Case report

Klippel-Trenaunay-Weber syndrome with visceral involvement and portal hypertension

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In 1900, Klippel and Trenaunay published two papers describing a syndrome they termed naevus variqueux ostéo-hypertrophique (naevus vasculosus osteohypertrophicus) characterized by (1) a vascular nevus extending over the lower limb in a segmental distribution, (2) varicosities, limited to the affected side and appearing early in childhood, if not at birth, and (3) hypertrophy of all tissues on the affected side and particularly the bones, which may increase in length, thickness, and width.[1,2] Weber[3,4] independently described a similar constellation of signs in 1907 and again in 1918 consisting of vascular or lymphangiomatous malformation, nevus flammeus, growth disturbances, and arteriovenous fistulae, which he termed hemangiectatic hypertrophy. Since then several authors have suggested combining the two syndromes under the name of Klippel-Trenaunay-Weber (K-T-W) syndrome or the more general term of naevus vasculosus osteohypertrophicus.[5,6] Fortunately, this disorder is rare, and no data exist concerning its exact incidence. We report a case of visceral involvement in K-T-W syndrome, and discuss the life-threatening complications of such involvement as the patient matures.

Case report

A 24-year-old white man was transferred to the Cleve-

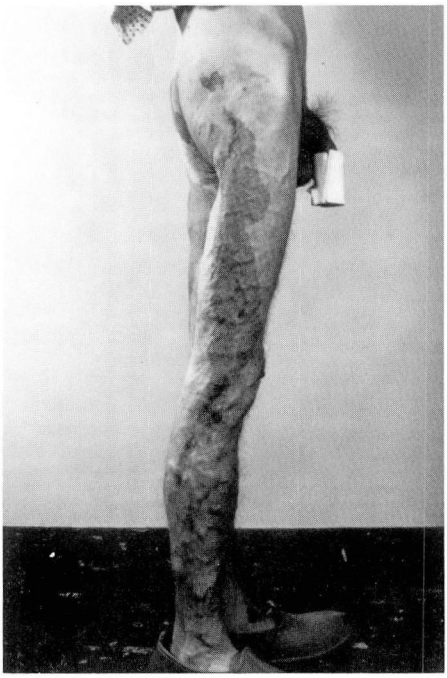

Fig. 1.

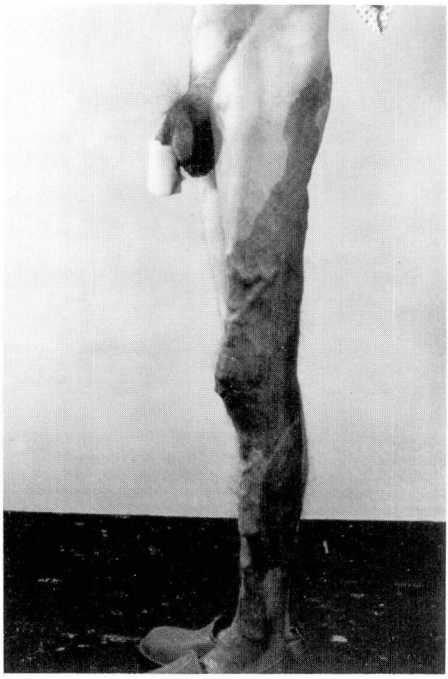

Fig. 2.

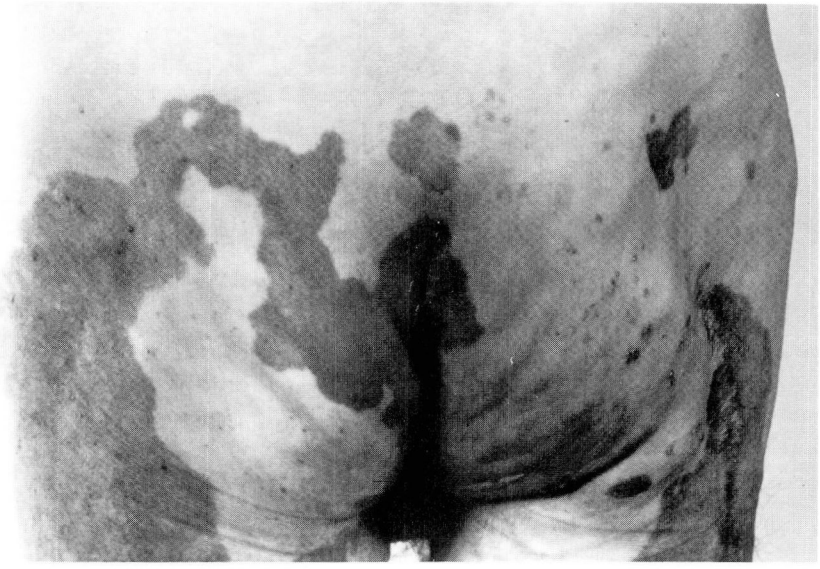

Fig. 3.

Figs. 1–3. Extensive vascular nevus involving buttocks and both legs.

land Clinic in March 1981 with a diagnosis of bleeding esophageal varices. The patient had an extensive nevus flammeus extending over both legs and the genitalia. At eight months of age, one toe of his left foot was excised because of a large hemangioma. At seven years of age he had an operation to curtail the growth of his left great toe, which

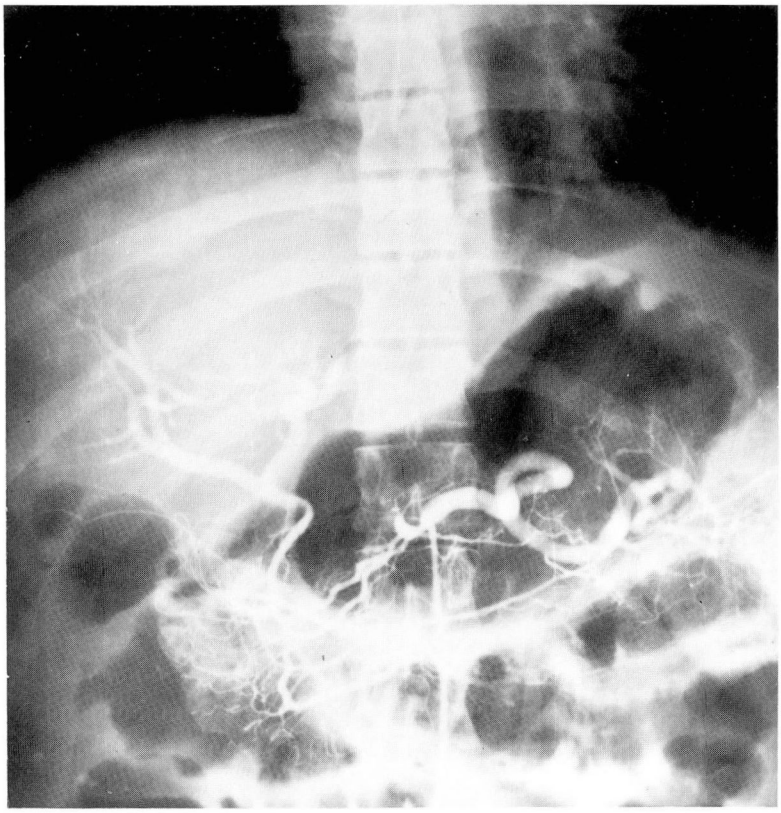

Fig. 4. Celiac angiogram demonstrating occlusion of proximal hepatic artery.

was hypertrophied; at age 14, varicose veins were excised, and at 16, a hemangioma around the penis and urethra was removed. He had also experienced periodic rectal bleeding from hemorrhoids and a hemangioma of the rectum. He had been admitted to his local hospital with a three-day history of melena and hematemesis and received a transfusion of 8 units of blood. An upper gastrointestinal radiographic series revealed esophageal varices. There was no history of alcohol ingestion or hepatitis.

On transfer to the Cleveland Clinic, his blood pressure was 160/88 mm Hg, and physical examination showed a poorly developed male in no acute distress. His head, eyes, ears, nose, and throat were normal. There was no scleral icterus. An extensive vascular nevus covered the left buttock, leg, and foot and the posterior aspect of the right buttock and thigh. There was also marked hypertrophy of the left leg (*Figs. 1–3*). The chest was clear to auscultation and percussion. The heart was normal. The abdomen was moderately distended with 4+ ascites. The liver was not palpable, and there were no masses or organomegaly. The external genitalia were enlarged, and there was a split-thickness skin graft on the penis. There was a vascular nevus around the rectum, and there were large external hemorrhoids with melanotic stool in the rectal ampulla.

An emergency upper gastrointestinal endoscopy was performed, which showed moderately large varices in the lower half of the esophagus. These were not actively bleeding on admission. The stomach and duodenum were normal. Celiac and SMA angiograms were done and demonstrated occlusion of the proximal hepatic artery with filling by anastomotic branches from the gastroduodenal to the distal hepatic artery (*Fig. 4*).

There were also collaterals extending from the superior mesenteric artery to the reconstructed hepatic artery. Extensive gastric and some distal esophageal varices were noted. There was suspected cavernous transformation of the portal vein and multiple phleboliths in the abdomen and pelvis.

The patient was treated with a Sengstaken-Blakemore tube and transfused with whole blood and fresh frozen plasma. His cardiac index was 7.8 L/min/m^2 with a systemic vascular resistance of 558 dynes · sec · cm^{-5} and a pulmonary capillary wedge pressure of 11 mm Hg. The Sengstaken-Blakemore tube was deflated, and the patient again began to bleed. Another upper gastrointestinal endoscopy was performed; the varices were injected with a sclerosant solution [0.5% sodium tetradecyl sulfate (Sotradecol)]; 70% glucose, and 3.5 units of thrombin per cc) and the patient was given intravenous vasopressin (Pitressin). Forty-eight hours later the patient became intensely jaundiced with a bilirubin of 20 mg/dl. The following day his bilirubin rose to 22 mg/dl. His albumin was 4 g/dl; serum calcium, 9.1 mg/dl; alkaline phosphatase, 75 U/L (normal, 30–85); serum glutamic oxaloacetic transaminase (SGOT), 65 U/L (normal, 7–40 U/L); lactate dehydrogenase (LDH), 860 U/L (normal, 100–225 U/L); and his prothrombin time was 16 seconds with a control of 12. A direct Coombs' test was positive, hemoglobin was 12.2 g/dl, and platelet count was 80,000. Another hematemesis followed, and the varices were again sclerosed. Following this procedure his temperature was 40.2 C, white blood cell count

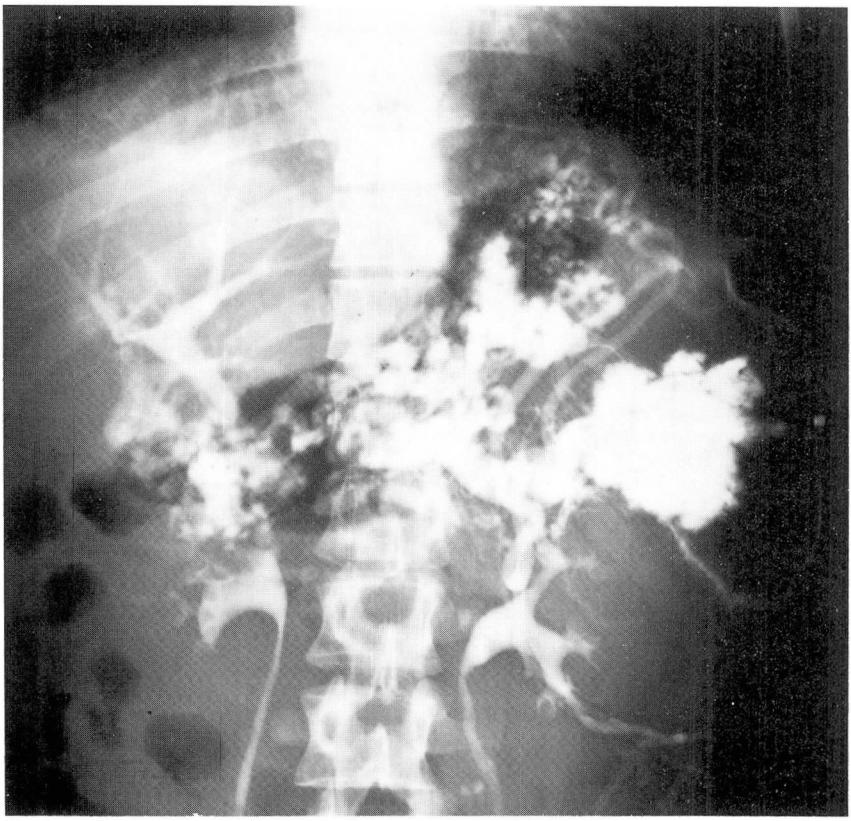

Fig. 5. Splenoportogram showing cavernous transformation of portal vein, occlusion of splenic vein, nonvisualization of superior mesenteric vein, and extensive gastric varices. Note notching of left ureter and phleboliths.

rose to 13,000, and hemoglobin fell to 8.1. A CT scan showed no evidence of biliary tree dilatation, and the jaundice cleared spontaneously with a decrease in the bilirubin to 12 mg/dl. The LDH increased to 1250 U/L. A splenoportogram confirmed cavernous transformation of the portal vein with occlusion of the superior mesenteric and portal veins; and the splenic pulp pressure measured 440 mm of water (*Fig. 5*). Another hematemesis occurred on April 11, and a third endoscopic sclerosing procedure was done. Following this, the patient's condition gradually improved with complete resolution of jaundice.

Because of the many previous episodes of bleeding he was taken to the operating room for better control of his varices. At surgery he was found to have markedly dilated veins and an arteriovenous malformation surrounding the terminal ileum, colon, rectum, and bladder (*Figs. 6 and 7*). There was hypertrophy of the colon, and especially of the rectosigmoid area. The superior mesenteric vein and splenic vein were thrombosed and replaced by multiple small collateral vessels. The spleen was massively enlarged. The liver was large and appeared congested, but was not cirrhotic. There was moderate ascites. Liver biopsy, splenectomy, and extragastric ligation of varices were performed. The liver biopsy showed only biliary stasis, and the spleen showed marked passive congestion with splenic infarction. One week postoperatively the patient had a mild episode of hematuria. Cystoscopy confirmed the presence of multiple hemangiomas in the bladder and urethra. An intravenous pyelogram showed left ureteral notching secondary to the markedly dilated retroperitoneal veins. There was also grade I right hydronephrosis with extrinsic obstruction of the right ureter at the pelvic brim. The bleeding stopped spontaneously, and the patient was discharged from the hospital two weeks after surgery.

A follow-up letter from his local physician in November 1981 noted that the patient had been hospitalized once more for colonic bleeding and had a positive test result for fibrin split products. The bleeding stopped with conservative medical management, and colonoscopy was performed by the patient's local gastroenterologist who suspected inflammatory bowel disease because of the degree of mucosal inflammation. He has had no further episodes of esophageal bleeding to date.

Discussion

Since the original reports by Klippel, Trenaunay and Weber, most authors

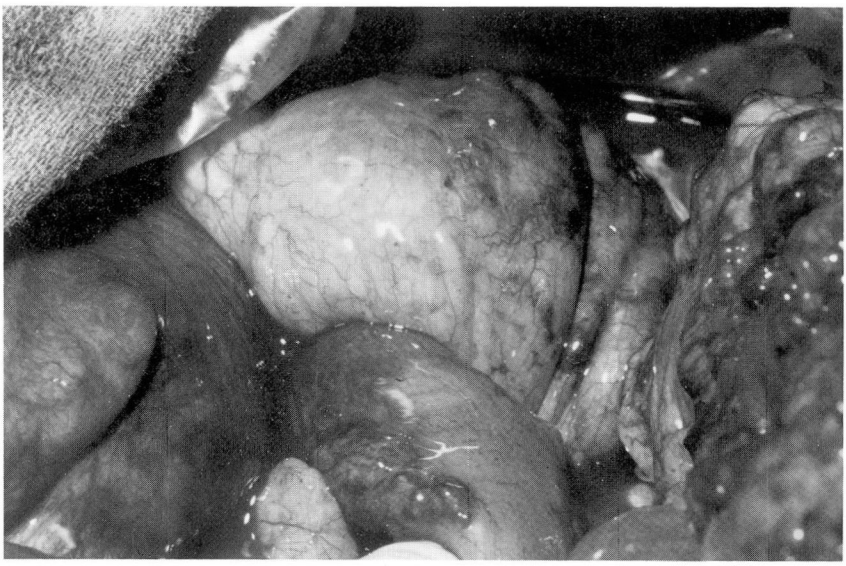

Fig. 6. Operative photograph showing arteriovenous malformation of terminal ileum (center) and colon.

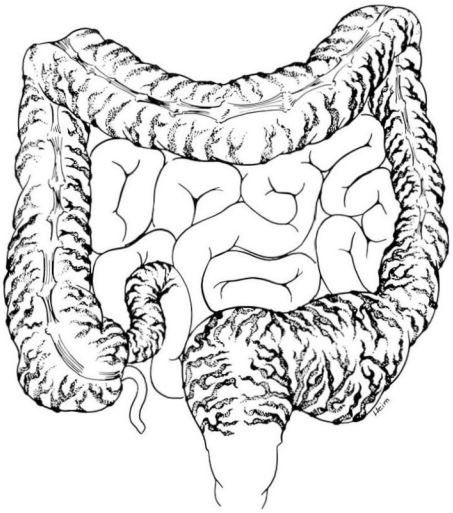

Fig. 7. The entire colon, colon mesentery, and rectosigmoid are surrounded by multiple dilated veins; rectosigmoid is hypertrophied.

have concentrated on the consequences of integumentary and limb involvement.[7–10] Speculation regarding etiology has been rife. Servelle and Babillot[11] believe the primary problem is congenital malformation of the deep veins with agenesis, atresia, or compression of the popliteal, femoral, or iliac veins resulting in venous stasis and hypertension. They reported an impressive operative experience of 614 cases between 1943 and 1976, with 559 of these for lower extremity involvement. Of this group, 78% had either popliteal vein obstruction, or popliteal and femoral vein obstruction combined, whereas 16% had femoral vein obstruction alone. Servelle et al[12] also described 6 children between 15 months and four years of age with severe rectal bleeding, vaginal bleeding, and hematuria. He speculated that the cause of the varicosities in the rectum, bladder, and vagina was an absence of the anterior venous pathway leading to abnormal hypertrophy of the sciatic nerve vein, deep femoral vein, and internal iliac vein. He concluded that high flow in the internal iliac vein hindered the venous drainage of the rectum, bladder, and vagina. He attempted to increase the anastomotic connections between the posterior venous pathway and the common femoral vein and external iliac vein. The technique seemed beneficial in 3 of his 6 patients; one died from recurrent bleeding, one required cystectomy and one proctectomy.

This view of the etiology has been disputed by others. Haven et al[9] presented 23 cases of K-T-W syndrome and concluded that there was a lack of correlation between limb hypertrophy and signs of venous stasis, and that there appeared to be a hereditary feature of the disease since it coexisted with other anomalies known to be transmittable. This syndrome may come under the more general term of phacomatosis, that is, a general embryological disorder involving the ectoderm or mesoderm expressed as cutaneous or visceral abnormalities.[13] Some support for this idea may be found in the literature. Owens et al[14] reported a case of K-T-W syndrome associated with a pulmonary vein varicosity. Pulmonary arteriograms showed otherwise normal pulmonary vasculature, and the rest of the cardiac catheterization studies were normal. Other cases have been reported involving the ears, oral cavity, upper extremities, and trunk.[15–17] Gourie-Devi and Prakash[18] reported a case of a vertebral and epidural hemangioma with paraplegia in K-T-W syndrome. They hypothesized that branches of the seventh dorsal intersegmental vessel were affected during embryonic life, giving rise to the vertebral and epidural hemangioma and a metameric cutaneous vascular nevus.

Apart from Servelle's cases we found only three published reports of K-T-W syndrome and visceral angiomatosis.

Kuffer et al[19] described an 11-year-old boy with bony and soft-tissue hypertrophy; varicosities and multiple hemangiomata of both lower extremities; hemangiomata of the bladder, glans penis, large bowel, mesocolon, the root of the small bowel mesentery, and retroperitoneal space; and a mild thrombocytopenia associated with persistent hemorrhage from multiple hemangiomas. This patient also had a small hemangioma of the anterior surface of the left lobe of the liver. Klein and Kaplan[20] reported 2 cases of K-T-W syndrome associated with urinary tract hemangiomas. The first of these required partial cystectomy at the age of three for hematuria. This patient had right lower extremity involvement with numerous varicosities and port-wine hemangiomas over the right buttock, thigh, and leg. Venography revealed numerous dilated and tortuous veins in the right leg, thigh, and buttock. The right external iliac vein was apparently normal, but the right internal iliac vein was extremely dilated. Thus, this case appears to be similar to those in Servelle's series. Their second patient developed hematuria at the age of 13 after a fall. He had varicosities and hypertrophy of the left ear, arm, axilla, and chest; a port-wine nevus of the left hand; and marked deformity of the left hand. He also had cavernous hemangiomas on the right side of the penis and scrotum as well as hypertrophy and varicosities of the right leg, and a large cavernous hemangioma obstructing the ureter. Ghahremani et al[21] described 2 patients with K-T-W syndrome with large, infiltrative cavernous hemangiomas of the distal colon. Both developed rectal bleeding at an early age. The first patient also had involvement of the dome of the bladder, retroperitoneal space, the colon distal to the splenic flexure, and the root of the small bowel mesentery. The second patient was noted to have thrombocytopenia; hypofibrinogemia; prolonged bleeding; and deficiency of factors V, VII, VIII, and IX; and a shortened half life of ^{131}I-fibrinogen consistent with the diagnosis of consumption coagulopathy. These authors noted that several cases reported in the literature as cavernous hemangiomas of the colon may in fact have been K-T-W syndrome.

The complications of K-T-W syndrome such as those listed by Mullins[5] are formidable enough in themselves without the added problem of visceral involvement. Mullins' list of complications includes edema, phlebitis, thrombosis, scoliosis, bone and joint abnormalities with resultant abnormality of function, stasis dermatitis, skin ulceration, phleboliths, hyperhydrosis, pulmonary hypertension, and paresthesias. Our patient appears to have had thrombosis of the portal and splenic veins and hepatic artery, presumably resulting from activation of clotting factors within the angiomas. Subsequent portal hypertension then caused bleeding esophageal varices. In addition, he suffered from periodic episodes of urinary and colonic bleeding. Fortunately, his hematuria and rectal bleeding have been relatively mild. An alternate explanation for the colonic varices is that the superior mesenteric vein, portal vein, and splenic vein thromboses were congenitally present, creating portal hypertension and generalized venous dilation. However, if portal hypertension had existed previously, one would have expected the development of esophageal varices to occur at an early age with consequent bleeding. Therefore, it seems logical to assume that the portal hypertension was a relatively recent phenomenon.

We know of one other case of K-T-W

syndrome associated with vaginal varices that became symptomatic after parturition necessitating an emergency hysterectomy (Robert D. Mercer, M.D., Department of Pediatrics, personal communication). When K-T-W syndrome involves the colon, it may cause rectal bleeding and endoscopically can mimic inflammatory bowel disease.[21] These colonic vascular malformations can occasionally be treated by ligation or embolization, but may necessitate colectomy. Similarly, bladder involvement may require partial cystectomy. Radiotherapy has been proposed as an alternative treatment; however, there are no data in the literature to suggest that it is effective. In our patient surgical removal of the colon would be exceedingly hazardous because of coexisting portal hypertension.

In summary, the K-T-W syndrome comprises not only cutaneous angiomas and skeletal hypertrophy, but may include visceral angiomas as well. It is not clear whether this involvement results from a generalized disturbance of the mesodermal and ectodermal tissues occurring in utero, chromosomal abnormalities, or from developmental problems secondary to venous hypertension and stasis. The complications of K-T-W syndrome are not limited to childhood growth disturbances and may appear as life-threatening bleeding in late adolescence or early adulthood.

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