

Analysis of Reversible Posterior Encephalopathy Syndrome in Relation to Various Pathologies: Series of Cases

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Summary

Posterior reversible encephalopathy syndrome is an entity with signs and neurological symptoms hypothetically triggered by a vasogenic edema or endothelial dysfunction. Children debut clinically with headache, visual impairment, altered consciousness and epileptic seizures. This review shows a series of six patients with PRES associated with various pathologies. The cause may be secondary to the underlying pathology by one of the three different theories of the disease which are hypertension / hyperfunction, dysfunction in vasogenic self-regulation and endothelial dysfunction. In our sample, the female sex and school stage predominate as shown in other case reports.

Objective: Describe the presence of reversible posterior encephalopathy syndrome associated with various pathologies.

Keywords: Encephalopathy, crisis, hypertension, dengue, lupus.

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is an entity in pediatric patients debuting clinically with headache, visual alteration, altered consciousness and epileptic seizures. The prognosis of the disease depends on the underlying disease. This review shows a series of six patients with PRES associated with various pathologies. The cause may be secondary to the underlying pathology by one of the three different theories of the disease which are hypertension / hyperfunction, dysfunction in vasogenic self-regulation and endothelial dysfunction.

DESCRIPTION OF CLINICAL CASES

Case 1

Female of 8 years of age with the diagnosis of alveolar rhabdomyosarcoma of the left pelvic limb with infiltration to the central nervous system and metastasis in the parietal lobe. The data suggestive of the syndrome were presented after radiotherapy with a total of 18 sessions in the skull area and 10 sessions in the neuro axial. The clinical debut was characterized by a treatment-refractory epileptic status, with generalized tonic- clonic epileptic seizures. An approach is performed with electroencephalogram

without the presence of alterations or discharges, as a whole of a magnetic resonance finding hyperintense lesions of posterior predominance extending to the left frontal temporal area and leukoencephalopathy in the corpus callosum and periventricular area. The duration of the episode was approximately 5 days. In the acute phase it was provided Benzodiazepines to control the status which were diazepam, midazolam and infusion propofol for control of it. In the maintenance phase, he left anti-crisis treatment based on magnesium valproate, oxcarbazepine, phenytoin and lacosamide.

Case 2

9-year-old male diagnosed with classic medulloblastoma with spinal cord infiltration and lung metastasis. The data suggestive of the syndrome were presented after radiotherapy with a total of 30 sessions covering the skull and neuroaxis area in a combination of chemotherapy with carboplatin, mesna, ifosfamide and etoposide.

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The clinical debut was characterized by fleeting amaurosis, irritability and generalized headache. A magnetic resonance approach is performed, finding asymmetric occipital hyperintense lesions. The duration of the episode was approximately 6 hours. In the acute phase, corticosteroid therapy was provided with dexamethasone as an anti-inflammatory and selective agonist of the alpha 2 receptors with dexmedetomidine for pain management. No treatment was provided in the maintenance phase.

Case 3

15-year-old female diagnosed with systemic lupus erythematosus. The suggestive data of the syndrome were presented after the initiation of immunosuppressive treatment based on mycophenolic acid, chloroquine, cyclophosphamide, and prednisone. The clinical debut was characterized by epileptic status with generalized tonic clonic seizures refractory to treatment accompanied by episodes of depression and psychosis prior to the seizures. An approach is performed with an electroencephalogram without the presence of alterations or discharges as a whole of a magnetic resonance of the skull, finding symmetrical frontoparietal hyperintense lesions. The duration of the episode was approximately 10 days. In the

acute phase, benzodiazepines were provided for status control, which were diazepam and midazolam in infusion. In the maintenance phase, he left anti-seizures treatment based on levetiracetam.

Case 4

1-year-old female diagnosed with pre-B acute lymphoblastic leukemia at high risk due to age. Data suggestive of the syndrome were presented after chemotherapy at high doses of methotrexate and intrathecal chemotherapy. The clinical debut was characterized by generalized tonic seizures. An approach is performed with an electroencephalogram without the presence of alterations or discharges as a whole of a magnetic resonance of the skull, finding bilateral symmetrical occipital hyperintense lesions. The duration of the episode was approximately 3 hours. In the acute phase, benzodiazepines were provided for status control, which were diazepam and midazolam in infusion. In the maintenance phase, he left anti-seizures treatment based on levetiracetam.

Case 5

15-year-old female diagnosed with systemic lupus erythematosus with diffuse proliferative lupus nephropathy

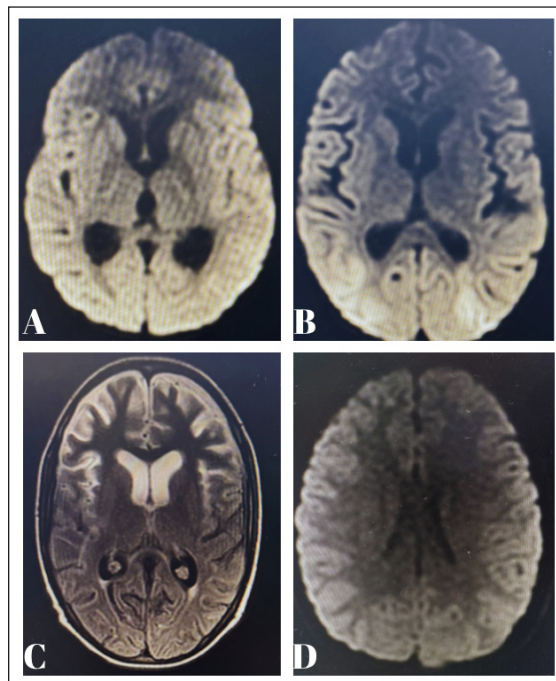


Figure 1. A) Magnetic resonance imaging of case 1 with hyperintense lesions of posterior predominance which extend to the left frontal temporal area in a set of leukoencephalopathy affecting corpus callosum and periventricular area. B) Magnetic resonance imaging axial section of case 2 showing asymmetric occipital - parietal hyperintense lesions. C) Magnetic resonance axial cut of case 3 showing symmetrical frontoparietal hyperintense lesions. D) Magnetic resonance axial cut of case 6 showing hyperintense lesions in the occipital area associated with edema.

and neurolupus. The data suggestive of the syndrome were presented after the initiation of immunosuppressive treatment based on hydroxychloroquine, mycophenolate, hydrocortisone bowls and rituximab infusion. The clinical debut was characterized by generalized tonic-clonic seizures, later accompanied by nystagmus, headache, amaurosis, episodes of delirium and psychosis. An approach is performed with an electroencephalogram without the presence of alterations or discharges as a whole of a magnetic resonance of the skull, finding bilateral symmetrical occipital parietal hyperintense lesions. The duration of the episode was approximately 10 days. In the acute phase, benzodiazepines were provided for status control which were diazepam and phenytoin impregnation. In the maintenance phase, he left treatment benzodiazepine clonazepam, antipsychotic such as olanzapine and anti- seizures treatment with levetiracetam

Case 6

Female of 10 years of age diagnosed with severe dengue in the interval of febrile - critical phase on the 4th day of evolution. The clinical debut is characterized by focal onset seizures with positive visual symptoms such as scotomas with secondary generalization tonic- clonic seizures accompanied by headache in post-ictal state. Approach is performed with electroencephalogram without the presence of alterations or discharges. Magnetic resonance imaging of the skull being in the occipital region with edema of the cortex, the interface between gray and white matter is not distinguished. The duration of the episode was approximately 2 days. No treatment was provided in the acute phase. In the maintenance phase, anti- seizures treatment levetiracetam was added at 48 hours of the epileptic episode.

PRES patients' clinical data							
Case	Sex	Age	Pathology of base	Clinical debut	Electroencephalogram	Resonance Magnetic	Treatment
Case 1	Female	8 years	Rabdomiosarcome Alveolar	Tonic-clonic seizures widespread	Without alterations	Hypertensive temporize frontal left	Lacosamide, Phenytoin, Oxcarbamaze pineapple, Valproate magnesium
Case 2	Male	9 years	Medulloblastoma Classic	Amaurosis/ Headache	It was not done	Hyperintensive parietal occipital symmetrical	None
Case 3	Female	15 years	Lupus erythematosus systemic	Status epileptic with tonic-clonic seizures widespread	Without alterations	Hyperintensive front parietal symmetrical	Levetiracetam
Case 4	Female	11 years	Leukemia Lymphoblastic Pre B	Tonic-clonic seizures widespread	Without alterations	Hyperintensive parietal occipital symmetrical	Levetiracetam
Case 5	Female	15 years	Lupus erythematosus systemic/ Neurolupus/ Nephropathy lupus	Tonic-clonic seizures widespread	Without alterations	Hyperintensive parietal occipital symmetrical	Clonazepam/ Levetiracetam
Case 6	Female	10 years	Severe Dengue	Tonic-clonic seizures	Without alterations	Edema of crust occipital and loss of the interface substance grey and white	Levetiracetam

Figure 2. The table shows a summary of the patients' clinical data.

DISCUSSION

The syndrome of reversible posterior encephalopathy is also known as PRES syndrome, reversible posterior leukoencephalopathy syndrome, reversible occipital parietal encephalopathy and reversible posterior cerebral edema syndrome; which is characterized by the abrupt appearance of neurological symptoms secondary to the alteration of the blood-brain barrier and extravasation of intrinsic fluid causing cerebral edema. The syndrome is triggered by medical conditions such as kidney diseases, autoimmune, oncological diseases, medications,

transplants, transfusions and other non-classifiable by atypical presentation secondary to a fluid extravasation as a complication of some disease (1)(2).

There are three pathophysiological theories of the syndrome in which the mechanism of hypertension / hyperfunction, self-regulation and endothelial syndrome is discussed (8). 1) Hypotension/hypoperfusion characterized by high systemic blood pressure exceeding the threshold of regulation at the brain level triggering an arterial dilation and cerebral hypoperfusion compromising the blood-brain barrier accumulating fluid causing vasogenic edema.

2) Vasogenic self-regulation dysfunction due to hypertension failing in the regulation of blood flow, considering that the increase in mean blood pressure exceeds the normal range of 40 mmhg.

3) Endothelial dysfunction which is secondary to hypoxia, the vascular endothelial growth factor is secreted by cerebral vessels increasing permeability causing vasogenic edema.

The incidence in the pediatric population is 0.04%, increasing to 0.7% in children with cancer and 0.4% in patients who are in intensive care. The highest prevalence is in females, being the most frequent stage of adolescence. In the literature, a presentation rate of less than 1% is reported in pediatric patients with systemic lupus erythematosus associated with antibodies being directed against the endothelium promoting the production of pro-inflammatory cells such as IL 6, IL1, FNTa generating a disruption of the blood-brain barrier with neurological repercussion. There is a relationship between moderate to severe lupus activity and progressive kidney damage in the PRES syndrome. In dengue it is an atypical presentation secondarily by an alteration of cytokines, presenting in serotypes DENV 2 and DENV 3, in any of three stages characterized by alteration of the level of consciousness, focal or generalized seizures (9).

The acute episode presents a debut with headache in 50%, epileptic seizures in 60-70%, alterations in vision such as amaurosis in 33% and alterations in behavior in 50%. The disease is usually associated with high blood pressure, but we can find normal blood pressure in 15 to 20% of patients.

In the algorithm proposed by Fugate et al. it helps us to make a diagnosis by meeting 4 requirements which are:

1. Acute neurological symptoms:

i. Migraine

ii. Encephalopathy

iii. Seizures

iv. Visual disturbances

2. >1 risk factor

i. Increased blood pressure

ii. Immunosuppressive drug

iii. Autoimmune disorders

iv. Kidney failure

V. Eclampsia

3. Neuroimaging

i. Bilateral vasogenic edema

ii. Cytotoxic edema with posterior encephalopathy syndrome pattern reversible

iii. Without alterations

4. No other alternative diagnosis.

To carry out an adequate approach, the image study of choice is the magnetic resonance of the skull in which we observe alterations within the first 24 hours of the appearance of the symptoms, characterized by a vasogenic edema in the white substance with predominance in the territory of the posterior cerebral circulation, being the occipital and parietal lobe the most frequent, the hyperintense lesions are symmetrical and bilateral in T2/Flair. We must take into account that it can affect other morphological injuries and different locations. This area is the most vulnerable due to lower sympathetic innervation and absence of cerebral self-regulation. In patients with some type of epileptic seizures it is complemented with an electroencephalogram which can be shown without alterations or acute focal spikes.

There is no specific treatment for reversible posterior encephalopathy, but it limits itself by controlling the precipitating cause, being able to supplement with anti-seizures medications if required. The prognosis is generally favorable with complete remission of the syndrome.

When analyzing our data, we found that all patients were in school age-adolescence with a greater predominance of female sex in 83.3% of patients. The most frequently associated pathologies are rheumatological and oncological at 33% each; we have an atypical presentation in the case of severe dengue. In 83.3% it was associated with immunosuppression generated by some type of treatment of which 33.3% by radiation at the level of the skull, 33.3% immunosuppressive medical treatment and 16% by intrathecal chemotherapy. Only one case was related to a complication of the same disease when it was in a period of capillary leakage. The predominant clinical debut was epileptic seizures in 83.3% of the population studied, 50% had generalized headache, psychosis and acute delirium, 33% had nystagmus, amaurosis and irritability. An MRI was performed where a temporofrontal hyperintense lesion was found in 16.3% and parietal occipital in 50%, with a predominance that the lesions were symmetrical. In 100% of patients there was no systemic arterial hypertension

A review of cases reported in the literature in the pediatric population was carried out, corresponding to their secondary presentation to immunosuppressive treatment by heart transplant, autolysis by venlafaxine presenting in both cases alterations in neuroimaging and the clinic with epileptic seizures and fugal amaurosis accompanying systemic arterial hypertension and associated renal failure, which we do not find in our patients. In another case study, patients with acute diffuse glomerulonephritis with hypertensive emergency secondary to streptococcal infection were evaluated. As we can see, the etiology is diverse, in most children it manifests with hypertension secondary to kidney disease, chemotherapy or immunosuppressive treatment, but the presentation of hypertension is only visible in 20% of the population. Brain self-regulation ensures constant cerebral blood flow in the MAP range of 60-150 mmhg, if it exceeds the upper limit it is transmitted to distal vessels resulting in dilation of cerebral arterioles, endothelial dysfunction and alteration of the blood-brain barrier. Blood pressure manifestations should be treated or prevented early, with nicardipine or labetalol being the drugs of choice. Systemic toxicity by some drugs can generate endothelial dysfunction and insufficient brain perfusion, explaining normotensive patients by another etiology(3).

The prognosis of the disease is good in 75 to 90% of cases, with resolution of signs and symptoms from days to weeks, only 10 to 20% have neurological sequelae. Our limitation is the small number of patients, so we must be aware of the data suggestive of the disease to make a correlation of the data found. We must perform a control neuroimaging study in search of atrophy or reversibility of the lesions, monitor if there was recurrence of the clinic associated with the syndrome.(4,5,6,7). PRES is a clinical, pathological syndrome evidenced in magnetic resonance imaging that frequently accompanies children with chronic diseases: rheumatological, hemato-oncological, metabolic or infectious, so raising the index of suspicion in a child who debuts with epileptic seizures is the main sign of this encephalopathy. There is no specific treatment and in general the prognosis is considered favorable in the vast majority of patients.

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