

Secondary Glaucoma in Sturge–Weber Syndrome

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Summary:

Sturge–Weber syndrome is a congenital neurocutaneous disorder involving abnormalities of blood vessels (hemangiomas) in the brain, face, and eyes. It is not hereditary or genetic, but it is present from birth. The syndrome may manifest as facial port-wine stains, seizures, diffuse choroidal hemangioma, and glaucoma.

Glaucoma is one of the most common ocular complications in Sturge–Weber syndrome, affecting approximately 30% to 70% of individuals. Open-angle glaucoma is the more frequently observed subtype. Glaucoma may be present from birth (early onset) or develop later in childhood or adolescence (late onset). The exact mechanisms leading to glaucoma in Sturge–Weber syndrome are complex and may include abnormal development of the anterior chamber angle, elevated pressure in the episcleral veins, and focal venous hypertension.

The most commonly used treatments for secondary glaucoma in Sturge–Weber syndrome include pharmacotherapy and surgical intervention. It is important to note that due to anatomical abnormalities, the incidence of surgical complications is higher. As an alternative, non-penetrating surgical procedures, which carry a lower risk of complications, may be preferred. A beneficial effect of brachytherapy has also been observed in cases of diffuse choroidal hemangiomas.

Key words:

Sturge–Weber syndrome, consecutive glaucoma.

Sturge–Weber syndrome (SWS) (classified among phakomatoses) is a rare congenital neurocutaneous disorder involving vascular malformations (hemangiomas) in the brain, face, and eyes. It is not hereditary or genetic, but it is present from birth. The syndrome may manifest as facial port-wine stains, seizures, diffuse choroidal hemangioma, and glaucoma. Neurological abnormalities in SWS include seizures, migraine headaches, and variable hemiparesis, with seizures being the most common manifestation [1]. Brain involvement in SWS is characterized by vascular malformations of the leptomeninges, visible on contrast-enhanced magnetic resonance imaging (MRI). Some studies suggest that a normal neurological examination result, absence of seizures in medical history, and a negative contrast-enhanced MRI after the first year of life may effectively rule out cerebral involvement in SWS.

Glaucoma is one of the most common ocular complications in SWS, affecting approximately 30% to 70% of individuals. The most frequently observed subtype is open-angle glaucoma. It may be present from birth (early-onset) or develop later in childhood or adolescence (late-onset).

Pathomechanism of secondary glaucoma development in SWS

A mutation in the *GNAQ* gene has been identified as the primary cause of SWS. However, recent studies suggest that macrophages, along with mutations in the *GNA11* or *GNB2* genes, may also contribute to the pathogenesis of the disorder.

Abnormal development of the anterior chamber angle, elevated episcleral venous pressure, and focal venous hypertension are key factors contributing to the development of secondary glaucoma in SWS. This form of glaucoma is often associated with

the characteristic facial distribution of port-wine stains, vascular malformations of the choroid such as diffuse choroidal hemangioma, and other ocular abnormalities.

The severity of glaucoma often correlates with the extent of facial skin hemangioma, and involvement of the eyelids – particularly the upper eyelid – is frequently associated with a higher risk of glaucoma [2, 3]. The presence of diffuse choroidal hemangioma is also correlated with secondary glaucoma (Fig. 1–5).

Elevated pressure in the episcleral veins may manifest as a dense, dilated vascular malformation external to the sclera. Weiss observed that in eyes affected by secondary glaucoma in SWS, blood reflux into Schlemm's canal occurs easily, and suggested that this may result from an arteriovenous shunt causing elevated episcleral venous pressure [4, 5].



Fig. 1. Facial hemangioma in SWS.

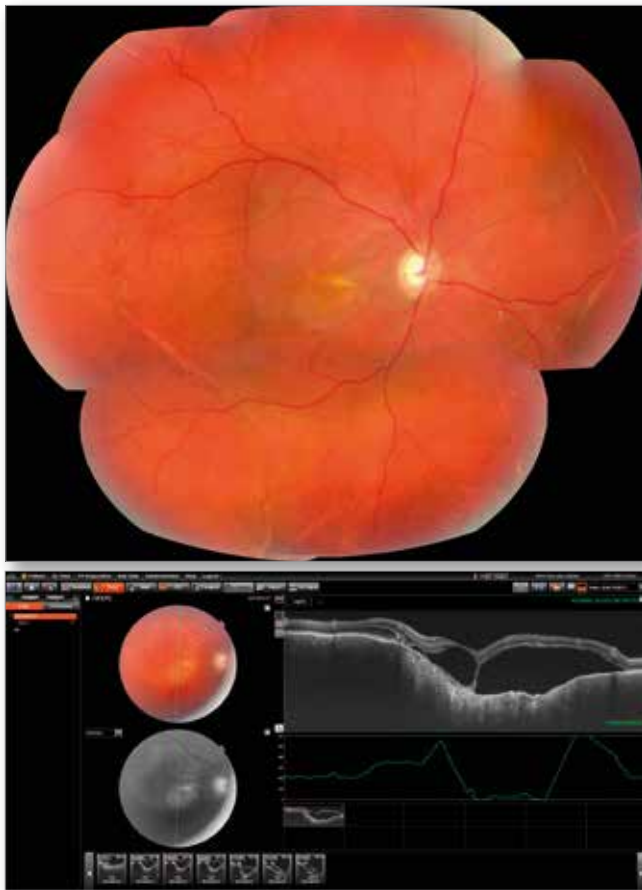


Fig. 2. Diffuse choroidal hemangioma in SWS. Fot. and OCT.



Fig. 3. Facial hemangioma in SWS.

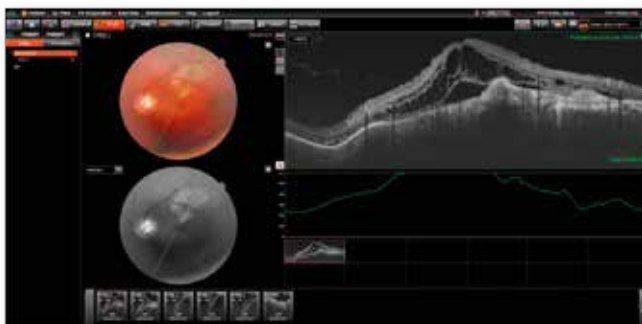


Fig. 4. Diffuse choroidal hemangioma in SWS. Fot. and OCT.



Fig. 5. Diffuse choroidal hemangioma in SWS after brachytherapy.

Focal venous hypertension

Abnormal development of cranial veins in SWS leads to cavernous sinus hypertension, which impairs normal venous drainage from the eye. Restricted choroidal outflow results in diffuse thickening of the choroid. The thickened choroid displaces the iris root anteriorly and obstructs the aqueous humor outflow channels.

Additionally, elevated venous pressure increases plasma protein exudation from the ciliary body into the iris base, further contributing to blockage of aqueous outflow. Histopathological and ultrastructural studies of the trabecular meshwork in patients with SWS have demonstrated intracellular flocculent material containing solid particles, as well as fine extracellular fibrillar deposits [6]. Clinical cases of isolated choroidal hemangioma with unilateral vascular malformations of the conjunctiva and episclera have also been reported, without signs of elevated intraocular pressure (IOP) [7].

SWS is commonly characterized according to the Roach classification (Tab. I) [8].

SWS classification according to Roach	Facial skin involvement	Brain involvement	Ocular involvement
Type I	+	+	It may occur (but is not always present)
Type II	+	-	
Type III	-	+	

Tab. I. SWS classification according to Roach.

Therapeutic management

Management of secondary glaucoma in SWS may involve pharmacological therapy and/ or surgical intervention.

Pharmacological treatment of secondary glaucoma in SWS

The treatment of choice for cutaneous hemangiomas in children is oral administration of β -blockers (propranolol). Topical β -blocker eye drops have proven effective in controlling elevated IOP in infants with glaucoma. Systemic administration of propranolol (at a dose of 2 mg/kg) has also demonstrated a short-term IOP-lowering effect, likely due to vasoconstriction [9]. Also, pe-

rioperative administration of propranolol has been shown to reduce the extent of choroidal effusion and alleviate exudative retinal detachment. This effect has not been observed in adults, supporting the hypothesis that one of the underlying mechanisms may involve propranolol's modulation of the mitogen-activated protein kinase (MAPK) pathway. While this pathway is hyperactive in infantile hemangiomas, cells with *GNAQ* mutations exhibit only a moderate increase in MAPK pathway signaling activity [3].

On the other hand, latanoprost has been shown to significantly reduce IOP in eyes with late-onset secondary glaucoma (SG), but not in eyes with early-onset SG [10]. Prostaglandin analogues may enhance matrix metalloproteinase activity and extracellular matrix turnover in aqueous outflow tissues, leading to tissue remodeling that increases uveoscleral outflow.

Surgical treatment

Pharmacotherapy is not always effective in treating secondary glaucoma in SWS, which is most commonly caused by anatomical abnormalities of the eye. Patients with glaucoma frequently require additional surgical interventions, which carry a higher risk and a greater number of postoperative complications compared to glaucoma caused by other etiologies.

Trabeculotomy or goniotomy is considered the optimal initial surgical approach for patients with early-onset SG in SWS, due to the presence of anatomical abnormalities and anterior chamber angle deformities.

In contrast, for patients with late-onset glaucoma, filtration surgery or implantation of a glaucoma drainage device is more commonly chosen [11]. Olsen et al. demonstrated that approximately half of the eyes initially treated with trabeculotomy required a secondary surgical procedure [12]. In patients with large corneas, high preoperative IOP, corneal edema, and extensive dilation of the episcleral vessels (in a net-like pattern), the prognosis is poorer [13].

Trabeculectomy can effectively lower IOP in individuals with SWS; however, it carries a risk of numerous complications, including anterior chamber shallowing, hypotony, subconjunctival fibrosis, and failure of the filtering bleb. Intraoperative hypotony can be avoided by ensuring a tight closure of the flap.

Glaucoma drainage methods

Creating a channel for external drainage of aqueous humor using a glaucoma drainage device can effectively reduce IOP, but it is associated with a relatively higher rate of postoperative complications, including hypotony, malposition of the drainage tube, tube obstruction, tube exposure, and corneal decompensation [14]. The most common types of glaucoma drainage devices include the Ahmed valve, Baerveldt tube, Molteno tube, and Ex-Press shunt.

Moreover, intraoperative addition of antimetabolites, such as mitomycin C (MMC), and the use of an implant (e.g., the collagen implant Ologen) reduce subconjunctival fibrosis, thereby increasing the long-term success rate of surgery.

Considering that SWS is associated with elevated pressure gradients within the choroidal vasculature, a rapid decrease in IOP following filtration surgery increases the likelihood of choroidal detachment, suprachoroidal hemorrhage, and retinal detachment.

Although pharmacotherapy and surgical treatment are the most commonly used methods for managing secondary glaucoma in SWS, it is important to note that due to anatomical abnormalities, the incidence of surgical complications is higher. Instead of these, non-penetrating surgical procedures – associated with a lower risk of complications – may be preferred, such as non-penetrating deep sclerectomy or cyclodestructive procedures. Cyclodestructive procedures exert a stronger hypotensive effect but carry a higher risk of intraoperative and postoperative complications, such as choroidal detachment.

Diffuse choroidal hemangioma may also be managed with brachytherapy as part of a combined approach alongside pharmacological methods. Patients with SWS are treated and monitored at the Department of Ophthalmology and Ocular Oncology, Jagiellonian University Medical College in Krakow. In three girls aged 6 to 9 years with SWS, diffuse choroidal hemangioma, and secondary glaucoma, brachytherapy using ^{106}Ru applicators led to scarring of the choroidal hemangioma, reattachment of the retina, and a reduction in IOP (Fig. 6) [15, 16].

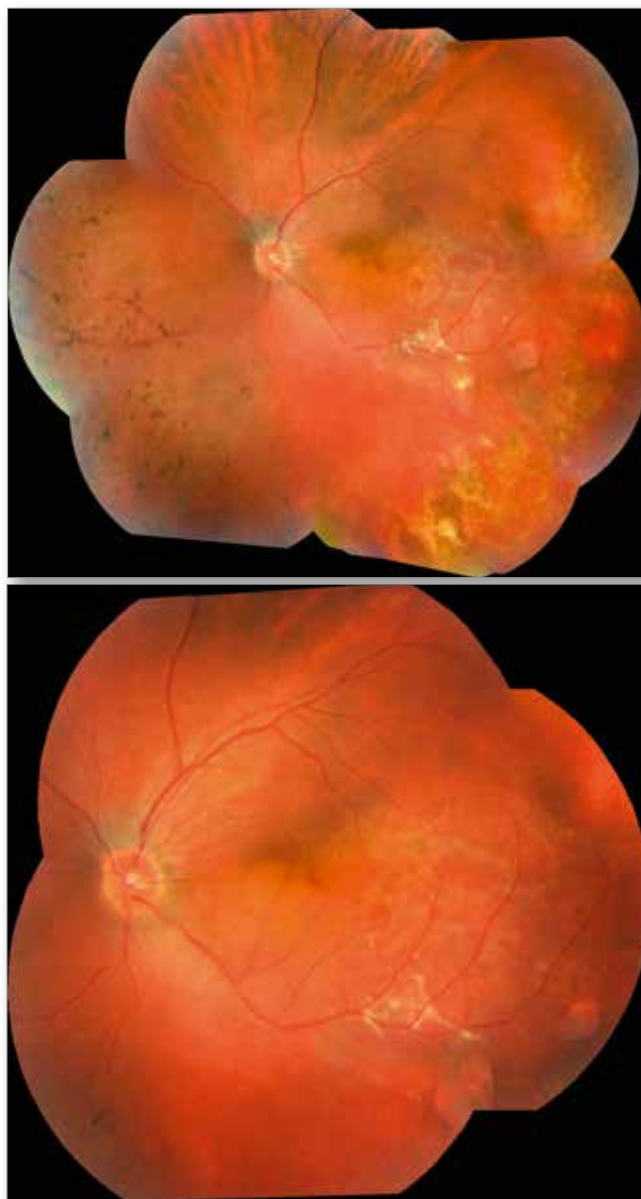


Fig. 6. Diffuse choroidal hemangioma in SWS following ruthenium brachytherapy.

In summary, the management of glaucoma in SWS remains a significant clinical challenge. Delayed or absent intervention frequently results in progressive deterioration and irreversible loss of visual function. Early detection and timely treatment of secondary glaucoma are essential for preserving useful vision in affected individuals.

Photographs by Piotr Bujak.

Disclosure

Conflict of interests: none declared

Funding: no external funding

Ethics approval: Not applicable.

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