Journal of Experimental and Molecular Pathology

Kowe P, J Exp Mol Pathol. 2026;3(1):8-11.

Commentary

# Expanding the phenotype of bilateral Sturge-Weber syndrome associated with soft tissue hypertrophy and trichomegaly

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Received date: March 26, 2026
Accepted date: May 20, 2026



## Abstract

Sturge-Weber Syndrome (SWS) is a rare congenital neurocutaneous disorder characterized by a facial port-wine stain (PWS), leptomeningeal vascular anomalies and ocular involvement, most commonly glaucoma. Bilateral SWS represents a clinically distinct and often more severe variant, frequently associated with bilateral glaucoma and complex intracranial findings. We present a commentary on a case report describing a young male in his 20s with bilateral SWS, soft tissue hypertrophy of the lower lip and trichomegaly, a triad not previously documented in the literature. The case report is noteworthy for several reasons. First, the bilateral distribution of PWS involving both ophthalmic and maxillary branches of the trigeminal nerve, confirmed by MRI brain with contrast, suggestive of a cerebellar venous anomaly and presenile atrophy, exemplifies the severe association of vascular anomaly in the SWS spectrum. Secondly, lower lip hypertrophy is a common finding in SWS with soft tissue involvement, representing a hamartomatous origin rather than a lymphovascular malformation. Third and most notably, the patient demonstrated trichomegaly, defined as eyelash overgrowth exceeding 12 mm. This finding appears to be rare or previously unreported in association with SWS. The underlying mechanism is likely multifactorial, involving port-wine stain related follicular hyperplasia of the eyelid, genetic influence, local cutaneous changes and the effects of long-term prostaglandin analogue therapy, which the patient had been receiving for glaucoma since childhood. This commentary highlights the expanding phenotypic spectrum of SWS, the importance of a systematic multidisciplinary approach, and the need for heightened clinical awareness of previously unrecognized associations such as trichomegaly in this syndrome.

**Keywords:** Bilateral Sturge-Weber Syndrome (SWS), Secondary glaucoma, Trichomegaly, Soft tissue hypertrophy

## Commentary

Sturge-Weber Syndrome (SWS) or encephalotrigeminal angiomatosis is a rare congenital neurocutaneous disorder belonging to the phakomatoses group, characterized by its classic triad of facial port-wine stain (PWS), leptomeningeal vascular anomalies, and ocular involvement, most notably glaucoma. The case report describing a bilateral SWS is a clinically compelling and highly illustrative report of a young man in his 20s with bilateral SWS accompanied by soft tissue hypertrophy of the lower lip and trichomegaly has not been documented previously. The rarity of this presentation, along with its comprehensive clinical, dermoscopic, and radiological workup, makes it a valuable contribution to the existing knowledge of this uncommon syndrome.

## Bilateral Presentation: A Clinically Distinct Entity

The bilateral nature of SWS in this patient represents a notably uncommon variant. While unilateral facial PWS involving the ophthalmic branch of the trigeminal nerve is the hallmark finding seen in approximately 96% of SWS cases, bilateral PWS involving both the ophthalmic and maxillary branches occurs in 10–30% of patients [1,2]. The bilateral pattern is particularly significant as it is associated with more severe neurological and ocular involvement, including bilateral glaucoma, seen in approximately 45% of bilateral SWS cases [1]. In the index case, bilateral secondary glaucoma with disc cupping and dilated tortuous retinal vessels confirmed ophthalmic involvement and MRI brain with contrast revealed an anomalous vein in the left cerebellar hemisphere with presenile atrophy. However, bilateral SWS, despite its more extensive involvement, does not always correlate with severely disabling neurological outcomes; for instance, the patient in this report had normal scholastic performance and no history of seizures, underscoring the importance of individualized prognostic assessment [2,5].

## Soft Tissue Hypertrophy: An Underappreciated Feature

Soft tissue hypertrophy is common in SWS, seen in approximately 55% of cases, and often receives less clinical attention than the neurological or ocular manifestations of the disease [3]. This case highlights the prominence of this feature, with the lower lip being the most frequently affected soft tissue site. Greene AK, *et al* (2009) reported 81% incidence of lip involvement among all soft tissue-affected patients [3]. The pathogenesis of soft tissue hypertrophy in SWS is attributed to hamartomatous changes involving epithelial, neural, and mesenchymal structures, rather than to arteriovenous or lymphatic malformations, an important distinction confirmed in this case via ultrasonography of the lower lip [3]. The clinical significance of distinguishing soft tissue hypertrophy in SWS from mimickers such as Capillary malformation of the lower lip, Lymphatic malformation of the face/neck, Asymmetry, and Partial/generalized Overgrowth (CLAPO) syndrome [6,13], Klippel-Trenaunay syndrome (KTS) [7,10], and Parkes-Weber syndrome [11] cannot be overstated, as management pathways differ considerably. The authors have provided a table describing differential diagnosis among these conditions, which serves as a practical reference for clinicians encountering similar presentations (**Table 1**).

## Trichomegaly: An Unrecognized and Clinically Significant Observation

One of the most noteworthy findings in the present case was the presence of trichomegaly, defined as excessive eyelash growth exceeding 12 mm in length, observed in direct association with SWS. The diagnosis was further substantiated by dermoscopic examination and was clinically associated with worsening pre-existing ocular discomfort. The occurrence of trichomegaly in a patient with bilateral

**Table 1.** Differential diagnosis of the index case.

| Differential diagnosis | Sturge Weber syndrome [1,9] | CLAPO syndrome [6] | Klippel-Trenaunay syndrome [7,10] | Parkes-Weber syndrome [11] |
|---|---|---|---|---|
| Synonyms | Encephalofacial angiomatosis<br>Encephalotrigeminal angiomatosis; Leptomeningeal angiomatosis | **C**apillary malformation of the lower lip, **l**ymphatic malformation of the face and neck, **a**symmetry and **p**artial/generalized **o**vergrowth | Angio-osteohypertrophy syndrome<br>Naevus varicosus osteohypertrophicus | Frederick Parkes Weber Syndrome, Capillary malformation-Arteriovenous malformation with associated limb overgrowth |
| Pathogenesis | Somatic mosaic mutation in *GNAQ* gene leading to aberrant overgrowth in endothelial cells resulting in capillary-venous malformations.<br>Aberrant vascular MAPK/PI3K signaling in early embryogenesis and/or sporadic somatic GNAQ/PI3K mutations. | Somatic mutation in the *PIK3CA* gene, leading to overactivation of the PI3K/AKT/mTOR pathway. This pathway is a major regulator in cell signaling and angiogenesis. | Somatic mutations in the *PIK3CA* gene cause abnormal activation of the phosphatidylinositol 3-kinase (PI3K) pathway, driving unchecked cell proliferation and tissue overgrowth. This primarily impacts blood vessels, bones, and soft tissues in a localized, segmental pattern. | Activating mutations in various components of the RAS/MAPK/ERK pathway.<br>*RASA1* mutations [8]. |
| Clinical features | Triad of skin (unilateral facial port-wine staining (PWS) frequently involves the ophthalmic branch of trigeminal nerve), central nervous system (intracranial leptomeningeal venous angiomas), and ocular (glaucoma and choroidal hemangioma) involvement.<br>Developmental delay and intellectual impairments may happen. | Midline capillary malformation of the lower lip.<br>Lymphatic malformation involving the lip, oral mucosa, neck, and tongue.<br>Asymmetric overgrowth with the presence of bony hypertrophy especially over face.<br>Limb overgrowth may be noticed in some patients. | Triad of capillary, venous, and lymphatic malformation without arteriovenous fistulas with associated limb overgrowth and PWS. | Triad of capillary, venous and lymphatic malformation combined with arteriovenous fistula. |

| Differential diagnosis | Sturge Weber syndrome [1,9] | CLAPO syndrome [6] | Klippel-Trenaunay syndrome [7,10] | Parkes-Weber syndrome [11] |
|---|---|---|---|---|
| Radiological investigations | Magnetic resonance imaging (MRI) brain with contrast is the gold standard modality for diagnosing SWS syndrome | Magnetic resonance imaging and angiography (MRI/MRA) | MRI is the gold-standard modality which can include the entire affected limb and capture the presence of a large embryonic vein | MRI, MR angiography and doppler ultrasound |
| Treatment options | Anticonvulsant if there is a history of seizures.<br>Low-dose aspirin.<br>Physiotherapy in case of hemiparesis.<br>Pulse dye laser for PWS.<br>Surgical intervention for secondary glaucoma. | Oral rapamycin for lymphatic malformation [12].<br>Laser therapy for capillary malformation [13].<br>Sclerotherapy.<br>Surgical intervention for lymphatic malformation.<br>Speech/occupational/ physical therapy. | Compression stacking for chronic venous insufficiency.<br>Limb elevation, physiotherapy.<br>Analgesics for pain management<br>Antibiotics if recurrent cellulitis.<br>Endovenous laser therapy for varicosities [13].<br>Radiotherapy in cases of hemangiomas to reduce the size [14]. | Compression stockings.<br>Embolization procedures for management of arteriovenous malformations (AVMs)/AV fistulas.<br>Surgical interventions for limb length discrepancies. Orthopedic procedures to correct bone deformities. |

glaucoma and extensive PWS adds considerable clinical complexity and underscores the need for meticulous ophthalmologic surveillance and management. This association remains underrecognized and sparsely reported in the literature, thereby potentially expanding the known phenotypic spectrum of this multisystem neurocutaneous disorder.

The pathophysiological basis of trichomegaly in this context is likely multifactorial. A plausible mechanism involves abnormal vascular development affecting the eyelid skin in regions supplied by the trigeminal nerve. These capillary-venous malformations may enhance local blood flow and nutrient delivery to adjacent hair follicles, thereby prolonging the anagen phase of the hair cycle and promoting excessive eyelash growth. Furthermore, most cases of Sturge-Weber syndrome are associated with somatic mutations in the *GNAQ* gene, resulting in dysregulated activation of downstream signaling pathways, including the MAPK pathway, which are known to influence cellular proliferation and differentiation within hair follicles. Although genetic testing could not be performed in the present patient because of financial constraints, such molecular mechanisms may have contributed to the observed follicular changes. Additionally, the presence of an extensive facial PWS may create an altered local microenvironment characterized by chronic vascular dilatation, altered oxygenation, and cytokine-mediated inflammatory signaling, all of which could further stimulate perifollicular activity and contribute to trichomegaly. A medication-induced component is also highly likely in the index patient, who had longstanding secondary glaucoma since childhood and had been receiving chronic therapy with the prostaglandin analogue (PGA) Latanoprost. Latanoprost, a prostaglandin F2α analogue, acts on prostaglandin FP receptors located within eyelid hair follicles. Chronic receptor stimulation prolongs the anagen phase, delays transition to the telogen phase, and enhances follicular melanogenesis and keratinocyte proliferation, thereby resulting in eyelashes that are longer, thicker, darker, and more numerous. Taken together, the trichomegaly observed in the present patient was most likely the result of a synergistic interplay between underlying vascular malformations, possible genetic dysregulation, local cutaneous microenvironmental changes, and prolonged prostaglandin analogue therapy. The delayed onset of trichomegaly several years after the development of glaucoma further supports the contributory role of chronic prostaglandin analogue exposure in this patient.

In clinical practice, trichomegaly has a broad differential diagnosis. Drug-induced causes are among the most common and include epidermal growth factor receptor (EGFR) inhibitors (such as Erlotinib and Cetuximab), Cyclosporine, topical Bimatoprost and Latanoprost (Prostaglandin analogues), Interferon-alpha, and Zidovudine. Systemic conditions associated with trichomegaly include hypothyroidism, malnutrition, anorexia nervosa, dermatomyositis, and HIV/AIDS. Rare congenital syndromes such as Cornelia de Lange syndrome, Oliver-McFarlane syndrome, and Goldblatt syndrome are also recognised causes. In the present case, these alternative etiologies would need to be systematically excluded,

From a clinical management standpoint, trichomegaly in SWS carries important practical implications. Elongated eyelashes can cause trichiasis, misdirected lashes contacting the ocular surface, leading to corneal irritation, punctate epithelial erosions, and increased risk of ocular surface disease. In a patient already predisposed to corneal complications from elevated intraocular pressure and glaucomatous optic neuropathy, even minor additional ocular surface stress may be clinically meaningful [1,4]. Management of trichomegaly in this setting should be individualized and may include careful epilation, electrolysis, or laser hair removal for symptomatic lashes. Ophthalmologists managing SWS patients should be sensitized to examine eyelash length as part of their routine assessment, particularly when patients report worsening ocular discomfort. Prospective documentation of trichomegaly in future SWS case series would be valuable in establishing its true prevalence and clinical significance within this condition.

## Role of Dermoscopy in Diagnosis

The use of polarized dermoscopy in this case is a notable methodological strength. Dermoscopy is a simple, non-invasive diagnostic tool that, when used in the appropriate clinical context, can supplement or even obviate the need for skin biopsy. In this patient, dermoscopy revealed dotted and globular vessels against a bluish-red background, consistent with the vascular nature of PWS. A study of 264 cases identified linear, reticular, sausage-like,

dotted, and globular vessels, and a whitish veil as the most frequently observed dermoscopic findings in PWS [15]. The predominantly globular pattern seen in this patient may reflect deeper dermal vascular ectasia characteristic of long-standing or extensive PWS. Wider use of dermoscopy in evaluating vascular birthmarks, particularly in resource-limited settings, could reduce unnecessary procedural interventions and improve diagnostic confidence.

## Multidisciplinary Management: A Necessity

The management of SWS, particularly in its bilateral form with multiple organ involvement, exemplifies the necessity of a coordinated multidisciplinary approach [4]. In this case, the involvement of dermatology (pulsed-dye laser for facial PWS), ophthalmology (management of secondary glaucoma), and plastic surgery (lip debulking) underscores the complexity of holistic patient care. The authors' emphasis on psychological support and quality-of-life considerations for young adults with visible, multisystem conditions aligns well with contemporary consensus recommendations in SWS management [4]. Future follow-up should include periodic neurological review given the MRI brain findings of presenile atrophy, an associated vascular anomaly, even in the absence of current seizures [5]. The addition of an ophthalmology review specifically addressing trichomegaly and its ocular surface implications would further strengthen the proposed management plan. For patients with a history of seizure disorder, recent studies suggest the use of low-dose aspirin and vitamin D in addition to anticonvulsants in the treatment of SWS, along with the usefulness of cannabidiol (CBD) and Sirolimus [16]. CBD is especially recommended as an adjunctive medicine for treatment-resistant seizures. mTOR inhibitor, Sirolimus, can reduce the risk of stroke by normalizing the function of affected vascular cells (leptomeningeal endothelial cells in the vascular malformation) [16].

## Conclusion

This case report makes a meaningful contribution to the clinical literature on Sturge-Weber Syndrome by documenting the first known association of bilateral SWS with both soft tissue hypertrophy and trichomegaly. The detailed clinical description, supported by dermoscopy, MRI imaging, and ultrasonography, along with a well-structured differential diagnosis, provides a practical framework for clinicians [1,3,4]. The report reinforces several key learning points: bilateral PWS may occur in up to 30% of SWS cases; soft tissue hypertrophy, particularly lip hypertrophy, is common and mechanistically linked to hamartomatous processes, and trichomegaly may represent an unrecognized component of SWS when capillary malformation involves the eyelid [1–3]. As rare disease reports remain foundational to advancing clinical understanding, this case serves as an important reminder that phenotypic variability in SWS extends beyond the classical triad and warrants broad clinical vigilance.

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