Sturge–Weber Syndrome

DESCRIPTION

Sturge–Weber syndrome (SWS) is a progressive congenital disease that is commonly associated with the port wine stain, an auburn colored birthmark, among other neurological and psychological deficits. SWS was first described by Sturge in 1879, as partial epilepsy caused by a lesion in the vasomotor brain center along with a characteristic neurocutaneous nevus. In 1922 and 1929, Weber described another case of SWS, although he named it “encephalotrigeminal angiomatosis.” Genetic causes of SWS are unknown, although rare monozygotic twin studies have led scientists to speculate that the syndrome originates from somatic gene mutation during early neonatal trimesters (Maiuri, Gangemi, Jaconetta, & Maiuri, 1989). SWS occurs in all sexes and races sporadically and equally. Treatments for SWS are symptomatically based and include aspirin, anticonvulsants, and dermal laser procedures.

NEUROPATHOLOGY/PATHOPHYSIOLOGY

The most common and apparent symptom associated with SWS is the trigeminal port wine stain, a birthmark most likely caused by agenesis of the cephalic venous plexus during the first neonatal trimester (Kossoff, Hatfield, Ball, & Comi 2004; McIntosh & Morse, 2006). Although the birthmark is seen in most cases of SWS, the majority (more than 50%) of infants born with the port wine stain birthmark do not have the associated neurological deficits found in SWS (Comi, 2003). The birthmark most frequently occurs unilaterally, although it does occur bilaterally, and develops on the face near the eyes. The port wine stain is caused by an overabundance of capillaries under the dermal layers. The birthmark has normal texture and can appear in a variety of colors, from light pink to deep red (Comi, 2003; McIntosh & Morse, 2006). The birthmark itself does not pose any neuropsychological or neurological symptoms.

The most common neurolopathological feature of SWS is angioma, which is the excessive and abnormal growth of blood vessels on the surface of the brain. Research suggests that the angioma found in SWS results from abnormal maturation of the most primitive cephalic venous plexus during the first neonatal trimester (Comi, 2003, pp. 9, 19). Animal models of the angioma seen in SWS have been replicated in horses, although few have been scientifically researched (Comi, 2003). Further studies regarding abnormal brain structures of SWS have shown abnormal vascular structures in the leptomeninges, showing atrophic tissue and brain calcifications (Comi, 2003). Evidence also indicates that the meninges are significantly more thin and narrow in SWS patients (Di Trapani, Di Rocco, & Abbamondi, 1982).

Brain calcifications frequently occur in SWS and are most commonly found in the cortical layers, which include the outermost layers of the brain. Brain calcifications consist of calcium and phosphorus deposits near parenchymal vessels and form within subcortical tissues in the cortex and vary greatly among patients (Comi, 2003). Although the structure of the brain calcifications is known, the origin and neuropsychological effect of brain calcifications in SWS are currently unknown and greatly disputed within scientific literature. According to Comi (2003), research suggests that SWS is caused by the complicated interplay between abnormal extracellular matrix, vascular innervations, and endothelium alongside the leptomeningeal angioma.

Other physical abnormalities associated with SWS include glaucoma, increased vascularity of jaw tissue, and growth hormone deficits. Various oral manifestations are also frequently present in SWS patients. These include increased vascularity of the jaw tissue, swelling of soft oral tissue, enlargement of the jawbone, and arched palate. Secondary symptoms associated with increased vascularity include the premature loss of permanent teeth (Comi, 2003).

Study results attribute abnormal brain structure to noradrenergic innervations in regard to the increased constriction in cortical vessels. It is hypothesized that such abnormalities would put SWS patients at a higher risk for chronic ischemia and seizures and in turn, brain injury (Comi, 2003). Studies have also shown that there is a high prevalence of growth hormone deficiency in SWS patients (61% in the SWS population and 0.03% in the general population) (Miller, Ball, Comi, & Germain-Lee, 2009).

NEUROPSYCHOLOGICAL/CLINICAL PRESENTATION

SWS is associated with several commonly occurring clinical symptoms including seizures, mental retardation (MR), migraines, glaucoma, and stroke-like episodes (Comi, 2003; Kossoff et al., 2004; McIntosh & Morse, 2006). Seizures are a frequent neurological symptom of SWS (occurring in approximately 70–80% of SWS patients), nearly 75% experiencing onset prior to 12 months of age, the mean age of onset being 9 months (Cody & Hynd, 1998; Kossoff, Buck, & Freeman, 2003; Morse & McIntosh, 2006). Seizures are not experienced by all SWS patients; while some SWS patients experience frequent and numerous seizures, others experience infrequent episodes. Seizures associated with SWS are generally focal in onset; however, they tend to generalize to other brain regions over time (McIntosh & Morse, 2006). Seizure type varies between patients. Seizure onset typically occurs within the first 2 years of the child's life, with the majority occurring prior to age 1 (approximately 75%) (Cody & Hynd, 1998; Comi, 2003; McIntosh & Morse, 2006).

Although SWS is not considered a fatal syndrome, seizures frequently give rise to the onset of morbid secondary symptoms, including motor delays, hemiatrophy and hemiplegia (30–50%) and brain lesions (Cody & Hynd, 1998; McIntosh & Morse, 2006). Hemiparesis and hemiplegia often occur as a result of acute seizure episodes and leave the SWS patient with either severe muscle weakness or paralysis of one or both sides of the body. Hemiatrophy and hemiplegia often cause permanent motor delays (Comi, 2003; McIntosh & Morse, 2006). Comi (2003) recently evidenced that SWS patients often experience weakness in the face or body that is contralateral to the port wine stain. In some cases, researchers have examined patients who have suffered acute ischemic brain injury resulting from acute seizure episodes (Comi, 2003). Studies show that the abnormal synaptic plasticity caused by seizures in the cortical tissue may lead to reoccurring epileptic episodes, supporting earlier research that seizures in SWS become more intense over time (Comi, 2003).

In addition, approximately 60–80% of SWS patients have mild to severe MR, with only 8% of patients considered to have average cognitive functioning (Cody & Hynd, 1998; Comi, 2003; McIntosh & Morse, 2006). A strong correlation between age of seizure onset and cognitive functioning has been shown; although there is also scientific speculation that age of seizure onset is not as predictive of cognitive functioning as seizure intensity (Cody & Hynd, 1998; McIntosh & Morse, 2006). Seizures occurring during the child's first year have been shown to significantly increase the risk for MR (Comi, 2003). This research is supported by the fact that MR is rarely seen in SWS patients who do not experience seizures (Aicardi, 1990).

Headaches are another secondary symptom of seizures. Approximately 50% of SWS patients complain of headaches, the majority of which are diagnosed as migraines. Headaches commonly occur directly after the onset of a seizure. In some cases, headaches are symptomatic of the pressure experienced as a result of glaucoma (Cody & Hynd, 1998; Comi, 2003; McIntosh & Morse, 2006). According to Kossoff et al. (2004), the most common symptomology associated with headache in SWS includes unilateral pain, nausea, photophobia, phonophobia, and throbbing sensations. Kossoff et al. (2004) also found that the most common type of headache was the migraine.

Neuropsychological symptoms associated with SWS include an increased risk for academic, intellectual, and behavioral problems. SWS patients are at a significantly high risk for pervasive developmental disorders (PDDs), particularly autism spectrum, MR, learning disabilities, and attention deficit hyperactivity disorder (ADHD) (close to 20% in SWS population and only 5–6% in the general population). PDDs develop at a significantly higher risk in SWS (Cody & Hynd, 1998). The most common PDD is autism, or autism spectrum disorders (Cody & Hynd, 1998). Depression has also been commonly seen in older children and adolescents. In general, early development appears more normal than later developmental stages in children diagnosed with SWS (Cody & Hynd, 1998). SWS patients often exhibit behavioral issues including increased disinhibition (Cody & Hynd, 1998). The majority of these children need to have specialized educational plans created for them. There is currently little research on specific neuropsychological deficits found in SWS.

DIAGNOSIS

SWS is categorized into three types. Type 1 is classified by the presence of the port wine stain along with leptomeningeal angioma, which consists of blood vessel tumors in the membranes covering the brain and spinal cord. In some Type 1 cases glaucoma is present. Type 2 consists of only the facial angioma, and glaucoma is sometimes present. Type 2 is categorized as having only the leptomeningeal angioma. Glaucoma is hardly ever present in Type 3 patients (Cody & Hynd, 1998; Comi, 2003; McIntosh & Morse, 2006). There are currently no known preventive methods for the development of SWS, and infants

born with the port wine stain should be screened periodically throughout infancy and into early childhood for diagnostics, since certain neurological symptoms associated with SWS, including brain calcifications and lesions, may not be present or visible in early neuro-imaging scans (Comi, 2003). Diagnostic methods most frequently used in the diagnosis of SWS include positron emission tomography (PET), MRI, and single-photon emission computed tomography (SPECT) (Comi, 2003).

TREATMENT

Laser treatment procedures are used to treat or decrease the visibility of the port wine stain. In certain circumstances, these procedures can be done on infants as early as 1 month old (McIntosh & Morse, 2006). The seizures found in SWS patients frequently intensify in severity and frequency as age increases, often becoming untreatable with anticonvulsants (Cody & Hynd, 1998). A study conducted by Wilfong, Buck, and Ball (2008) shows that the most common form of anticonvulsant prescribed to SWS patients are sodium channel blockers, including levetiracetam, carbamazepine, and oxcarbazepine. In acute cases, vagus nerve stimulation or epilepsy surgery, known as hemispherectomy, can be used to treat seizures. A study by Wilfong et al. (2008) found that 81% of SWS patients who had undergone vagus nerve stimulation or hemispherectomy experience no postoperative seizures, with 53% of these patients no longer having to take anticonvulsants. Surgery is still highly controversial and considered to be a last resort for treating SWS, since studies show that approximately 47% of patients experience postoperative complications (Wilfong et al., 2008). Glaucoma is often treated with eye drops, corrective lenses, as well as surgery. Headaches are generally treated with aspirin.

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