ISSN (Online): 2455-3662
EPRA International Journal of Multidisciplinary Research (IJMR) - Peer Reviewed Journal
Volume: 9| Issue: 8| August 2023|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2023: 8.224 || ISI Value: 1.188

ANALYSIS OF THE CLINICAL MANIFESTATIONS CAUSED BY STURGE WEBER SYNDROME

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Article DOI: https://doi.org/10.36713/epra14146
DOI No: 10.36713/epra14146

ABSTRACT

Introduction: *Sturge-Weber syndrome is a congenital disease with activating somatic alteration of the GNAQ gene, causing a failure in the regression of the primitive cephalic venous plexus so it is specifically associated with Port Wine stain with leptomeningeal angioma, it is associated with venous and capillary malformations in the brain and eye; causing glaucoma and leptomeningeal angioma.*

Objective: *detail and analyze the clinical manifestations related to Sturge Weber syndrome.*

Methodology: *the work presented is a descriptive analysis based on research studies by different authors and on a clinical case found in the province of Cañar, that is to say that its incidence is 1 in 100,000 inhabitants. A total of 20 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 14 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, SciELO, Google Scholar, Medigraphic and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: Sturge-Weber syndrome, Port Wine Stain, Leptomeningeal angiomatosis.*

Results: *based on some authors, it is argued that the Sturge-Weber syndrome presents different forms, even presenting incompletely in which there are two manifestations, being angiomatosis and encephalo-facial, but according to the Roach scale there are three types: type 1 with facial port wine stain and leptomeningeal angiomatosis, with or without associated glaucoma that would correspond to classic Sturge Weber Syndrome; type 2, which is the most frequent, with facial MVO without leptomeningeal involvement, with or without the presence of glaucoma; and type 3, which is the less frequent form, with the presence only of leptomeningeal angiomatosis.*

It is currently known that the evolution of the clinical manifestations should be treated respectively, since the most serious complication of this disease are partial or complex seizures, taking into account that the occipital lobe is affected in most cases, but also the occipito-parietal lobe or even the frontal lobe in the frontonasal area may be affected. Sturge-Weber syndrome is a congenital disease affecting the brain, spine and nerves (neuro) and skin (cutaneous), with an incidence of about 1 in 20,000 to 50,000 people, but not inherited.

Medical treatment includes anticonvulsants, symptomatic and prophylactic, glaucoma treatment to reduce intraocular pressure, and laser therapy to reduce facial nevus. It should be clarified that the medical treatment will be based on how much the area is affected, especially in the neurological symptoms due to the development of the leptomeningeal malformation.

Conclusions: *Sturge-Weber syndrome is a highly complex disorder of very low incidence in our country, because it is caused by a mutation of one of the genes at birth, affecting mainly the blood vessels and causing severe neurological disorders due to the lack of flow to the affected areas, thus compromising the life of the patients who suffer from it, who are mainly newborns and children, This makes its approach difficult, due to the mutation and the affection that they entail, which hinders therapeutic decisions, so it is extremely important to make a correct diagnosis based on a clinical, genetic and symptomatological analysis taking into account the condition and age of the patient, so that in this way the treatment can provide adequate survival to the patient.*

KEYWORDS: SSW: Sturge-Weber Syndrome.

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MVO: Port Wine Stain.
Leptomeningeal angiomatosis: It is an excess of venous vascularization, producing an alteration in cerebral venous drainage, leading to venous stasis and hypoperfusion causing cerebral atrophy and cerebral calcifications.
Port wine stain: It is a birthmark that is related to the growth of blood vessels.
Roach scale: Used for grading.

INTRODUCTION

Sturge Weber syndrome (SSW) was first described by Schirmer in 1860, its main cause and manifestations were not exactly known, but, from 1879 William Allen Sturge investigated in depth about the syndrome in a six year old patient who presented a clinical picture of neurological disorders associated with seizures, mental retardation and unilateral ocular disease.
From this case in 1901 Siegfried Kalischer manifested more clinical features in new studies of children. In 1922, Parkes Weber described the typical radiological changes of the disease: intracranial calcification(1).
Finally, in the years 1923 to 1934 Vicente Dimitri and Krabbe concluded that it is a rare hereditary syndrome. Cases are described as autosomal recessive and dominant, and can affect both sexes equally. According to the analysis performed, the most visible signs of the disease are birthmarks or "port wine stains" on the face, which are flat areas that vary in color from red to dark purple and are characteristic of at least one upper part in the area of the eyelids and forehead. The cause of the spots is the formation of small blood vessels under the skin(1).
Based on all the research carried out, it is currently proposed that it is a hereditary neurocutaneous disease, which occurs in 1 in 20,000-50,000 live births. Characteristically presenting with a vascular malformation (VM), from a somatic change that activates the GNAQ gene, leading to the failure of the degeneration of the primitive cranial plexus, so it is particularly associated with Port Wine Stain with visible leptomeningeal hemangiomas and patchy distribution of blood vessels.(2). Its severity is based on the control of epilepsy and degree of brain involvement(3).

METHODOLOGY

The work presented is a descriptive analysis based on research studies by different authors and on a clinical case found in the province of Cañar, that is to say that its incidence is 1 in 100,000 inhabitants. A total of 20 articles were analyzed in this review, including review and original articles, as well as clinical cases, of which 14 bibliographies were used because the other articles were not relevant to this study. The sources of information were PubMed, SciELO, Google Scholar, Medigraphic and Cochrane; the terms used to search for information in Spanish, Portuguese and English were: Sturge-Weber syndrome, Port Wine Stain, Leptomeningeal angiomatosis.
The choice of literature presents elements related to an overview of Sturge-Weber syndrome; in addition to this factor, a description and analysis of the clinical manifestations of the disease is presented.

DEVELOPMENT

Clinical Manifestations.

Port-Wine Stain, Capillary or Venular Malformation.

Present at birth, it is characteristic of Sturge Weber syndrome, is pink or purple in color, is usually lateralized, or may be bilateral. On the other hand, the risk of association to leptomeningeal or ocular damage is determined by its extension, that is to say, as the trigeminal branch is mainly affected, it can alter any of its branches, being the frontal branch (V1), maxillary branch (V2) and the mandibular branch (V3)(4).

Velasquez describes the physiopathology of Sturge Weber syndrome, emphasizing that it is neurodegenerative.
From the point of view of the authors, all agree that the frontal branch is the most frequently affected, extending through the upper eyelid, frontonasal prominence and optic vesicle that derive from the frontal placode. The V2 and V3 branches are less frequent and there is no risk of causing leptomeningeal involvement or glaucoma. Those that present a higher risk are bilateral and extensive(5).
In addition, it has been suggested that in some cases MVO can develop up to 60% soft tissue hypertrophy, 13.8% bone hypertrophy and 43.8% proliferative nodule formation(5).

Neurological Manifestations

The leptomeningeal capillary venous manifestation presents with tortuous and abnormal vascular structures in the thickened leptomeninges, usually affecting the occipital lobe, occipitoparietal lobe and sometimes the entire hemisphere. It is usually ipsilateral to the MVO. There are also alterations in the deep draining veins which are dilated, the underlying brain tissue may show neuronal loss, be atrophic with calcifications in perivascular distribution or in the cerebral cortex due to hypoxia causing neurological symptoms(6).

The cortical irritability that is generated will cause hypoxia and ischemia in patients with WSS resulting in seizures, which occur in 80 to 90% during the first 2 years of life and are associated with progressive hemiparesis in 60%, migraine, neuropsychological developmental delay, cerebrovascular events, glaucoma and behavioral problems. The first seizures are usually partial, and may even be triggered by a febrile condition; these partial seizures usually evolve into generalized seizures(7).

Angiomas

63% of cases are associated with unilateral cutaneous nevus, i.e. Port Wine stain, the other 40% of cases occur bilaterally. Kuchenbunch in 2016 states that the presence of angiomas in some cases occurs with Klippel Trenaunay syndrome, i.e. angiomas can be found at the level of the thorax, abdomen or upper or lower extremities, it is a bony hypertrophic syndrome. Since the angioma can affect branches V1, V2, V3 depending on its distribution, whether uni or bilateral, it has close structural consequences, such as facial mucosa, facial asymmetry and dental occlusion, which are usually unilateral(7).

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Liao, Yao, Huang and Zeng, determine that neurodegenerative symptomatology can appear even within the first two years being even more serious to treat.

Ocular Manifestations

It consists mainly of a vascular malformation of the eye, with dilated, tortuous venous vessels caused by an increase in episcleral venous pressure in Schlemm's canal or failure of aqueous humor drainage that causes optic atrophy and blindness. It appears during the first year of life and it is mentioned that glaucoma is the most frequent ocular clinical manifestation, in up to 40-60% of patients(7).

Sturge-Weber syndrome does not occur frequently, it is a congenital disorder and based on Roach's study includes in one of his classifications of encephalo-facial angiomatosis the classic Sturge-Weber syndrome within type I, while the cases without facial angioma would be included within type III. Type II, which would not correspond to this syndrome, is the most frequent, and includes all those cases of facial angioma without leptomeningeal involvement, whether or not they have glaucoma. Although most newborns with SSE are usually neurologically asymptomatic at birth, up to 70-80% of patients present with seizures at some time during their evolution, usually of a focal type. These seizures usually appear in the first eighteen months of life, and may be accompanied by a febrile process(8).

Several studies have shown that WSS is characterized by a wine-colored spot on the face, epilepsy, mental retardation, other neurological deficits (hemiparesis, hemianopsia) and glaucoma that must be controlled to avoid total neurological atrophy(8).

The most frequent complication of this pathology is seizures, so its treatment is based on the control of epileptic seizures. Regarding the treatment of epilepsy, it is important the correct selection of the antiepileptic drug according to the type or types of seizures shown by the patient and it is important to be energetic because of the importance of seizures in the prognosis and thus avoid total neurological atrophy(9).

Huang, Couto, Pinto, determine that the evolution of a patient becomes more severe depending on the age of the patient.
In few young patients, with exclusively unilateral involvement, with refractory epilepsy and without profound mental retardation, surgical treatment is indicated, by means of resection of the affected area, lobectomy or even hemispherectomy. In these cases it is important to ensure that the other hemisphere is completely healthy, which requires a thorough neuroimaging (structural and functional) and electroencephalographic evaluation(9).

Treatment with low-dose aspirin has been proposed for the prevention of venous thrombosis and thus neurological deterioration; however, this is disputed in patients with small facial lesions and little neurological involvement; laser therapy can be used for aesthetic treatment(9).

Treatment.

In most cases the control of epileptic seizures constitutes the only element to be treated; however, there are other possibilities and options that we will describe below(10).

Regarding the treatment of epilepsy, it is important the correct selection of the antiepileptic drug according to the type or types of seizures shown by the patient(10).

In different cases with minor patients, with unilateral involvement exclusively, with refractory epilepsy and without profound mental retardation, surgical treatment is indicated, by resection of the affected area, lobectomy and even hemispherectomy(10).

Treatment with low-dose aspirin has been proposed for the prevention of venous thrombosis and thus neurological deterioration; however, this is disputed. In patients with small facial lesions and little neurological involvement, laser therapy can be used for cosmetic treatment(11).

The onset of seizures below the age of 2 years makes it more prevalent in cases of mental retardation. Only about 7% of patients start their seizures after 5 years of age. Total seizure control is achieved in 47% of patients; others report that epileptic seizures are more frequent when there is bihemispheric involvement. Mental retardation affects 50-70% of patients with WSD and its presence is noted after the onset of epileptic seizures. Severe mental retardation develops in 2.5% of patients(12).
Fernandez, Gomez, Hernandez, describe that incidence studies are rare but exist and depending on the severity, neurological signs, mainly seizures, will be treated.

Complementary Examinations

- **Skull X-ray:** It is not a study of choice, but gyriform cortical calcifications called "railroad tracks" can be observed, which are commonly shown as a late finding in children older than 2 years(13).
- **Computed Axial Tomography:** It is a study used in the emergency department, from one year of age onwards, tomography can be used to observe calcifications.
- **Brain MRI:** It is the study of choice to observe the degree of brain involvement. The technique of choice is with gadolinium and the vascular leptomeningeal malformation, dilatation of the ipsilateral choroid plexus and loss of volume of the affected hemisphere will be observed. This can be observed after one year.
- **Perfusion imaging:** Since it is in a state of hypoperfusion, hypoxia, ischemia and lack of glucose in the parenchyma, neurological deterioration can be observed(14).
- **Angiography:** It is used to see other associated vascular alterations, but above all to know if there is bleeding in case it is necessary to opt for a craniotomy(14).

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RESULTS

Sturge-Weber syndrome is a congenital disease with activating somatic alteration of the GNAQ gene, causing a failure of primitive cephalic venous plexus regression and is therefore specifically associated with Port Wine stain with leptomeningeal angioma.

Nevus flammeus type facial angiomas appear in approximately three out of every thousand live births. The first controversies arise when including a patient with a facial angioma within the diagnosis of Sturge Weber syndrome, since only 5-10% of patients with congenital facial angioma will correspond to this syndrome, while the remaining 90-95% are not accompanied by leptomeningeal malformations. Thus, neuromeningeal and ocular involvement is limited to cases in which the extension of the facial angioma affects the first trigeminal branch.

This disorder produces seizures, weakness, intellectual disability and increased pressure in the eye (glaucoma), it can increase the risk of stroke, if children present a characteristic birthmark, physicians suspect SSW disorder and request an imaging test to look for angiomas.

Higueros, Roe, Granell, Baselga, state that among the complementary examinations, the study of choice is the brain MRI in which the loss of volume of the hemisphere can be observed.

Sturge-Weber syndrome is a congenital disease with cerebral, spinal column and nerve (neuro) and skin (cutaneous) involvement, with an incidence of about 1 in 20,000 to 50,000 people, but it is not inherited.

Several authors specify that it is a disorder that affects the blood vessels, particularly those of the skin, the tissues lining the brain and the blood vessels in the eye. Congenital port-wine stain is caused by an overgrowth of small blood vessels (capillaries) just beneath the skin. Angiomas which are the overgrowth of capillaries located in the tissues lining the brain cause seizures and can cause weakness on one side of the body by reducing blood flow to the part of the brain below.

The cause of the gradual onset of neurological symptoms is due to the progressive nature of the brain injury. The neurological manifestations correlate well with the extent of cerebral angiomatosis, the extent of white matter involvement, and the degree of parenchymal atrophy. All these parameters are best assessed by contrast-enhanced MRI, which is considered the procedure of choice for the diagnosis of the disease.

Its diagnosis and treatment should be multidisciplinary, since processes associated with disabilities such as deficits in maturational factors, infection by various viruses, action of cytotoxic agents, association with mutations and other types of conditions should be ruled out. The objective of the treatment is to improve the survival of the patients and to treat their symptoms.

CONCLUSIONS

Sturge-Weber syndrome is a highly complex disorder of very low incidence in our country, because it is caused by a mutation of one of the genes at birth, affecting mainly the blood vessels and causing severe neurological disorders due to the lack of flow to the affected areas, thus compromising the life of the patients who suffer from it, who are mainly newborns and children, This makes its approach difficult, due to the mutation and the affection that they entail, which hinders therapeutic decisions, so it is extremely important to make a correct diagnosis based on a clinical, genetic and symptomatological analysis taking into account the condition and age of the patient, so that in this way the treatment can provide adequate survival to the patient.

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Conflict of Interest Statement
The authors report no conflicts of interest.

Funding
The authors report no funding by any organization or company.