References

1. Lamiell JM, Salazar FG, Hsia YE. Von Hippel-Lindau disease affecting 43 members of a single kindred. Medicine 1989;68:1–29.
2. Go RCP, Lamiell JM, Hsia YE, Yuen JW, Paik Y. Segregation and linkage analysis of von Hippel-Lindau disease among 220 descendants from one kindred. Am J Hum Genet 1984;36:131–42.
3. Bradley WG, Duroff RB, Fenichel GM, Marsdser CD, eds. Neurology in clinical practice the neurologic disorders. Stoneham, Massachusetts: Butterworth-Heineman, 1991:1332–3.
4. Matthews AJ, Halshaw J. Epidural anaesthesia in von Hippel-Lindau disease. Anaesthesia 1986;41:853–5.
5. Donaldson JO. Neurology of pregnancy. 2nd ed. Philadelphia: WB Saunders, 1989:198–9.
6. Tuttelman RM, Gleicher N. Central nervous system hemorrhage complicating pregnancy. Obstet Gynecol 1981;38:651–6.
7. Hughes SJ, Short DJ, Usherwood MM, Tebbutt H. Management of the pregnant woman with spinal cord injuries. Br J Obstet Gynaecol 1991;98:513–8.

Address reprint requests to:
Keith K. Ogasawara, MD
Department of Obstetrics and Gynecology
Women's Hospital, 5K40
1240 North Mission Road
Los Angeles, CA 90033

Received March 4, 1994.
Received in revised form August 2, 1994.
Accepted August 15, 1994.

KASABACH-MERRITT COAGULOPATHY COMPLICATING KLIPPEL-TRENAUNAY-WEBER SYNDROME IN PREGNANCY

A. George Neubert, MD, Michael A. Golden, MD, and Nancy C. Rose, MD

***Background*: Klippel-Trenaunay-Weber syndrome is a sporadic genetic syndrome characterized by localized hemangiomas, venous varicosities, and asymmetric osseous hypertrophy of the ipsilateral extremities. Most commonly seen in association with hemangiomas, Kasabach-Merritt syndrome is defined by the presence of thrombocytopenia and a consumptive coagulopathy.**

***Case*: A 22-year-old primigravida with a prior diagnosis of Klippel-Trenaunay-Weber syndrome presented for genetic counseling and delivery management at 37 weeks' gestation. Large varicosities of the vulva required cesarean delivery. Multiple hemangiomas in the right lower quadrant of the abdomen necessitated the use of a left paramedian cutaneous incision. The patient subsequently developed Kasabach-Merritt syndrome and required the transfusion of blood products as well as heparin and aminocaproic acid therapy for her postoperative management.**

Conclusions*: Klippel-Trenaunay-Weber syndrome in pregnancy is rare. The potential for a refractory coagulopathy presenting as Kasabach-Merritt syndrome should be considered in any patient who presents with extensive hemangiomas. *(Obstet Gynecol 1995;85:831–3)

Obstetric patients with large vascular malformations present difficult management issues at delivery. Klippel-Trenaunay-Weber syndrome is a sporadic genetic syndrome characterized by localized cutaneous hemangiomas, venous varicosities, and asymmetric osseous hypertrophy of the ipsilateral extremities.[1] Complications at delivery can include disseminated intravascular coagulation (DIC) and massive hemorrhage. Coagulopathic events may be due to persistent blood loss or may reflect the development of Kasabach-Merritt syndrome. First reported in 1940, this syndrome has been described most commonly in children; it is defined by thrombocytopenia of varying degrees and a consumptive coagulopathy seen in association with hemangiomas.[2] A microangiopathic hemolytic anemia may also be present. To our knowledge, no other cases of a pregnancy complicated by Klippel-Trenaunay-Weber and subsequent Kasabach-Merritt syndrome have been reported.

From the Divisions of Maternal-Fetal Medicine and Reproductive Genetics, the Departments of Obstetrics and Gynecology and Surgery, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania.

Case Report

A 22-year-old primigravida was first seen in consultation for genetic counseling and delivery management at 37 weeks' gestation. A diagnosis of Klippel-Trenaunay-Weber syndrome had been made previously, and she had undergone an uncomplicated amputation above the right knee in 1988 because of recurrent hemarthrosis. Her medical history was otherwise unremarkable. Her pregnancy course had been without complication.

On physical examination, she displayed multiple subcutaneous hemangiomas distributed over the right lower quadrant of the abdomen, extending to the posterior gluteal region and over the right anterior thigh. Ipsilateral hypertrophy of the right thigh was also present. In addition, massive hypertrophy of the right labia majora was noted. Closer inspection revealed the labia majora to contain a large complex of varicosities measuring 15 × 5 cm (Figure 1). The varicosities partially obstructed the introitus and, on bimanual examination, were noted to extend along the entire length of the right vaginal-side wall.

Based on these findings, we recommended a cesarean

0029-7844/95/$9.50 **831**
SSDI 0029-7844(94)00349-I

Figure 1. Antepartum photograph of the patient presenting at term with Klippel-Trenaunay-Weber syndrome. In addition to the hypertrophy of the right labia majora, multiple subcutaneous hemangiomas were distributed over the right lower quadrant of the abdomen, posterior gluteal region, and right anterior thigh.

delivery. Before admission, both the vascular surgery and anesthesia services were consulted; plans were made for delivery in the vascular surgery suite with the ready availability of red blood cell salvage equipment. The preoperative magnetic resonance imaging demonstrated the lumbar spine and epidural space to be free of vascular abnormalities, and a combined spinal and epidural anesthetic was given.

The patient underwent an uncomplicated, primary low vertical cesarean delivery through a left paramedian incision at 39 weeks' gestation. A viable female infant was born weighing 3730 g and having an Apgar score of 9 at both 1 and 5 minutes. The neonate displayed no evidence of Klippel-Trenaunay-Weber syndrome. The patient's course was uncomplicated until postoperative day 4, when she reported incisional pain after ambulation. We found the incision to be intact, but noted a small amount of bleeding. A pressure dressing was applied, and a complete blood count and coagulation studies revealed a hemoglobin and hematocrit of 9.0 g/dL and 26%, respectively; a platelet count of 135 × 1000/uL; prothrombin time (PT) of 13.1 seconds; and partial thromboplastin time (PTT) of 32.4 seconds.

The next morning, the patient was noted to have active bleeding along the incision line, as well as a palpable mass consistent with a wound hematoma. She was returned to the operating room, where the wound was explored and a large hematoma was evacuated. The fascial suture line was intact, no active bleeding sites were identified, and the incision was closed with staples. Treatment with 2 g of intravenous (IV) cefotetan, every 12 hours was begun. Both during and after the procedure, laboratory studies indicated evidence of DIC. A complete summary of the patient's pertinent laboratory values is provided in Table 1. The patient was transferred to the intensive care unit, and despite transfusion with packed red blood cells, platelets, and fresh frozen plasma, she remained anemic, thrombocytopenic, and coagulopathic. Continued bleeding at the incision site and the development of a new wound hematoma required a second exploration on postoperative day 6. A large hematoma was evacuated again, and no active bleeding sites were identified. The wound was packed with sterile gauze and left to heal by secondary intention.

No further bleeding occurred at the operative site. We noted no evidence of internal bleeding on computed tomography scan or peripheral bleeding on physical examination. Despite these findings, coagulation studies remained abnormal. In total, the patient received 20 U packed red blood cells, 72 U platelets, 59 U fresh frozen plasma, and 240 U cryoprecipitate during her hospitalization. Given her refractory coagulopathy, a diagnosis of Kasabach-Merritt syndrome was considered, and the patient was started on IV heparin (1000 U IV bolus followed by 100 U/hour) and aminocaproic acid therapy (4 g orally, then 1 g orally every hour thereafter for 12 doses). The patient had minimal immediate response to this therapy, but did show slight improvement in her coagulation profile over the next several days. Therapy was continued until postoperative day 16, when the patient's hemoglobin and hematocrit were stable and her thrombocytopenia resolved. Coagulation studies remained abnormal, but the patient displayed no evidence of bleeding, and the incision was healing well. She was discharged on postoperative day 20. The patient's labo-

Table 1. Laboratory Values

Postoperative day	Hemoglobin (g/dL)/ hematocrit (%)	Platelets* (×1000/ μL)	PT† (sec)	aPTT‡ (sec)	FBG§ (mg/ dL)	FSP‖ (μg/ mL)
0	10.9/32	202	9.7	24.4	272	
4	9.0/26	135	13.1	32.4		
5¶	5.9/17	126	>50	26.1	66	142
5#	6.8/23	113	14.3	37.6	64	220
6	7.1/21	78	14.0	37.0	100	395
7	9.0/26	82	12.9	31.6	158	340
16	10.5/30	156	14.9	36.0	55	100
20	12.6/37	169	15.1	35.9	50	176
34	12.8/37	186	12.4	26.5	158	10–40
91			11.3	24.7	204	<10

PT = prothrombin time; aPTT = activated partial thromboplastin time; FBG = fibrinogen; FSP = fibrin split products.

* Normal value 130,000–400,000/μL.

† Normal value 10–12.5 seconds.

‡ Normal value 24–34 seconds.

§ Normal value 170–410 mg/dL.

‖ Normal value 0–18 μg/mL.

¶ Intraoperative.

Postoperative.

ratory values showed continued improvement on postoperative day 34, and by her follow-up visit at 13 weeks postpartum, all laboratory values had returned to normal.

Discussion

Klippel-Trenaunay syndrome, first described in 1900, is defined as a triad of clinical features, including unilateral cutaneous hemangiomas, varicose veins, soft tissue, and asymmetric osseous hypertrophy of the ipsilateral extremities.[1] Weber[3] described several similar cases and, in 1918, reported the additional feature of arteriovenous fistulae. A review[4] of 768 cases of Klippel-Trenaunay-Weber syndrome described a consistent absence or major atresia of the deep venous vascular system, causing limb elongation, venous stasis, varicosities, and edema. A venogram had previously demonstrated a similar absence of the deep venous vascular system of the right lower extremity in our patient. The etiology of Klippel-Trenaunay-Weber syndrome has been reviewed by Baskerville et al,[5] who suggested that a mesodermal defect operative at angiogenesis may explain the vascular abnormalities that define the syndrome. Complications in the affected extremity may include stasis dermatitis, skin ulceration, and recurrent hemarthrosis—all of which may require amputation of the limb for management.

Our patient's refractory coagulopathy prompted the diagnostic consideration of Kasabach-Merritt syndrome. First reported in 1940, the syndrome consists of thrombocytopenia and a consumptive coagulopathy seen in association with hemangiomas.[2] Consistent laboratory abnormalities include thrombocytopenia, decreased fibrinogen, and coagulation factors II, V, and VIII. Increased PT, PTT, and fibrin split products are also invariably present. A similar clinical presentation has been reported in association with Klippel-Trenaunay-Weber syndrome.[6]

The exact mechanism by which the thrombocytopenia and coagulopathy develop is unknown. It has been suggested that a combination of venous stasis and abnormal endothelial cells within the hemangiomas functions to increase platelet pooling and destruction with activation of the coagulation cascade, resulting in a localized and self-perpetuating coagulopathy.[7] Inceman and Tangun[8] reported a case in which an 8-year-old boy with a giant hemangioma of the lower extremity demonstrated a difference in PT and PTT values in blood obtained from a peripheral site in comparison with blood obtained from the hemangioma. We suspect that a similar mechanism occurred in our patient. Despite choosing a left paramedian incision, a subtle disruption of the right-sided hemangioma, exacerbated by increased ambulation, may have initiated the coagulopathy. Once established, the local consumption of clotting factors and platelets persisted in the hemangioma and resulted in hemorrhage at the incision site.

A number of therapeutic modalities have been used in the management of Kasabach-Merritt syndrome. These include platelet transfusion, IV heparin, aminocaproic acid, radiotherapy, alpha 2a interferon, corticosteroids, and intermittent pneumatic compression of the extremities. A prominent feature of this patient's persistent coagulopathy was the markedly elevated fibrin split products. This finding prompted our decision to use the plasminogen-activator inhibitory effects of aminocaproic acid after the failure of blood product replacement therapy to correct her coagulopathy.

Although a pregnancy presenting with Klippel-Trenaunay-Weber syndrome is rare, many patients with known deep or superficial hemangiomas can and do become pregnant. The potential for a refractory coagulopathy presenting as Kasabach-Merritt syndrome should be considered in any patient who presents with extensive hemangiomas.

References

1. Klippel M, Trenaunay P. Du noevus variqueux osteohypertrophique. Arch Gen Med 1900;3:641–72.
2. Kasabach HH, Merritt KK. Capillary hemangioma with extensive purpura: Report of a case. Am J Dis Child 1940;59:1063–70.
3. Weber FP. Haemangiectatic hypertrophy of limbs: Congential phlebarteriectasis and so called congenital varicose veins. Br J Child Dis 1918;15:13–7.
4. Servelle M. Klippel and Trenaunay's syndrome: 768 operated cases. Ann Surg 1985;201:365–73.
5. Baskerville PA, Ackroyd JS, Browse NL. The etiology of the Klippel-Trenaunay syndrome. Ann Surg 1985;202:624–7.
6. D'Amico JA, Hoffman GC, Dyment PG. Klippel-Trenaunay syndrome associated with chronic disseminated intravascular coagulation and massive osteolysis. Clev Clin Q 1977;44:181–8.
7. Hillman RS, Phillips LL. Clotting and fibrinolysis in a cavernous hemangioma. Am J Dis Child 1967;113:649–53.
8. Inceman S, Tangun Y. Chronic defibrination syndrome due to a giant hemangioma associated with microangiopathic hemolytic anemia. Am J Med 1969;46:997–1002.

Address reprint requests to:
A. George Neubert, MD
Department of Obstetrics and Gynecology
University of Pennsylvania Medical Center
3400 Spruce Street
Philadelphia, PA 19104

Received July 14, 1994.
Received in revised form September 16, 1994.
Accepted September 29, 1994.