INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Research Article

Case Report on Tacrolimus – Associated Pres

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ARTICLE INFO

Published: 15 Dec. 2024
Keywords:
Posterior reversible encephalopathy syndrome, tacrolimus, Calcineurin inhibitors
DOI:
10.5281/zenodo.14487244

ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a disorder characterized by grey and white matter abnormalities in the temporal, parietal, and occipital lobes of the brain. Clinical findings involve headache, mental status changes, focal neurological deficits, as well as visual disturbance which are also associate with characteristic imaging features of subcortical white matter lesions on computed tomography (CT) and magnetic resonance imaging (MRI). it may lead to significant morbidity and mortality if it is not diagnosed instantly. The study sheds light on importance of magnetic resonance imaging in prompt recognition of this syndrome, withholding tacrolimus may be consider to be diagnostic tool, if symptoms persists or other complications require this approach. We aimed to present our 44 years old secondary membranous nephropathy with nephrotic syndrome secondary to lupus nephritis with ANA profile S1RNP positive, right lower limb DVT provoked due to nephrotic syndrome, complicated pyelonephritis S/P D-J stent removal patient in whom we observed press following tacrolimus treatment in the light of clinical and MRI findings.

INTRODUCTION

PRES was initially described by Hinchey et.al in 1996 as a clinicoradiology entity and shortly after two other case series were published.[3] It is a neurological disorder which is characterized by variable symptoms which includes headache, vomiting, altered consciousness, seizures and visual disturbances.[4] There are numerous underlying causes of the PRES syndrome, which can arise from medical interventions (such as antineoplastic therapy) or from a PRES-related ailment (such as eclampsia or autoimmune disorders).[1] Although PRES can strike anyone at any age, with a mean age of 45, it most commonly affects young or middle-aged adults. Even after removing patients who have eclampsia, there still seems to be a female majority. Adult patients with PRES include those with up to 98% eclampsia,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

2.7%–25% after bone marrow transplantation, 7.4%–6% after solid organ transplantation, and 0.4%–0.8% in patients with end-stage renal illness or systemic lupus erythematosus[3]. Tacrolimus is a macrolide lactone derived from the bacteria Streptomyces tsukubaensis, which is used to treat a number of immune-mediated illness. This medication forms a drug receptor complex with cyclosporine. After that, this compound binds to calcineurin competitively and inhibits it. It works by preventing T-helper lymphocytes from transcriptionally expressing interleukin (IL-2), as well as preventing T-helper lymphocytes proliferation and expansion. Regretfully, tacrolimus is associated with renal and neural toxicity tacrolimus, among its other side effect of immunosuppression. One of the most uncommon presentation neurotoxicity is Posterior reversible encephalopathy syndrome (PRES).[1]

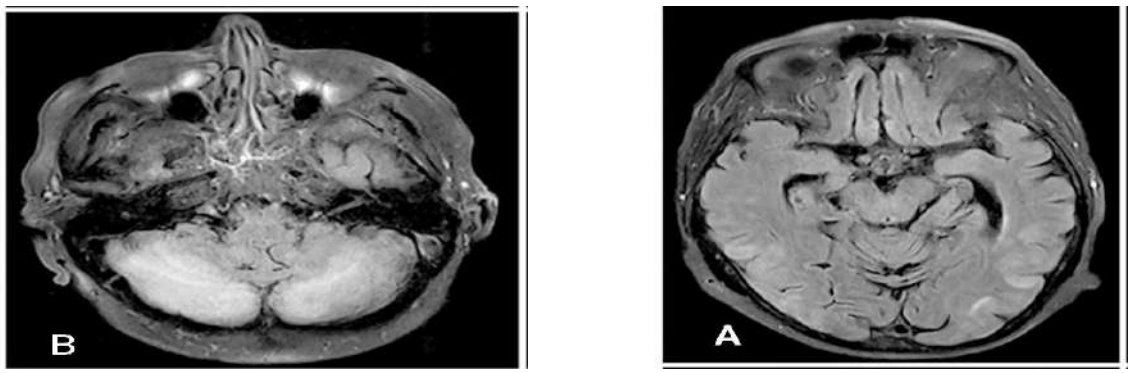
CASE REPORT

A 45year old female patient admitted to Bellary medical college and research centre, known case of secondary membranous nephropathy with nephrotic syndrome secondary to lupus nephritis with ANA profile S1RNP positive, right lower limb DVT provoked due to nephrotic syndrome, complicated pyelonephritis S/P D-J stent removal, Patient came with the complaints of convulsion 4 episodes and weakness of right upper limb and lower limb since morning at the day of admission on arrival patient is drowsy and the vitals BP 170/100mmhg, PR 110bpm, GRBS 144mg/dl, SPO2 96% On room air, on general examination B/L pitting pedal edema present. on systemic examination CNS- drowsy, pupil B/L equally reactive to light, plantar -B/L Extension, and all other investigations were within normal limits. Patient initial blood workup included a complete blood count, chemistry panel including electrolytes, renal function test, liver function test and bleeding time and all were within a normal range. MRI – vasogenic edema in the parietooccipital lobe and cerebellum in axial FLAIR.

On the basis of subjective, objective and past medical, medication history patient was on Tacrolimus twice a day for a week i/v/o secondary membranous nephropathy with nephrotic syndrome secondary to lupus nephritis after continuing for a 1 week suddenly she came with the complaints of convulsions, blood pressure 170/100mmhg as she was not hypertensive and her workup excluded any infectious or metabolic causes. Therefore, Tacrolimus toxicity was considered the most probable suggested cause for PRES and accordingly immunosuppressive change into a mycophenolate mofetil 360 mg twice a day along with this anti-convulsant, anticoagulants, antihypertensive, steroids, calcium supplement and other supportive measure were given, during hospital stay patient had no further episodes of convulsions, no bleeding manifestations. Patient was hemodynamically stable symptomatically better, hence a being discharged with the below advised medications.

LABORATORY INVESTIGATION

DAYS	CBC			RFT		LFT				COAGULATION		
	HB %	WBC Cells/cumm	PLT Lacs/Cumm	SR.CR mg/dl	UREA mg/dl	TOTAL BILIRUBIN mg/dl	SGOT U/L	SGPT U/L	ALP U/L	PT sec	INR	APTT sec
DAY 1	10.1	13150	2.08	0.9	22	0.5	12	16	108	14	1.15	32.8
DAY 2	8.6	5800	1.68	0.7	17	0.5	17	12	113			



MRI : **vasogenic edema in the Parieto-occipital lobe and cerebellum in axial FLAIR.**

TREATMENT GIVEN DURING HOSPITALIASATION

Sr. No	Medication	Dose	Route	Frequency	Duration
01	TAB.PHENYTOIN	100mg	PO	1-0-1	2 Days
02.	TAB. LEVETIRACETUM	500mg	PO	1-0-1	5 Days
03.	INJ. CEFTRIAXONE	1g	IV	1-0-1	5 Days
04.	TAB. PREDNISOLONE	10mg	PO	1-0-0	7 Days
05.	TAB. PANTOPRAZOLE	40mg	PO	1-0-0	7 Days
06.	TAB. APIXIBAN	5mg	PO	1-0-1	7 Days
07.	TAB. NICARDIARETARD	20mg	PO	1-0-1	7 Days
08.	TAB. ATORVASTATIN	40 Mg	PO	0-0-1	7 Days
09.	TAB. CALCIUM AND VITAMIN D3	500mg	PO	1-0-1	7 Days
10.	TAB. MYCOPHEOLATE MOFETIL	360mg	PO	1-0-1	7 Days

DISCGARGE MEDICATIONS

Sr. no	MEDICATION	DOSE	ROUTE	FREQUENCY	DAYS
01.	TAB. AZITHROMYCIN	500mg	PO	1-0-0 1-0-1	5 days
02.	TAB. MYCOPHEOLATE MOFETIL	360mg	PO	1-0-1	30 days
03.	TAB. PREDNISOLONE	20mg	PO	1-0-1	30 days
04.	TAB. LEVETIRACETUM	500mg	PO	1-0-1	30 days
05.	TAB. APIXIBAN	5mg	PO	1-0-1	30 days
06.	TAB. NIFEDIPINE	20mg	PO	1-0-1	30 days
08.	TAB. CALCIUM AND VITAMIN D3	500mg	PO	1-0-1	30 days
09.	TAB. ATORVASTATIN	40mg	PO	0-0-1	30 days
10.	TAB. PANTOPRAZOLE	40mg	PO	1-0-0	10 days

DISCUSSION

PRESS is clinicoradiological diagnosis that is based on combination of typical clinical features and risk factors, and supported by magnetic resonance imaging findings.[2] PRES , as the name suggests, is a constellation of symptoms associated with vasogenic edema, most commonly, the posterior cerebral vasculature, of the posterior cerebral vasculature, often affecting the parietal occipital region. Other vascular territories can also be affecting in PRES, such as the posterior portion of frontal lobe and temporal lobe.[10] Numerous investigations have noted varying frequency of signs and symptom in PRES by Fisher M et al i.e Encephalopathy 28-92% Disorder of consciousness 67-90% Acute arterial hypertension or blood pressure fluctuations 61-80% Epileptic seizures 70-74% Visual disturbance 20-67% Headache 26-53% Focal neurological signs 5-15%.[5] Our patient developed sudden onset of convulsions 4 episodes, and weakness of right upper and lower limb (symptoms consistent with PRES). Tab. tacrolimus can cause hypertension, as the risk factor mentioned in literature, our patient also had high blood pressure while on oral Tab. Tacrolimus therapy which promptly responded to discontinuations of accused medication. Although the precise pathogenesis of PRES remains unclear, Hypertension & endothelial damage appear to be constant feature. Hypertension is the most common precipitating factor with endothelial dysfunction, the pathogenesis of PRES can be explained by multiple process such as (i) Failure of auto regulation causing vasogenic edema (ii) Disruption or damage of Blood Brain Barrier (BBB) (iii) cerebral vasoconstriction. Upon disruption of autoregulation, which mains as steady blood supply to the brain despite variations in systemic pressure, elevated perfusion pressure leads to disruption resulting in hyper perfusion and extravasation of protein and fluid into interstitial space, which inter cause vasogenic edema.[4]

Diagnosis fugate et al. suggested the following criteria for the diagnosis of PRES 1. Acute onset of Neurological symptoms 2. Neuroimaging abnormalities of vasogenic edema (focal / confluent) 3. Reversibility of clinical and/or radiological findings. The most sensitive routine magnetic resonance imaging (MRI) sequence for identifying subcortical and cortical lesions in PRES is fluorescence-assisted inversion recovery, or FLAIR. Vasogenic edema-induced bilateral and symmetrical regions of hyperintensity in the posterior parietal and occipital lobes have been the traditional descriptions of PRES on T2-weighted MRI and FLAIR. In our patient, MRI finding that symmetric bilateral white matter lesions with cortical involvement in parietooccipital lobe and cerebellum. In our case unlike those described in literatures. [5] Treatment early diagnosis and therapy beginning are crucial components of PRES management. An intensive care unit (ICU) may be necessary for many patients in order to aggressively manage symptoms such seizures, encephalopathy, and status epilepticus.[4] Tacrolimus dose adjustment involves immediate reduction or discontinuation of tacrolimus to resolve symptoms and prevent permanent neurological damage. The acute management of PRES is supportive and includes removing or reversing any suspected cause. supportive measures such as controlling blood pressure, manging seizure or other cause and correcting electrolyte imbalances. Blood pressure control is still the cornerstone of management. In order to prevent fluctuations, continuous IV infusion is typically necessary. However, the selection of antihypertensive medications is based on standard guidelines for the treatment of hypertensive emergencies or crises in the general public. The objective is to lower blood pressure to 160/100 mmHg in the first six hours and to lower MAP by

20 –25% in the first two hours. Nevertheless, despite a known link between hypertension and other conditions.[5] The management of PRES primarily adopts a symptomatic approach , with a key emphasis on regulating blood pressure. Additionally, when feasible, discontinuation of the causative drug is recommended. In cases where immediate cessation is impractical, considering dose reduction becomes a viable alternative. For individuals presenting with seizures , the administration of anti-seizures medications (ASMs) may be necessary. A standard practice involves tapering ASMs as symptoms alleviates and MRI findings show resolutions, a trend observed in majority of patients.[9] PRES is generally reversible with timely intervention, but delays in recognizing symptoms or adjustment in tacrolimus levels can lead to lasting neurological deficits. prevention strategies include regular monitoring of the blood levels for patients taking Tab tacrolimus, particular in patient with renal or hepatic impairment. propose routine neurological assessment for patient with risk factors to help detect PRES symptoms early. an individualized treatment plan, tailored to each patient need and risk profile is critical for achieving a balance between effective immunosuppression and neurological safety. This careful, proactive management strategy is essential for maximizing the risk of adverse neurological outcomes.[6]

CONCLUSION

Tacrolimus associated PRES is a rare and serious complication. This syndrome should be promptly recognised as it recognised potentially reversible and generally response to withholding or decreasing the dose of tacrolimus in addition to controlling hypertension and seizures[1]. PRES generally has good prognosis; prompt recognition and management are important in preventing significant disease morbidity and mortality.[7]

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HOW TO CITE: Dr. Harris Kajal S. K*, Dr. Bhavani, Case Report on Tacrolimus – Associated Pres, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 12, 2175-2180. https://doi.org/10.5281/zenodo.14487244