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Case Report

Posterior reversible encephalopathy syndrome (PRES) following cannabis consumption: A rare association ☆

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ARTICLE INFO

Article history:
Received 11 September 2024
Accepted 17 September 2024

Keywords:
Posterior reversible encephalopathy syndrome
Cannabis
Altered consciousness
Magnetic resonance imaging
Psychoactive substance use

ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a clinical-radiological syndrome that combines nonspecific neurological manifestations, sometimes severe (coma, status epilepticus), with typical brain imaging showing mostly bilateral, symmetrical abnormalities, predominantly affecting the white matter. Termed "reversible," the norm is a return to the previous neurological state. However, this recovery is not always guaranteed, with potential neurological sequelae or even progression to death. PRES has multiple etiologies. The primary etiology associated with PRES is substance consumption. However, cases of PRES following cannabis consumption are rare. Here, we present the case of a 27-year-old man admitted for the management of a feverless altered state of consciousness, whose investigations eventually revealed PRES due to cannabis consumption.

Introduction

Posterior Reversible Encephalopathy Syndrome (PRES) is a rare [1] but serious neurological condition characterized by a combination of clinical and radiological signs [2], including severe headaches, visual disturbances, seizures, altered consciousness, and bilateral white matter abnormalities in the posterior parieto-occipital regions.

Various medical conditions and risk factors may contribute to the development of PRES [3]. Particularly, drug intoxications are often cited as potential triggers for this condition [3,4].

Among them, cases of PRES due to cannabis intoxication [5,6] are only documented in a few publications.

The focus of our work is to report a case of PRES following cannabis intoxication in a patient admitted to our facility for the management of an altered state of consciousness without fever.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2024.09.084

Patient and observation

This concerns a 27-year-old patient, with a history of smoking 10 pack-years and chronic cannabis use, consumed by smoking "joints" daily, admitted to the intensive care unit for the management of a feverless altered state of consciousness.

The disease history dates back to 4 days before admission with the onset of headaches and vomiting. The course was marked by the development of confusion and right hemiparesis, evolving in a context of afebrile condition, prompting emergency department consultation 2 days later.

A brain CT scan was inconclusive.

The patient was admitted to neurology for further management.

Two days later, the patient experienced neurological deterioration, leading to admission to the intensive care unit.

The initial examination revealed a patient who, neurologically, had a Glasgow Coma Scale score of 11, with a motor response of 5, a verbal response of 2, and an eye-opening response of 4. The patient was agitated. He had equal and reactive pupils. Additionally, he suffered from right hemiparesis evaluated at 4/5 and exhibited signs of seizures, including urinary incontinence.

Regarding his hemodynamic status, his heart rate was 56 beats per minute, and his blood pressure was 14/7 mmHg, without signs of peripheral hypoperfusion.

Respiratory-wise, his oxygen saturation was 98% on room air, he was eupneic, and had normal breath sounds.

Regarding his general condition, the patient was afebrile, with capillary blood glucose measured at 2 g/dL.

The management involved admitting the patient to the intensive care unit, placing him in a semi-recumbent position at a 30-degree angle, performing noninvasive monitoring including pulse oximetry, electrocardiography (ECG), and blood pressure (BP) monitoring with peripheral venous access.

In the intensive care unit, there was neurological deterioration upon arrival (GCS decreased from 11 to 8), necessitating the patient's intubation.

As part of the etiological assessment, metabolic testing was performed, a lumbar puncture with concurrent glucose measurement was carried out, and toxicological screening in blood and urine was requested.

The lumbar puncture was negative, while the metabolic panel did not reveal any electrolyte disturbances that could explain the neurological disorder.

The toxicological screening found very high urinary cannabinoid levels, exceeding 200 ng/mL. The rest of the toxicological screening was negative.

Concurrently with the etiological investigation, the patient was maintained under deep sedation, with management of systemic cerebral insults. Transcranial Doppler was used for cerebral hemodynamic monitoring. The next day, cerebral Angio-MRI was requested.

The MRI revealed bilateral posterior parieto-occipital ischemic areas with T2 hypersignal, consistent with bilateral occlusion of the posterior cerebral arteries visualized in the TOF sequence. This radiological appearance primarily suggests reversible posterior leukoencephalopathy or PRES syndrome (Figs. 1 and 2).

The fifth day was marked by the development of bilateral mydriasis and abolition of brainstem reflexes. A CT Angiography was performed, confirming brain death. The patient was considered for organ donation but experienced cardiac arrest the following day.

Discussion

Definition

PRES, or reversible leukoencephalopathy syndrome, is a clinical-radiological entity that combines, on 1 hand, nonspecific neurological symptoms ranging from headaches, visual disturbances to focal neurological deficits, seizures, and alterations of consciousness, and on the other hand, radiological findings strongly suggestive of this syndrome [1,2].

In reality, one can even speak of constellations of clinical and radiological signs, given the diversity of symptoms and radiological images [2].

It is noteworthy that hypertension is a frequently associated sign [7].

Pathophysiology

Two major theories are proposed to explain PRES [8].

The first is related to vasogenic edema following elevated blood pressure. This theory would explain the association between PRES and hypertensive emergencies [7].

According to this hypothesis, the elevation of blood pressure beyond the cerebral autoregulation capacity would lead to cerebral hyperperfusion, vascular leakage, and thus vasogenic edema. This is the theory of cerebral hyperperfusion.

Cerebral autoregulation maintains continuous cerebral blood flow despite variations in systemic blood pressure [9].

Thus, during hypotensive episodes, cerebral vasodilation occurs. Conversely, hypertensive episodes are marked by reflex vasoconstriction, maintaining cerebral blood flow. In a healthy individual, the lower and upper autoregulatory limits generally correspond to a cerebral perfusion pressure between 50 and 150 mmHg [9,10] (Fig. 3).

To induce "hyperperfusion," according to this theory, either a very high systemic blood pressure inducing a cerebral perfusion pressure higher than the autoregulatory limit, or a modification of autoregulatory thresholds, would be required. Chronic hypertension is one of the reasons for cerebral vascular dysregulation [11].

The preferential posterior cerebral localization is attributed to the unequal sympathetic innervation between the anterior and posterior cerebral circulations. The lack of innervation of the posterior circulation (compared to the anterior circulation) could explain a lack of vasoconstriction in response to increased systemic blood pressure, explaining vasogenic edema.

However, nearly 30% of PRES patients show normal or slightly elevated blood pressure values inconsistent with the theory of cerebral hyperperfusion [12].

It is on this basis that the second theory, called the "toxic" theory, developed. PRES would be the result of endothelial dys-

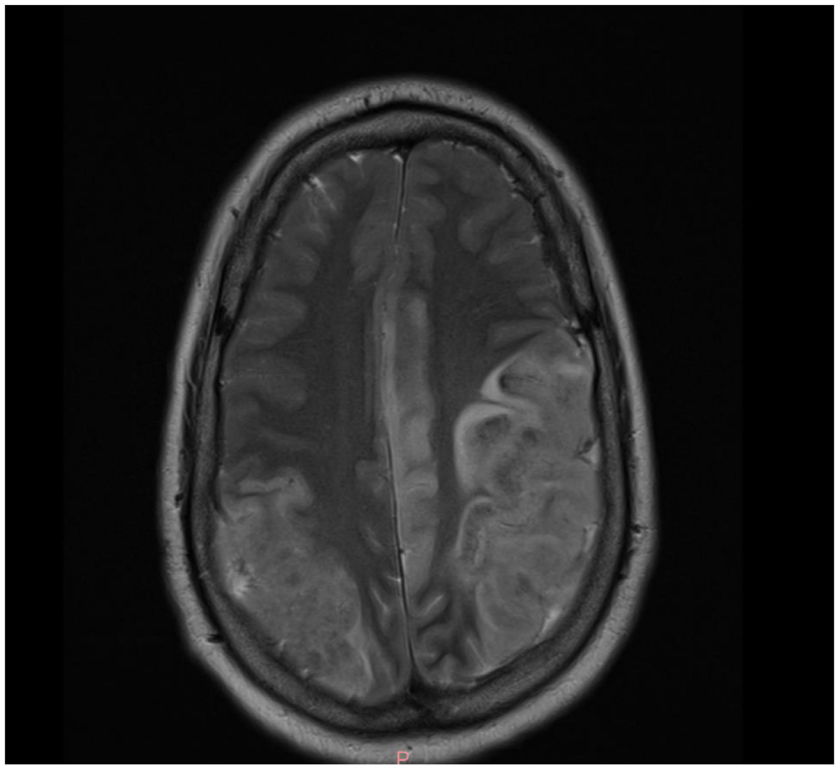

Fig. 1 – MRI image in T2 sequence showing bilateral parieto-occipital hypersignal related to bilateral posterior lobe ischemia.

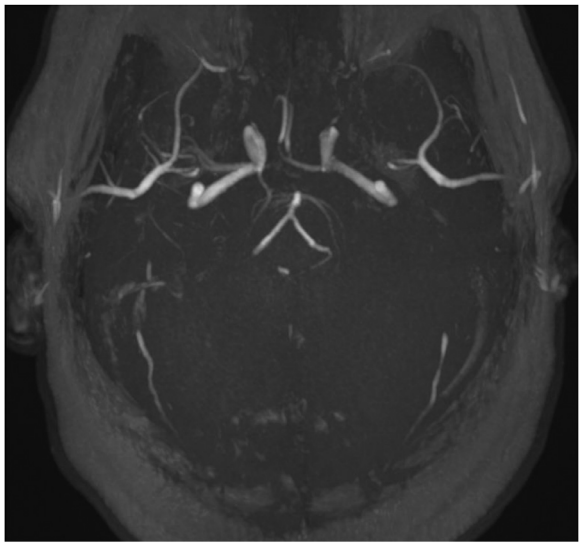

Fig. 2 – MRI image in TOF sequence showing bilateral occlusion of the posterior cerebral arteries.

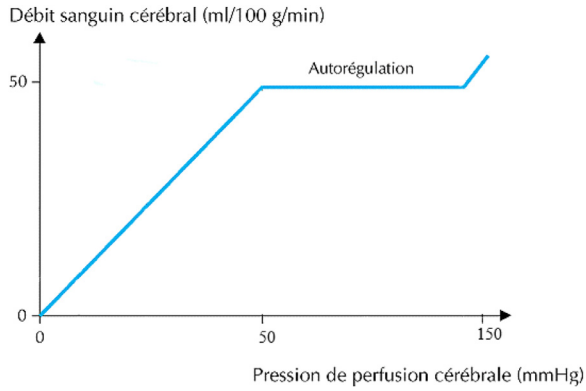

Fig. 3 – Cerebral blood flow autoregulation curve in healthy individuals.

function triggered by circulating endogenous or exogenous toxins [13]. Circulating toxins could trigger vascular leakage and edema formation on 1 hand, and lead to endothelial activation resulting in the release of immunogenic and vasoactive substances on the other hand. Thus, in this theory, hypertension is a consequence of endothelial dysfunction, not the cause of edema.

Etiologies

Etiologies can be classified according to whether they belong to the cerebral hyperperfusion theory or the toxic theory [14].

Related to cerebral hyperperfusion: hypertensive emergencies in primary or secondary hypertension, vasculitis, or other autoimmune conditions.

Related to the toxic theory: drug intake, toxic exposure, sepsis, pre-eclampsia or eclampsia, autoimmune conditions.

In our case, cannabis consumption was the cause of PRES.

Points on cannabis

Cannabis contains several active compounds. However, the main compound responsible for its psychoactive effects is tetrahydrocannabinol (THC) [15]. Consumed THC interacts with cannabinoid receptors in the brain, particularly with CB1 receptors.

CB1 receptors are widely present in various limbic system structures, which play a crucial role in emotion regulation. This localization explains the feelings of euphoria or relaxation experienced by consumers. At high doses, some patients may experience anxiety, paranoia, or even psychotic episodes [16].

Memory impairment and cognitive alterations frequently observed after chronic cannabis use could be associated with the presence of CB1 receptors in the cortex, especially in the hippocampus, a brain structure essential for memory formation [17].

Finally, the presence of these receptors in the thalamus, which relays peripheral sensory information, could explain the sensory perception alterations often reported by cannabis users [18].

Clinical features

PRES is characterized by a variety of neurological signs, often associated with hypertension. Its onset can be acute, sometimes subacute [7], developing over hours, days, or several weeks.

This was the case with our patient, whose symptoms developed over several days.

A variety of neurological symptoms are encountered. Nausea, vomiting, and headaches have been observed.

Patients may present with encephalopathy signs, with neurological deficits, drowsiness, or coma [19].

Visual disturbances such as decreased visual acuity, visual field deficits up to cortical blindness, or visual hallucinations are described [20].

Seizures, both focal and generalized, which can evolve into status epilepticus, are also noted.

Radiological aspects

The diagnosis of PRES is typically made based on MRI findings, which commonly reveal bilateral and symmetrical ischemic lesions with hypersignal on T2-weighted sequences and variable diffusion appearances depending on the syndrome's duration and the imaging delay. However, the main element of radiological diagnosis remains the topography of lesions, often involving the parieto-occipital regions in 98% of cases [21]. Other sites may be involved in association with posterior involvement, including the frontal lobes or even the brainstem and basal ganglia in the context of central PRES [22].

Imaging may also reveal other signs that are a direct consequence of cerebral artery vasoconstriction, such as intracranial hemorrhage or vasogenic edema, defining advanced radiological forms of PRES [23].

In cases where angiography is performed, it confirms arterial involvement characterized by vasoconstriction up to arterial occlusion [24]. However, the indication for this modality is often unnecessary, as MRI is considered the sufficient imaging choice for diagnosis.

- Acute onset neurological symptoms;
- Vasogenic (focal) edema on cerebral imaging;
- Reversibility of clinical and/or radiological findings.

Fig. 4 – Diagnostic criteria suggested by Fugate et al. [25].

Diagnostic criteria

Fugate et al [25] established diagnostic criteria to identify PRES (Fig. 4).

It should be noted that while the norm for PRES is complete recovery after appropriate treatment, the course can nevertheless be marked by complications, with persistent sequelae and sometimes death [26].

Some authors therefore suggest an alternative designation highlighting the potential reversibility of PRES rather than its systematic nature: PRES would become the "potentially reversible encephalopathy syndrome" [27].

This was the case for our patient, who died from PRES sequelae.

Treatment

The treatment of PRES combines general symptomatic measures with correction of the underlying cause.

Symptomatic treatment involves hemodynamic stabilization in case of hypertension, with lowering of blood pressure values by 20 to 25% within the first 2 hours, aiming to reduce blood pressure below 160/100 mmHg within the first 6 hours. Overly aggressive antihypertensive management exposes the patient to the risk of ischemia.

In case of altered consciousness or development of refractory status epilepticus, airway protection should be implemented. If intubation is required, rapid sequence induction should be recommended.

Concurrently, rapid correction of the underlying cause is essential to improve the prognosis of PRES patients.

Conclusion

In conclusion, Posterior Reversible Encephalopathy Syndrome (PRES) remains a complex and rare clinical entity, characterized by a constellation of distinct clinical and radiological signs. Our case highlights the uncommon association between PRES and cannabis consumption. Although several toxins have been implicated in triggering PRES, it is noteworthy that the association of PRES with cannabis remains rare and poorly described in the literature. Better understanding of the underlying mechanisms and increased awareness among healthcare professionals are essential for early diagnosis and effective management of this condition. Further studies are needed to elucidate the specific pathogenic pathways

involved in the development of PRES related to cannabis consumption.

Author contributions

Each author contributed to imaging interpretation or the work done in intensive care unit.

Patient consent

The written consent of the patient was obtained before submission.

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