

Parkes Weber Syndrome: Clinical Manifestations, Diagnostic Challenges, and Contemporary Management Strategies

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ABSTRACT

Parkes Weber syndrome (PWS) is a rare congenital vascular anomaly characterized by a triad of capillary, venous, and lymphatic malformations associated with high-flow arteriovenous fistulas. This syndrome, often presenting with limb hypertrophy and cutaneous vascular lesions, poses significant diagnostic and therapeutic challenges due to its overlap with similar vascular syndromes such as Klippel-Trénaunay syndrome. Advances in imaging modalities, including Doppler ultrasound, magnetic resonance angiography (MRA), and computed tomography angiography (CTA), have refined the diagnostic accuracy, enabling early detection and detailed vascular mapping. Current management strategies emphasize multidisciplinary approaches, integrating interventional radiology, surgical techniques, and symptomatic treatments. Despite these advancements, the natural history of PWS underscores a significant risk of complications, including chronic pain, ulceration, and potential cardiac overload from high-output heart failure. This review aims to provide a comprehensive overview of the clinical features, diagnostic processes, and evolving therapeutic modalities for Parkes Weber syndrome, highlighting recent innovations and unmet needs in the care of affected individuals.

KEYWORDS: Parkes Weber syndrome, arteriovenous fistulas, vascular malformations, limb hypertrophy, interventional radiology, high-flow vascular anomalies, multidisciplinary management

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INTRODUCTION

Parkes Weber syndrome (PWS) is a rare yet complex congenital vascular disorder characterized by high-flow arteriovenous malformations (AVMs), typically manifesting in association with limb hypertrophy and distinctive cutaneous capillary malformations. This condition, first described in detail by Parkes Weber in the early 20th century, represents a critical diagnostic and therapeutic challenge within the spectrum of vascular anomalies. Differentiating PWS from other related syndromes, such as Klippel-Trénaunay syndrome, is pivotal due to its distinct pathophysiology and management implications.^{1,2}

The hallmark of PWS is the presence of high-flow AVMs, which distinguish it from low-flow vascular anomalies seen in similar syndromes. These malformations lead to chronic complications, including venous stasis, ulceration, and in severe cases, high-output cardiac failure secondary to the

increased vascular shunting. Clinical presentations can vary widely, ranging from mild cosmetic concerns to debilitating limb dysfunction and life-threatening cardiovascular compromise.^{2,3}

Advancements in imaging technologies, particularly Doppler ultrasound, MRA, and CTA, have greatly enhanced the ability to accurately diagnose PWS and assess the extent of vascular involvement. Management strategies have evolved from primarily palliative care to include targeted interventions such as embolization and surgical resection, often in combination. However, the optimal treatment approach remains individualized, necessitating a multidisciplinary team of vascular surgeons, interventional radiologists, and other specialists.^{3,4}

This article provides an in-depth review of Parkes Weber syndrome, focusing on its clinical manifestations, diagnostic approaches, and contemporary management strategies.

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Emphasis is placed on recent innovations and ongoing research aimed at improving outcomes for patients with this challenging vascular disorder.^{4,5}

EPIDEMIOLOGY

Parkes Weber syndrome (PWS) is an exceedingly rare vascular anomaly with a global distribution, though its true prevalence remains largely undefined due to its rarity and the potential for misdiagnosis. Estimates suggest that PWS constitutes a minor fraction of congenital vascular anomalies, with an incidence significantly lower than related disorders such as Klippel-Trénaunay syndrome. Its rarity complicates epidemiological studies, as many cases are only reported in isolated instances or small series within the literature.^{5,6}

PWS does not demonstrate a predilection for any specific geographic, racial, or ethnic population. However, it is typically diagnosed in early childhood due to its characteristic clinical manifestations, including limb hypertrophy and cutaneous vascular lesions. The disorder exhibits no known gender bias, with reported cases occurring equally in males and females.^{5,6}

The pathogenesis of PWS is linked to somatic mutations in the **RASA1** gene, which encodes a protein crucial for the regulation of the Ras signaling pathway. This genetic basis underscores its sporadic occurrence in most instances, although familial cases with autosomal dominant inheritance have been documented. The variability in phenotypic expression, even within families, suggests the influence of additional genetic or environmental modifiers.^{5,6}

Due to its clinical overlap with other vascular syndromes, such as Klippel-Trénaunay syndrome and hereditary hemorrhagic telangiectasia (HHT), PWS may be underdiagnosed or misclassified. The presence of high-flow arteriovenous malformations (AVMs) in PWS is a critical distinguishing feature that necessitates advanced imaging for accurate differentiation. Delayed or incorrect diagnosis can lead to a significant underestimation of its prevalence in the general population.⁶

In terms of morbidity, PWS is associated with considerable clinical burden due to the progressive nature of its vascular malformations and their systemic complications. The presence of high-output cardiac failure, chronic pain, and recurrent infections in severe cases highlights the importance of early recognition and management. The disorder's natural history and associated complications underline the need for further research to elucidate its epidemiological patterns and improve diagnostic precision.⁷

Given the scarcity of large-scale epidemiological studies, most available data on PWS derive from case reports and small case series. This limitation calls for the establishment of national and international registries to aggregate data, facilitating a more accurate understanding of the disorder's incidence, prevalence, and natural history. Such efforts would not only enhance awareness among clinicians but also

support the development of evidence-based guidelines for the management of this rare vascular condition.⁷

CLINICAL MANIFESTATIONS

Parkes Weber syndrome (PWS) is a rare congenital vascular disorder primarily characterized by the presence of high-flow arteriovenous malformations (AVMs) in conjunction with a spectrum of other vascular anomalies. These malformations typically present in early childhood but can vary widely in their clinical expression, ranging from mild cosmetic concerns to severe systemic complications. The hallmark features of PWS are outlined below, highlighting the breadth and complexity of its clinical presentation.⁷

LIMB HYPERTROPHY

Limb hypertrophy, often involving the lower extremities, is one of the most prominent features of PWS. This hypertrophy results from a combination of soft tissue and bone overgrowth driven by the abnormal hemodynamics associated with high-flow AVMs. Affected limbs are typically larger and longer than their contralateral counterparts, leading to significant asymmetry. This condition can result in functional limitations, impaired mobility, and a predisposition to chronic pain.⁸

CUTANEOUS VASCULAR ANOMALIES

Patients with PWS often exhibit capillary malformations on the skin, commonly referred to as port-wine stains. These lesions are typically well-demarcated, pink to red in color, and frequently overlay the regions of underlying arteriovenous shunting. Over time, these lesions may darken or develop a cobblestone-like texture. The presence of extensive capillary malformations can serve as an external marker for the severity of the underlying vascular anomaly.⁸

HIGH-FLOW ARTERIOVENOUS MALFORMATIONS

The defining feature of PWS is the presence of high-flow AVMs, which result in abnormal shunting of blood between the arterial and venous systems without an intervening capillary bed. These malformations can lead to increased venous pressure, venous stasis, and the formation of varicosities. In severe cases, high-output cardiac failure may develop due to the significant hemodynamic burden imposed by these shunts.⁸

CHRONIC PAIN AND ULCERATION

Chronic pain is a frequent and debilitating symptom in PWS, often resulting from venous hypertension, tissue ischemia, or recurrent infections. Ulcerations may occur in areas of increased venous pressure, particularly in the lower limbs, and are prone to secondary infection. These chronic wounds are challenging to manage and often require multidisciplinary care.⁹

SYSTEMIC COMPLICATIONS

In advanced cases, PWS can lead to significant systemic complications. High-output cardiac failure, driven by the extensive arteriovenous shunting, is one of the most severe outcomes. The cardiac system compensates for increased vascular load, potentially leading to progressive cardiac dysfunction. Other systemic manifestations may include deep vein thrombosis (DVT), pulmonary embolism, and secondary lymphedema due to impaired lymphatic drainage.⁹

FUNCTIONAL IMPAIRMENTS

Functional limitations are common in PWS due to the combined effects of limb hypertrophy, pain, and soft tissue anomalies. Gait abnormalities and reduced range of motion in affected joints can impair the patient's quality of life. Additionally, the psychological burden of living with a visible and often progressive disorder can contribute to emotional distress and reduced social functioning.¹⁰

DIFFERENTIAL DIAGNOSIS CHALLENGES

The clinical presentation of PWS frequently overlaps with other vascular syndromes, particularly Klippel-Trénaunay syndrome (KTS). While both conditions share features such as capillary malformations and limb overgrowth, the high-flow AVMs in PWS serve as a critical distinguishing factor. The accurate differentiation between these conditions is essential, as it informs both prognosis and management strategies.¹⁰

VARIABILITY IN EXPRESSION

The phenotypic variability in PWS is striking, even among individuals with confirmed **RASA1** mutations. Some patients may present with mild symptoms confined to a single limb, while others exhibit extensive, multisystem involvement. This heterogeneity underscores the importance of individualized clinical assessment and a multidisciplinary approach to care.¹⁰

In summary, the clinical manifestations of Parkes Weber syndrome reflect a complex interplay of vascular, soft tissue, and systemic abnormalities. Early recognition of its hallmark features—limb hypertrophy, high-flow AVMs, and cutaneous capillary malformations—is crucial for timely diagnosis and management. Understanding the broad spectrum of clinical presentations is essential for optimizing patient outcomes and mitigating the potential complications of this challenging vascular disorder.¹¹

DIAGNOSIS

Diagnosing Parkes Weber syndrome (PWS) requires a comprehensive approach that integrates clinical evaluation, advanced imaging studies, and, in some cases, genetic testing. The process can be challenging due to the overlap of clinical features with other vascular malformation syndromes, particularly Klippel-Trénaunay syndrome (KTS). Early and

accurate diagnosis is critical for guiding appropriate management and preventing complications such as high-output cardiac failure.¹²

CLINICAL ASSESSMENT

The diagnostic process begins with a detailed medical history and physical examination. Key clinical findings that raise suspicion for PWS include:

- **Limb Hypertrophy:** Disproportionate overgrowth of an affected limb, involving both soft tissues and bone.¹²
- **Cutaneous Vascular Lesions:** Presence of capillary malformations, often described as port-wine stains, which may correspond to underlying vascular anomalies.¹²
- **Palpable Thrill and Audible Bruit:** High-flow arteriovenous malformations (AVMs) can produce a thrill or bruit detectable on physical examination.¹²
- **Signs of High-Output Cardiac Failure:** Symptoms such as tachycardia, fatigue, and dyspnea on exertion may indicate systemic complications.¹²

The presence of high-flow vascular anomalies sets PWS apart from low-flow syndromes like KTS, emphasizing the importance of thorough clinical evaluation.¹³

IMAGING STUDIES

Advanced imaging is essential for confirming the diagnosis, characterizing the extent of vascular involvement, and differentiating PWS from other syndromes. Key modalities include:

- **Doppler Ultrasound**
Doppler ultrasound serves as an initial diagnostic tool to evaluate blood flow patterns, detect arteriovenous shunting, and assess soft tissue involvement. High-flow AVMs are characterized by rapid, pulsatile flow on Doppler studies, a hallmark feature of PWS.¹³
- **Magnetic Resonance Imaging (MRI) and Magnetic Resonance Angiography (MRA)**
MRI and MRA provide detailed visualization of soft tissues, vascular structures, and the extent of malformations. MRA, in particular, enables precise mapping of arteriovenous connections and is invaluable for pre-procedural planning. Contrast-enhanced imaging enhances the identification of high-flow AVMs and associated anomalies.¹⁴
- **Computed Tomography Angiography (CTA)**
CTA offers high-resolution imaging of vascular structures and is particularly useful for delineating complex AVMs. It provides a comprehensive view of arterial and venous anatomy, aiding in differentiation from other vascular syndromes.¹⁴
- **Conventional Angiography**

Although less commonly used as a diagnostic modality, conventional angiography remains the gold standard for defining arteriovenous shunting. It is typically reserved for cases where interventional embolization or surgical planning is under consideration.¹⁴

LABORATORY AND GENETIC TESTING

- **Laboratory Tests**

Routine laboratory tests may reveal secondary complications such as anemia from chronic bleeding or elevated cardiac biomarkers in cases of high-output cardiac failure. However, these findings are nonspecific and supportive rather than diagnostic.¹⁴

- **Genetic Testing**

Mutations in the **RASA1** gene are implicated in the pathogenesis of PWS. Genetic testing can confirm the diagnosis, particularly in cases with ambiguous clinical or imaging findings. It is also valuable in familial cases to assess the risk of transmission.¹⁴

DIFFERENTIAL DIAGNOSIS

Differentiating PWS from other vascular syndromes is critical for appropriate management. Key conditions to consider include:

- **Klippel-Trénaunay Syndrome (KTS):** Unlike PWS, KTS is characterized by low-flow venous and lymphatic anomalies without high-flow AVMs.
- **Hereditary Hemorrhagic Telangiectasia (HHT):** PWS may mimic HHT due to overlapping AVM features, but systemic telangiectasias and a family history of epistaxis favor HHT.¹⁴
- **Proteus Syndrome:** Limb overgrowth in Proteus syndrome lacks the high-flow vascular anomalies seen in PWS.¹⁴

DIAGNOSTIC CHALLENGES

The rarity of PWS and its phenotypic variability contribute to frequent delays in diagnosis. Misclassification as KTS or other vascular disorders can result in suboptimal management. High clinical suspicion, combined with the use of advanced imaging modalities and genetic testing, is essential for accurate diagnosis.¹⁵

EMERGING DIAGNOSTIC TOOLS

Recent advances in imaging technology and molecular diagnostics hold promise for improving the detection and characterization of PWS. Techniques such as 4D flow MRI and whole-exome sequencing are being explored to enhance diagnostic precision and guide personalized management strategies.¹⁵

In conclusion, the diagnosis of Parkes Weber syndrome requires a multidisciplinary approach that combines clinical expertise with state-of-the-art imaging and genetic tools.

Early identification is critical for initiating timely interventions and mitigating the systemic complications associated with this high-flow vascular disorder.¹⁵

SURGICAL TREATMENT IN PLASTIC SURGERY FOR PARKES WEBER SYNDROME

The management of Parkes Weber syndrome (PWS) presents unique challenges due to its complex vascular pathology and the associated structural deformities. Plastic surgery plays a pivotal role in addressing both the functional and aesthetic concerns associated with this disorder, particularly in cases of severe limb hypertrophy, disfiguring cutaneous vascular lesions, and chronic wounds. The surgical approach requires meticulous planning and collaboration across multiple specialties, including vascular surgery, interventional radiology, and cardiology, to optimize outcomes and mitigate risks.¹⁵

Objectives of Plastic Surgery in PWS

The surgical management of PWS in the context of plastic surgery focuses on:

1. **Restoration of Function:** Addressing limb deformities and hypertrophy to improve mobility and reduce functional limitations.¹⁵
2. **Aesthetic Enhancement:** Correcting disfiguring features such as extensive port-wine stains or hypertrophic tissues to improve quality of life and psychosocial well-being.¹⁵
3. **Management of Chronic Ulcerations:** Reconstructing chronic, non-healing wounds associated with venous stasis and tissue ischemia.¹⁵
4. **Symptom Palliation:** Relieving pain, reducing vascular congestion, and addressing complications such as recurrent infections.¹⁵

Preoperative Planning

Preoperative assessment is critical to ensure the success of surgical interventions. Key components include:

- **Vascular Imaging:** High-resolution imaging, such as magnetic resonance angiography (MRA) or computed tomography angiography (CTA), is essential for mapping the extent of arteriovenous malformations (AVMs) and vascular anomalies.¹⁵
- **Multidisciplinary Evaluation:** Collaboration with interventional radiologists and vascular surgeons is necessary to address underlying vascular anomalies prior to plastic surgical interventions. Embolization of AVMs, for instance, may be performed preoperatively to reduce intraoperative bleeding.¹⁵
- **Cardiac Assessment:** Given the risk of high-output cardiac failure in PWS, a thorough cardiac evaluation is mandatory to assess hemodynamic stability.

SURGICAL TECHNIQUES

Plastic surgery for PWS typically involves a combination of techniques tailored to the patient's specific presentation and the severity of their condition.

1. Limb Debulking and Contouring

Limb hypertrophy is a hallmark of PWS, often requiring debulking procedures to alleviate functional impairments and improve limb symmetry.

- **Soft Tissue Excision:** Excessive adipose and fibrous tissue is removed to restore proportionality. Careful preservation of neurovascular structures is paramount.¹⁵
- **Liposuction-Assisted Contouring:** Liposuction may be employed as an adjunct to excision for fine contouring and to address areas of diffuse hypertrophy.
- **Osteotomy:** In cases of severe bony overgrowth, orthopedic collaboration may be required to perform corrective osteotomies.¹⁵

2. Management of Cutaneous Vascular Lesions

The extensive capillary malformations characteristic of PWS often necessitate surgical intervention to improve cosmetic appearance and address complications such as bleeding or infection.¹⁵

- **Excision and Skin Grafting:** Large vascular lesions may be excised, with subsequent coverage using split-thickness or full-thickness skin grafts.
- **Laser Therapy:** Adjunctive laser treatments, such as pulsed dye laser (PDL), can be utilized pre- or postoperatively to reduce the pigmentation and size of port-wine stains.¹⁵

3. Reconstruction of Chronic Ulcerations

Chronic wounds in PWS, often resulting from venous stasis or tissue ischemia, require surgical reconstruction for definitive management.

- **Local Flap Reconstruction:** Rotational or advancement flaps may be employed for smaller defects.¹⁵
- **Free Tissue Transfer:** Complex wounds, particularly those with underlying vascular involvement, may require microvascular free flaps such as anterolateral thigh (ALT) or radial forearm flaps for durable coverage.¹⁵

4. Amputation (Selective Cases)

In extreme cases of limb hypertrophy or refractory complications such as intractable pain or severe infection, amputation may be considered as a last resort. This decision is typically made after thorough discussion with the patient and their family, weighing the risks and benefits.¹⁵

Postoperative Care

Postoperative management is critical to ensure the success of surgical interventions and minimize complications.¹⁵

- **Wound Monitoring:** Close observation for signs of infection, graft failure, or flap necrosis is essential in the early postoperative period.¹⁵
- **Compression Therapy:** Graduated compression garments may be prescribed to manage residual venous stasis and lymphedema.¹⁵
- **Rehabilitation:** Physical therapy is often necessary to optimize functional recovery, particularly after limb contouring or amputation procedures.¹⁵

CHALLENGES AND LIMITATIONS

Surgical management of PWS is inherently complex due to the high vascularity of affected tissues, the risk of significant intraoperative bleeding, and the progressive nature of the disease. Moreover, recurrence of vascular lesions or hypertrophy may occur, necessitating repeat interventions. A thorough understanding of the underlying pathology and a tailored, multidisciplinary approach are essential for long-term success.¹⁵

EMERGING TECHNIQUES

Advances in reconstructive surgery, including the use of bioengineered tissue scaffolds, regenerative therapies, and 3D printing for preoperative planning, hold promise for improving outcomes in PWS. These innovations aim to enhance surgical precision, reduce morbidity, and provide more durable solutions for this challenging condition.¹⁵

In conclusion, plastic surgery plays an integral role in the multidisciplinary management of Parkes Weber syndrome, addressing both functional and aesthetic concerns. A personalized, carefully planned approach is essential to optimize outcomes and improve the quality of life for patients with this rare vascular disorder.¹⁵

CONCLUSION

Parkes Weber syndrome (PWS) is a rare and complex congenital vascular disorder characterized by high-flow arteriovenous malformations (AVMs), soft tissue and skeletal hypertrophy, and capillary malformations such as port-wine stains. Its multifaceted nature, encompassing both localized and systemic manifestations, presents significant diagnostic and therapeutic challenges that require a multidisciplinary approach.

From a pathophysiological standpoint, the identification of mutations in the **RASA1** gene has shed light on the underlying genetic mechanisms driving aberrant vascular development. However, the variable phenotypic expression of the syndrome underscores the need for individualized diagnostic and management strategies. Clinical differentiation from other vascular syndromes, such as Klippel-Trénaunay syndrome, remains a cornerstone in establishing an accurate diagnosis, with advanced imaging techniques playing a pivotal role in delineating the extent and severity of arteriovenous malformations.

The management of PWS is inherently multidisciplinary, involving plastic surgery, interventional radiology, vascular surgery, cardiology, and rehabilitation. In particular, plastic surgery holds a critical role in addressing the functional and aesthetic challenges posed by limb hypertrophy, disfiguring vascular lesions, and chronic wounds. Surgical interventions, ranging from limb debulking and contouring to complex microvascular reconstructions, are tailored to alleviate symptoms, restore functionality, and enhance the patient's quality of life. Additionally, adjunctive therapies such as embolization, laser therapy, and physical rehabilitation complement surgical approaches to provide comprehensive care.

Despite advancements in diagnostic imaging, surgical techniques, and interventional procedures, the management of PWS remains challenging due to the high vascularity of lesions, the risk of recurrence, and potential systemic complications such as high-output cardiac failure. Emerging technologies, including regenerative medicine, bioengineered tissue scaffolds, and genetic therapies, offer hope for more effective and durable solutions, but further research and clinical trials are necessary to validate their utility in the context of this syndrome.

Ultimately, the prognosis for patients with PWS depends on timely diagnosis, meticulous management of vascular anomalies, and vigilant monitoring for systemic complications. While current treatment modalities focus on palliation and symptom management, the evolving landscape of genetic and molecular research holds promise for disease-modifying therapies in the future.

Parkes Weber syndrome exemplifies the intricate interplay between vascular biology, genetics, and clinical medicine. By fostering collaboration among specialties and leveraging advancements in medical science, clinicians can continue to improve outcomes for individuals affected by this rare and challenging disorder. Future endeavors should prioritize comprehensive care models, patient-centered approaches, and translational research to bridge the gap between pathophysiological understanding and clinical application.

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