking prophylactic therapy with enoxaparine. This pulmonary embolism case can be accepted as a postoperative complication, but we think that also it can be accepted as a part of KTWS since he had venous thrombosis on the affected leg (left leg). Nevertheless we believe that none of the reasons can be excluded exactly.

In the literature there is no established treatment regimen for the thromboembolism in patients with KTWS. It is recommended that firstly some preventive procedures should be done like not using oral contraceptive drugs, to use deep venous thrombosis prophylaxis regimens after surgical procedures etc. We recommend medical treatment if patients have one thrombosis source and have one attack. Medical treatment includes anticoagulation with warfarin to a goal INR between 2.5 and 3 for at least one year or life long therapy according to patient’s clinical findings. If patient has recurrent multiple pulmonary embolism attacks despite anticoagulation, pulmonary thromboendarterectomy can be applied (11,15), and an inferior vena cava filter can be placed (1,16).

As a conclusion; KTWS is a rare and complex disease. To be aware of this syndrome and its clinical implications are necessary to improve the prognosis and to avoid misdiagnosis.

REFERENCES