CHAPTER **40**

LOWER EXTREMITY DEFORMITY CAUSED BY PARKES WEBER SYNDROME: Literature Review and Case Report

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INTRODUCTION

Parkes Weber Syndrome (PWS) is a rare form arteriovenous malformation (AVM) causing overgrowth of bone and soft tissue of both upper and lower extremities; however, the lower extremity is more commonly affected. PWS was first described in 1907 by the English dermatologist Frederick Parkes Weber, who presented multiple case reports of children with "hypertrophy of one limb," which was found to be associated with "tumor-like overgrowth in the corresponding portion of vascular system" (1). In his further publications, Dr. Weber referred to the above phenomenon as "congenital or developmental phlebarteriectasis," characterized by "communication between arterial channels and the venous channels...as in cases of arterio-venous anastomosis of traumatic origin" (2). PWS is often erroneously muddled in the literature into Klippel-Weber-Trenaunay Syndrome (KTS), causing a lot of confusion and uncertainty for both physicians and patients. KTS is a well-known form of vascular malformation often characterized by malformed capillary, lymphatic, and venous elements (3). PWS differs from KTS in hemodynamic and biologic factors, therefore requiring a separate unique diagnosis and novel approach to treating patients affected by this rare disorder. Most literature and research has been focused on describing KTS while very little has been published on PWS.

CASE REPORT

A 53-year-old female with a known diagnosis of PWS and significant cutaneous manifestations affecting the right lower extremity presented to the clinic for management of recurrent ulcerations on the dorsum of the right foot. At the time of the presentation, the wounds had been open for 5 months; however she has had recurrent ulcerations since adolescence. The patient denied any local and systemic symptoms of infection. The patient was able to care for the wounds in the past with local wound care and strict adherence to compression stocking therapy.

On physical examination, there were 2 small ulcerations measuring <1.0 cm each in diameter. The wound beds were shallow with mild fibrotic debris that did not probe to bone. There was no active purulent drainage, no proximal streaking, or sinus tracts. The skin of the dorsal forefoot and digits 1 through 3 was thickened with purple-violaceous discoloration resembling a port wine stain (Figure 1). There was increased temperature of the right foot as compared to the contralateral side. The right ankle and foot were significantly larger in diameter as compared to the left. Dorsalis pedis and posterior tibial pulses were palpable, however, the perforating peroneal pulse was not appreciated.

In order to reduce unnecessary radiation exposure to the patient, previous studies were used to evaluate the vasculature and bony deformity. Magnetic resonance arteriogram (MRA) obtained in 2008 revealed a right midfoot AVM supplied by the anterior and posterior tibial arteries with venous drainage predominantly via superficial

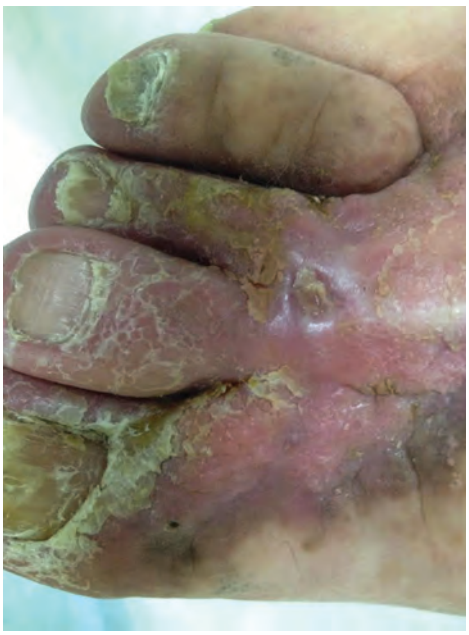

Figure 1. Clinical appearance.

veins along the medial calf and thigh as well as into the deep venous system at the level of the calf. The patient's left lower extremity was found to have normal arterial and venous distribution (Figure 2).

Magnetic resonance imaging (MRI) obtained in 2008 revealed subcutaneous edema involving the dorsum of the foot superior to the normal-appearing first and second metatarsals. There was no bone marrow edema or pathological post-contrast enhancement of marrow, which ruled out osteomyelitis. The study did not reveal any evidence of abscess within the soft tissues, however, it did reveal generalized atrophy of the intrinsic muscles of the forefoot (Figure 3). Arterial duplex ultrasound obtained in 2012 revealed minimal plaques in the arteries of the right lower extremity. Arterial flows were noted to be lower in resistance, which is consistent with the patient's multiple AVMs. Venous duplex ultrasound revealed a normal deep venous system of both legs with normal wave forms, morphology, and coaptation upon probe pressure.

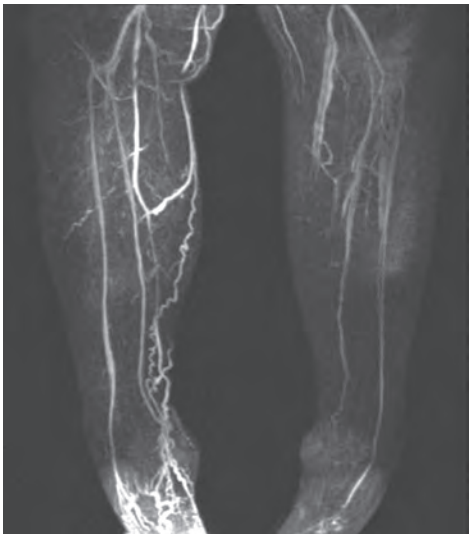

Figure 2. Normal arterial and venous distribution of patient's left lower extremity.

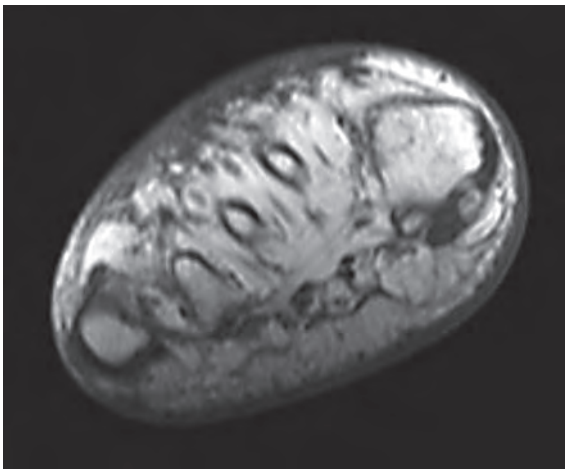

Figure 3. Magnetic resonance imaging showing subcutaneous edema.

DISCUSSION

PWS is a rare form of vascular malformation that occurs sporadically, however, familial dominance has been recorded (4). Recent studies suggest that it may result from mutations in the RASA1 gene that provides instructions for making a protein known as p120-RasGAP (5). PWS has had a complex evolution as an eponym for a group of fast flow arteriovenous anomalies. It was wrongfully combined into triple eponym KTS due to multiple publications describing similar findings by physicians who were not aware of each other's work. In 1900, Drs. Klippel and Trenaunay described a triad of vascular stain, soft tissue and bony hypertrophy, and venous varicosities in the lower extremity (6). Unaware of the earlier publication, in 1907 Dr. Frederick Parkes Weber described multiple patients with angio-formation in connection with hypertrophy of the limb (1). The triple eponym was finally disjoined in 1988 into two unique vascular anomalies with limb overgrowth (7). KTS and PWS are now differentiated based on flow characteristics and presence or absence of arteriovenous fistulas (8) (Table 1).

PWS is a high flow disorder characterized by malformed communication of arterial and venous channels made unique by the presence of arteriovenous fistulas, however it can also be associated with microscopic arteriovenous shunting instead of overt fistulas (9). KTS is a slow flow form of vascular malformation characterized by malformed capillary, lymphatic, and venous system communications. The arterial component, which is present in PWS, is absent in KTS.

Besides being different in their underlying etiology, both KTS and PWS result in marked disfiguring deformities due to bony and soft tissue hypertrophy. The hypertrophy in KTS is caused by venous hypertension that develops as a result of congenital deep vein anomaly (10). Patients with KTS who elected to undergo surgical intervention were found to have malformation of deep venous system that leads to elongation and edema of the affected limb (11). To prove that venous hypertension leads to hypertrophy, Servelle ligated veins in dogs at the groin or popliteal region and found that elongation of an extremity ranged between 2.6 and 7.6 percent within 1 to 1.5 years (12). In a different experiment he ligated popliteal veins in the normal limb on 48 children with KTS and found that differences in lengths between the two limbs was significantly reduced or even absent by adult life (10). Bony hypertrophy in PWS has been attributed to increased vascularization of the nearby cartilage growth center due to constant increased vascular inflow (13). This theory leads less to limb overgrowth since growth plates close by the time child reaches adulthood, though limb overgrowth caused by PWS continues to progress with age. Soft tissue overgrowth is responsible

Table 1. Flow characteristics and presence or absence of arteriovenous fistulas*

Type of association	Flow characteristics	Associated growth disturbance and traditional eponymous terminology
CLM	Slow-flow	
CVM	Slow-flow	
CLVM	Slow-flow	With undergrowth of the limb: Servelle-Martorell syndrome
CVM	Slow-flow	With overgrowth of the limb: Klippel-Trenaunay syndrome
CLVM	Slow-flow	With overgrowth of the limb: Klippel-Trenaunay syndrome
CAVM	Fast-flow	With overgrowth of the limb: Parkes Weber syndrome
CLAVM	Fast-flow	With overgrowth of the limb: Parkes Weber syndrome

CLM = capillary lymphatic malformation; CVM = capillary venous malformation; CLVM = capillary lymphatic venous malformation; CAVM = capillary arteriovenous malformation; CLAVM = capillary lymphatic arteriovenous malformation.

for the majority of limb deformity. Hypoxia due to the local vascular steal phenomenon created by the fistulas could be the culprit for associated hypertrophy (13). As fistulas siphon blood away proximally, this creates hypoxia distally causing the release of vascular endothelial growth factors. This leads to proliferation of endothelial cells and fibroblasts, causing hypertrophy (14). We hypothesize that soft tissue hypertrophy in PWS is similar to the digital clubbing phenomenon observed in patients with COPD and other pulmonary disorders.

Other clinical findings of PWS includes cutaneous red stain, dilated veins, cutaneous warmth, pedal edema, and pigmentation due to high flow arterial blood being siphoned through an unaccustomed venous network. Pseudo-Kaposi sarcoma skin changes that manifest as purple shiny plaques with a tendency to ulcerate, have been associated with PWS, which is likely due to proliferation of fibroblasts and local dermatitis (14-16) (Figure 4).

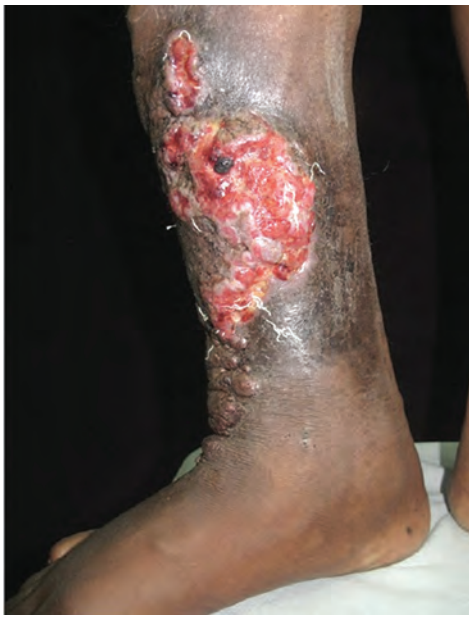

Figure 4. Pseudo-Kaposi sarcoma skin changes manifest as purple shiny plaques and have a tendency to ulcerate.

It is important to note that the vascular malformations are present at birth, but often go neglected for years due to their innocent appearance. PWS is also at times confused with hemangioma and gets mislabeled as port wine stain (17). Physical examination usually confirms the diagnosis of PWS, however, further confirmation can be done by ultrasound and color Doppler flows. MRA is the best way to document the extent of the disease, but is not necessary until surgical intervention is warranted.

Treatment of AVMs is a challenge for many surgeons. The few available research publications have shown great success with conservative treatments, however none address the underlying etiology. The mainstay conservative treatment options for these patients is control of edema with compression stockings, pain management, accommodative shoe gear that compensates for lower extremity deformity and leg length discrepancy, local wound care, and patient education regarding their condition. Surgical treatment of these patients is often delayed until there are ulcerations, ischemic pain, bleeding, increased cardiac output, or the patient falls into the Schobinger category III-IV (8) (Table 2). Surgical treatment should be approached on

a multi-specialty basis as the surgeries are very complex. Consultations should be made to interventional radiologists, plastics, and vascular surgeons.

As mentioned earlier, MRA should be obtained to evaluate for the extent of the disease during surgical planning. The usual treatment is arterial embolization for temporary occlusion of the AVM, which is then followed up by surgical excision of the skin and nidus. These surgeries can only be done if the defect does not create a deformity. Embolization procedures carry their own risk and should be performed by an appropriately trained and experienced interventional radiologist (18). Sclerotherapy, which involves direct puncture of the nidus, is dangerous in untrained hands given the high flow nature of the disease. Epiphysiodesis has been utilized to prevent bone hypertrophy, however, it is useless once growth plates have closed. Local bony resection can serve its purpose to relieve local bony overgrowth. Amputation has been offered to patients with severe deformity and medical complications, which in some cases offers much relief to the patient.

In conclusion, we aimed to shine light on a unique and rare vascular disorder which podiatric physicians may encounter during the course of their career. We believe each case should be treated with special care and that more research needs to be instituted pertaining solely to PWS.

Table 2. Schobinger Clinical Classification

Stage	Features
I.	Cutaneous blush / warmth
II.	Bruit, audible pulsations, expanding lesions
III.	Same as above with pain, ulceration, bleeding, infection
IV.	Same as above with cardiac failure

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