

Sturge-Weber Syndrome

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Abstract

Sturge-Weber syndrome (SWS) is a neurocutaneous disorder caused by somatic mutations in the *GNAQ* and *GNA11* genes. These mutations affect blood vessel development, causing abnormalities in the brain, skin, and eyes from birth. The major features of SWS include a port-wine birthmark, leptomeningeal angiomas, and glaucoma. If SWS is suspected, MRI is recommended for further evaluation.

Keywords: Neurocutaneous Syndrome, Brain, Skin

Case Summary

An adolescent with a facial port-wine birthmark extending from the forehead to the lower eye and known Sturge-Weber syndrome (SWS) presented to the emergency department with left-sided weakness.

Imaging Findings

Brain MRI (Figure 1) showed multiple findings of SWS with asymmetric volume loss of the right cerebral hemisphere, increased thickness of the leptomeninges, and diffuse leptomeningeal enhancement involving the right cerebral hemisphere. Calcifications were present in the right cortical and subcortical white matter of the posterior temporal and occipital lobes. There were no findings of stroke.

Diagnosis

Sturge-Weber syndrome.

The differential diagnoses of SWS are other malformation syndromes that

mimic SWS, including venous angiomas, cerebral arteriovenous malformations, hemimegalencephaly, Rasmussen encephalitis, hypoxic-ischemic injuries, tuberous sclerosis, and neurofibromatosis.

Discussion

SWS is a congenital, sporadic, and rare neurocutaneous disorder that affects 1 in 20,000-50,000 children without gender or racial predilection.¹ It causes abnormal development of blood vessels, specifically in the skin, brain, and eyes.² SWS is characterized by the presence of a facial port-wine birthmark with ipsilateral brain abnormalities, glaucoma, and neurological manifestations including leptomeningeal angiomatosis and seizures.¹

SWS can be caused by somatic mutations in either the *GNAQ* gene, specifically an arginine to glutamine substitution, or in the *GNA11* gene.³ The mutation ultimately results in overactive endothelial cells, capillary overgrowth, or poorly differentiated endothelial cells

with progressively dilated immature, venule-like vasculature.⁴

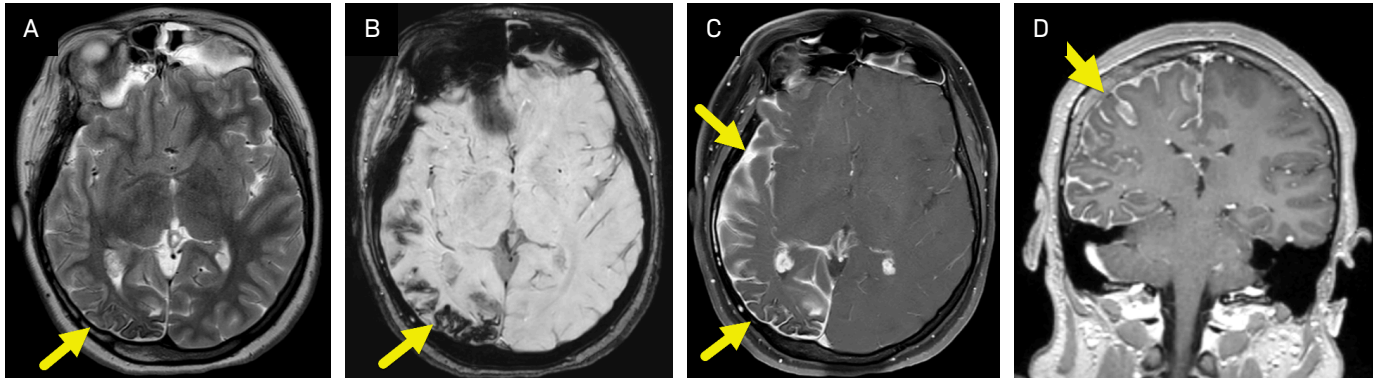
Individuals with SWS may be identified at birth due to the presence of the port-wine birthmark on the forehead, temple, or eyelid. The size of the birthmark correlates positively with the extent of brain involvement seen on MRI.⁵ Hence, neuroimaging is an important first step for evaluating children with possible SWS and identifying patients at a higher risk of significant brain involvement and subsequent neurological complications.^{1,6} MRI sequences should include pre- and post-contrast T1-weighted and FLAIR images and susceptibility-weighted imaging (SWI) to detect venous abnormalities and calcifications.⁷ Leptomeningeal enhancement is a diagnostic feature of SWS. However, the finding can be absent in young children. Hence, other imaging findings are important to identify. These include cortical atrophy, abnormal venous drainage, choroid plexus asymmetry, focal areas of abnormal white matter signal, and calcifications.⁶ Follow-up MRIs are not indicated for patients with SWS with well-controlled clinical symptoms but may be recommended for patients with new-onset or progressive neurological symptoms.¹

Other imaging modalities can be useful to monitor disease. CT (with or without contrast) can also detect calcification, cortical atrophy, and an enlarged ipsilateral choroid plexus.⁷ US can

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Figure 1. (A) Axial T2-weighted MRI image showing right-sided cerebral volume loss with small gyri in the right posterior parietal lobe. Abnormal cortical and subcortical white matter signal (arrow) suggesting calcification is present. (B) Susceptibility-weighted image highlighting the susceptibility artifact (arrow) related to cortical calcification. (C) Axial and (D) coronal T1-weighted postcontrast MRI highlighting the diffuse leptomeningeal thickening and enhancement (arrows) over the right convexity.



demonstrate enlarged vessels, increased Doppler flow, and asymmetric enlargement of the choroid plexus. Transcranial Doppler shows lower peak systolic and end-diastolic velocities in the anterior, middle, and posterior cerebral arteries.¹ F-18 fluorodeoxyglucose PET can also be informative by detecting changes in brain glucose levels, a marker for cognitive decline and seizure activity in SWS. Additionally, electroencephalography can aid in detecting seizure and nonconvulsive status epilepticus in patients with SWS.¹

The prognosis of patients with SWS depends on the presence and severity of neurological complications. Complications can involve multiple systems and may vary widely in affected individuals. Problems can affect the brain, endocrine system, eyes, and skin. These complications typically occur within the first year of life and can worsen over time. Neurologic problems include seizures, stroke-like episodes, and cognitive and developmental delays. The most frequent ocular complication is glaucoma. Choroidal hemangiomas may occur, and eye enlargement (buphthalmos) from congenital glaucoma. The skin can become hypertrophied, and asymmetric growth of bone and soft tissue may occur. Thus, early diagnosis is crucial for identifying at-risk patients. To date, there is no single treatment for SWS. Pulsed-dye laser

and eye drops that decrease intraocular pressure are the current standards of care for the cutaneous and ophthalmologic manifestations, respectively.⁸ The primary method for seizure management continues to be antiseizure medication.⁶ In a few clinical trials, patients taking sirolimus demonstrated improvements in cognitive impairment, especially those with neurological features of SWS.^{9,10} Sirolimus functions as an mTOR inhibitor, a downstream target likely upregulated by the mutated, *GNAQ* or *GNA11* gene.

Conclusion

SWS is a neurocutaneous disorder caused by somatic mutations in the *GNAQ* and *GNA11* genes. These mutations affect blood vessel development, causing abnormalities in the brain, skin, and eyes from birth. The major features of SWS include a port-wine birthmark, leptomeningeal angiomas, and glaucoma. If SWS is suspected, MRI is recommended for further evaluation.

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