Case Report

Sturge weber syndrome with phenytoin toxicity - A deeper pandora’s box

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**Key Words:** Sturge weber, Port wine stain, leptomeningeal angioma

**Abstract**
A neuro-cutaneous disorder with angiomas involving the leptomeninges and the face, Sturge weber syndrome is a crippling entity with devastating outcomes at times. Although known to conglomerate other markers like seizures, mental retardation, hemiplegia, intracerebral calcifications etc, atypical variants have been noted and we bring forth one such case complicated by the adverse effects of long term phenytoin use.

**Introduction:**
Sturge weber syndrome (SWS) is an encephalofacial angiomatosis with a facial capillary hemangioma, termed the Port wine stain (PWS) and angiomata of the leptomeninges. With an incidence of about 1 in 50,000 SWS is a rare entity with considerable morbidity.1 We report a case with the quintessential features of SWS associated with phenytoin toxicity and review the literature.

**Case report:**
A 22 year old male presented with gradually worsening shortness of breath and cough from 10 days. He had an erythematous patch on the left side of the face and left upper limb by birth (a full term normal vaginal delivery). He had been having recurrent seizures (starting 3 months of age) persisting despite treatment with phenytoin for more than 7 years (later switched to carbamazapine and sodium valproate due to gum hypertrophy). His milestones were delayed and sported short stature and mental retardation (IQ-40). He had repeated fractures (long bones and ribs) making him bedridden most of the time. His family history was not contributory. Examination revealed nonblanchable erythematous patches involving left side of the face, upper limb and the trunk (Figure 1).
Figure 1: Clinical photograph showing nonblanchable erythematous patches involving the left side of the face, upper limb and the trunk along with gum hypertrophy.

On auscultation, lungs revealed left sided crepitations. His motor power was 2/5 on the left side (both upper and lower limbs) compared to 4/5 on the right with left plantar upgoing. Labs showed Hb-7.7g/dl, TWBC-10,300; Alkaline phosphatase - 1238 U/L; Thyroid profile showed T3 -0.65ng/ml, T4- 5mcg/dl, TSH-0.41 mIU/L suggesting central hypothyroidism. Xray chest showed left upper zone haziness. His growth hormone (GH) assay after clonidine stimulation was low at 6ng/ml.USG abdomen was essentially normal. His CT brain showed extensive serpiginous gyriform cortical calcifications seen as a linear parallel "railroad-track" like configuration with atrophic right hemisphere (Figure 2).
Figure 2: CT brain showing extensive serpiginous gyriform cortical calcifications seen as linear parallel "railroad-track" like configuration with atrophic right hemisphere.

Figure 3: Gadolinium contrast MRI brain (axial T1W image) showing gross calvarial thickening with hypertrophy of the choroid plexus and leptomeningeal enhancement on contrast.

EEG showed bilateral polymorphic delta activity, attenuation and excess of slow activities (1-1.5Hz). Ophthalmic exam was normal. Patient was started on azithromycin (for community acquired pneumonia), carbamazapine, calcium, Vitamin D supplements and GH along with supportive care.

Discussion:
SWS is mostly sporadic though rarely familial cases have been reported. It is hypothesized that early on in the pregnancy, chromosomal abnormalities (mainly somatic mosaicism) in fetal ectodermal tissues, increased gene expression of
fibronectin\textsuperscript{2} (role in blood vessel proliferation), dysregulation of hypoxia-inducible factor-alpha expression and enhanced endothelial turnover in SWS vessels\textsuperscript{3} may all contribute to the pathophysiology of SWS. In brain, the stasis, poor venous drainage/venous hypertension and decreased glucose utilization (consistent with an ischemic process) are incriminated in the progressive gliosis and atrophy of the cortical and subcortical regions.\textsuperscript{4}

There are three types of SWS described, complete trisymptomatic (involvement of eye, skin and nervous system), incomplete bisymptomatic (two of either eye, skin or nervous system involved which in our case were the latter two) and incomplete monosymptomatic (only one organ). Our case featured the quintessential PWS, seizures, hemiplegia, intracerebral calcifications, and mental retardation. The classical PWS is commonly seen and restricted to the periorbital area, forehead or scalp (V1 and/or V2 of trigeminal nerve distribution), but in our case it extended on to the upper trunk and the ipsilateral upper limb. About 90 percent of cases with the port wine stain involving both the upper and lower eyelids sport a leptomeningeal angioma, compared to 10 percent when only one eyelid is affected\textsuperscript{5} and 10% of SWS cases may not feature PWS at all. The leptomeningeal angioma is usually ipsilateral to the PWS and is in the parieto-occipital region or the entire hemisphere (commonly unihemispheric). Generalized tonic-clonic seizures are the most common seizure type in SWS (as described in our patient) although infantile spasms, myoclonic and atonic seizures have also been noted. Choroidal angioma, buphthalmus, glaucoma and vascular anomalies of conjunctiva, episclera, choroid, and retina and rarely megalocornea may be seen in the ipsilateral eye (absent in our patient). Our patient demonstrated growth hormone deficiency and central hypothyroidism (low TSH despite low T3) both of which are documented in SWS and owing to the treatable nature, appropriate screening tests should be done when indicated.\textsuperscript{6}

The diffuse osteoporosis and osteomalacia in our patient can be explained by long term phenytoin usage which could have been responsible for the repeated long bone fractures and the resulting bedridden/immobilization state could have fuelled a vicious cycle. The associated GH deficiency could have further contributed to his short stature. The calvarial thickening prominent in our case is an established adverse effect of phenytoin and is probably mediated by stimulation of osteoblast-associated markers such as bone nodule formation, alkaline phosphatase, Osteocalcin, Osteopontin, and type I collagen apart from the creation of a pseudo-hypoparathyroid and/or Vitamin D deficient state.\textsuperscript{7} The chronic anemia noted in our case, probably from the poor nutrition and/or folic acid deficiency induced by phenytoin, could also have contributed to the calvarial thickening (marrow expansion).

Gadolinium enhanced magnetic resonance imaging (MRI) is superior to CT (except when delineating the extent of calcification) in demonstrating the extent of the leptomeningeal angioma, the associated vascular anomalies and recent ischemic damage at an early and often presymptomatic stage. Astute anticonvulsant treatment and in refractory cases, surgical treatment options like hemispherectomy (lobar/multilobar) and corpus callosotomy have shown some benefit in curbing the seizure related morbidity. Prophylactic low dose antiplatelet therapy has also shown
promise. PWS may be ameliorated by laser treatment and glaucoma needs appropriate medical/surgical treatment. Our case is different in many ways like the intracerebral calcifications not being ipsilateral to the PWS, the PWS extending on to the trunk and the ipsilateral upper limb, associated features of phenytoin toxicity like extensive calvarial thickening, osteoporotic fractures and anemia thus highlighting the need for clinicians to be aware of the umbrella of manifestations SWS encompasses and their management options.

References:
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