PRES, A Lethal and Rare Side Effect of Cyclosporine: A Case Study and Review of Literature.

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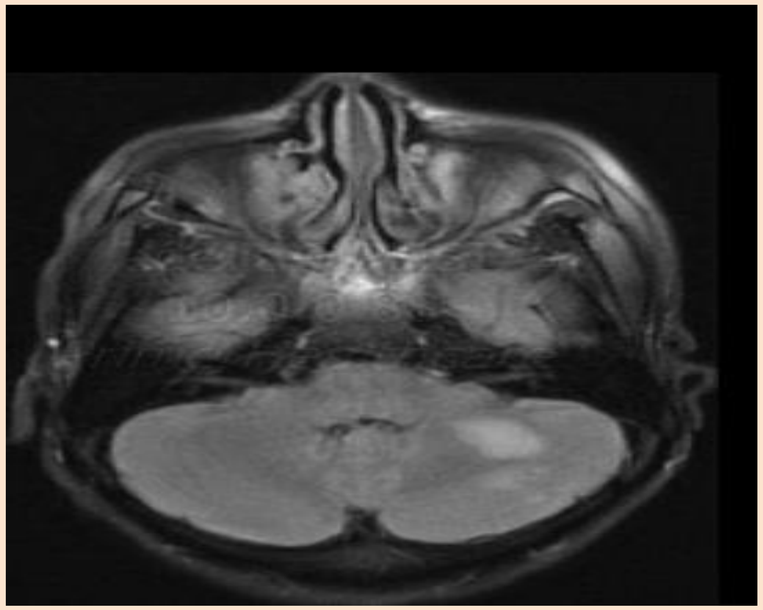
Background

Posterior Reversible Encephalopathy Syndrome (PRES) is a lethal but reversible condition caused due to impairment of cerebral perfusion autoregulatory mechanism[1].Although PRES is mostly associated with the use of immunomodulators, there are very few cases reported from the use of Cyclosporine. This is a case of a 22-year-old male on Cyclosporine who developed PRES. We want to alert the physician community to be more vigilant about close surveillance of this population who present with acute neurological changes.

However, the name used to describe the syndrome is misleading because the edema is not localized necessarily to the posterior cerebrum white matter and can appear in watershed zones other than parietal-occipital regions, thalamus, and sometimes in anterior circulation. Moreover, the syndrome is not always reversible.

Imaging

MRI showing Hyperintense FLAIR in Left Cerebellum.



Discussion

PRES occurs when cerebral perfusion autoregulation is impaired resulting in radiographic evidence of vasogenic edema[2]. It is commonly associated with Tacrolimus but can be caused by any immunosuppressive or cytotoxic medications[3]. Proposed mechanism includes direct toxic effect on vascular endothelial cells causing the release of thromboxane, endothelin and prostacyclin which disrupts the blood-brain barrier[4]. Presentation includes neurological symptoms ranging from headache to seizures. Due to its vague symptoms, PRES is occasionally missed. PRES is reversible and patients can recover within weeks if diagnosed timely. If diagnosis is delayed or missed, patients can have permanent neurological injury or even death due to high intracranial pressure. Recognition of this syndrome is critical to the institution of appropriate therapy and prevention of this lethal outcome. Treatment includes control of BP and withdrawal of offending drugs. These patients mostly present with hypertensive emergency and Nicardipine and Labetalol is the drug of choice, but nitroglycerine should never be used as it can aggravate cerebral edema[5]. PRES can even happen when the cyclosporine levels are normal[4]

Case Report

A 22-year-old male with history of Cystic Fibrosis; status post double lung and liver transplant, on Cyclosporine presented to the Emergency Department (ED) after a witnessed seizure. Patient woke up with severe occipital headache radiating to the neck, with nausea and an episode of vomiting. Within an hour he had a witnessed tonic-clonic seizure that lasted for <30 seconds. While in the ED he had another seizure episode, accompanied by transient hypertension (180/121 mmHg). Patient was treated with IV Ativan and Keppra. On physical examination he was in post -ictal state with labile blood pressures. Neurology and transplant team were consulted. They recommended to continue Keppra and to hold Cyclosporine along with checking of Cyclosporine levels. Level was found to be normal. EEG was negative. MRI showed hyperintense FLAIR and T2 signal within cortical/subcortical region of the bilateral occipital, frontal lobes, and left cerebellum along with multifocal gyral swelling. The diagnosis of PRES was established. Cyclosporine was discontinued and conservative therapy was administered. He had favorable response to cyclosporine discontinuation and had near-full reversal of encephalopathy. As per neurology and transplant team patient was continued on Prednisone and Mycophenolic acid. Rapamycin was started instead of Cyclosporine.

References

1. Gaillard, F., Smith, D. Posterior reversible encephalopathy syndrome. Reference article, Radiopaedia.org. (accessed on 23 Nov 2021) https://doi.org/10.53347/rID-1915
2. Hinduja A. Posterior Reversible Encephalopathy Syndrome: Clinical Features and Outcome. Front Neurol. 2020;11:71. Published 2020 Feb 14. doi:10.3389/fneur.2020.00071
3. Gaillard, F., Smith, D. Posterior reversible encephalopathy syndrome. Reference article, Radiopaedia.org. (accessed on 23 Nov 2021) https://doi.org/10.53347/rID-1915
4. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996;334:494–500.
5. Posterior Reversible Encephalopathy Syndrome (PRES): A Case Report and Review of the Literature Kevin G. Lazo, DO, Steven Mandel, MD, Bidyut Pramanik,MD, Jane Lee, MD, Maria V. Devita, MD, David Coven, MD, PhD, and Sandra Gelbard, MD

Conclusion

If a patient on cytotoxic agents or immunomodulators, with acute neurological symptoms and is either in hypertensive emergency or having labile blood pressure, PRES should be considered.

Clinical Symptoms To Look Out