International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

A Case Report on Systemic Lupus Erythematosis, Lupus Nephritis, Acute Pancreatitis, Posterior Reversible Encephalopathy Syndrome (PRES), Macrophage Activating Syndrome (MAS)

S. Mohamed Ashik Ali[1], P. Muhammed Nishad[2], A. Priya[2], K. Arun Chander[3]*

Department of Clinical Pharmacology, Apollo Children's Hospital, Chennai, Tamil Nadu, India

*Correspondence:
Dr. K. Arun Chander
Consultant and Head,
Department of clinical pharmacology
Apollo Children's Hospital,
Greams Road, Thousand Lights
Chennai
Email: clinicalpharmaach_cni[at]apollohospitals.com

Abstract: ***Systemic lupus erythematous is an autoimmune disease. Healthy tissues mistakenly damaged by the immune system of its own. Skin, joints, of the body brain, kidneys and other organs of the body were damaged. It is characterized by antibodies to nuclear and cytoplasmic antigens, multisystem inflammation, protean clinical manifestation and a relapsing and remitting course. More than 90% of cases of SLE occur in women, frequently starting at childbearing age. Lupus nephritis is a frequent complication of SLE. It damages structures of kidneys that filter out waste. It causes inflammation and may lead blood and protein in the urine and creates high blood pressure sometimes kidney failure too. Inflammation of the pancreases indicates pancreatitis and of two types depending upon the degree of abdominal pain and pancreatic damage. One is acute pancreatitis and another one will be chronic pancreatitis. Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by a headache, seizures, altered mental status and visual loss and characterized by white matter vasogenic oedema affecting the posterior occipital and parietal lobes of the brain predominantly. This clinical syndrome is increasingly recognized due to improvement and availability of brain imaging specifically magnetic resonance imaging (MRI). Macrophage activation syndrome (MAS) is a severe complication of rheumatic disease in childhood, particularly in systemic Juvenile Idiopathic Arthritis (SJIA). It is characterized by an uncontrolled activation and proliferation of T lymphocytes and macrophages.***

Keyword: Systemic Lupus Erythematosus, Lupus Nephritis, Acute Pancreatitis, Posterior Reversible Encephalopathy Syndrome (PRES), Macrophage Activating Syndrome (MAS)

1.Introduction

Systemic Lupus Erythematous and Lupus Erythematous:

Systemic lupus erythematous is an autoimmune disease. Healthy tissues of the body mistakenly damaged by the immune system of its own. Skin, joints, brain, kidneys, and other organs of the body were damaged. It is characterized by antibodies to nuclear and cytoplasmic antigens, multisystem inflammation, protean clinical manifestation, and a relapsing and remitting course. More than 90% of cases of SLE occur in women, frequently starting at childbearing age. Lupus nephritis is a frequent complication of SLE. It damages structures of kidneys that filter out waste. It causes inflammation and may lead blood and protein in the urine and creates high blood pressure sometimes kidney failure too.

Diagnosis procedure for SLE and Lupus Nephritis:

Auto immune work up will perform to diagnose SLE. Positive tests of ANA, Anti ds DNA, low C3 and C4 levels, direst coomb's test indicates presence of SLE. Also, protein urine with plenty of RBC will be present indicates lupus nephritis.

Treatment for SLE:

Steroids and Anti biotic.

Acute Pancreatitis:

Inflammation of the pancreases indicates pancreatitis and of two types depending upon the degree of abdominal pain and pancreatic damage. One is acute pancreatitis and another one will be chronic pancreatitis.

Diagnosis procedure for Acute pancreatitis:

Acute abdominal pain and tenderness in the upper abdomen, elevated levels of pancreatic enzyme in the blood, urine, or ascitic fluid and abnormal imaging findings in the pancreas associated with acute pancreatitis.

Treatment for acute pancreatitis:

H2 receptor antagonist
Proton pump inhibitors

Antibiotics

Pancreatic surgery if needed.

Posterior Reversible Encephalopathy Syndrome (PRES):

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome characterized by a headache, seizures, altered mental status and visual loss and characterized by white matter vasogenic oedema affecting the posterior occipital and parietal lobes of the brain predominantly. This clinical syndrome is increasingly recognized due to improvement and availability of brain imaging specifically magnetic resonance imaging (MRI).

Diagnosis procedure for Posterior reversible encephalopathy syndrome (PRES):

Neurological symptoms of acute onset
Neuroimaging abnormalities of vasogenic oedema
Reversibility of clinical and radiological findings and Magnetic Resonance imaging (MRI).
Treatment for Posterior reversible encephalopathy syndrome (PRES):
There is no direct treatment for PRES, other than removing or treating any underlying cause.

Macrophage Activating Syndrome (MAS):

Macrophage activation syndrome (MAS) is a severe complication of rheumatic disease in childhood, particularly in systemic Juvenile Idiopathic Arthritis (SJIA). It is characterized by an uncontrolled activation andproliferation of T lymphocytes and macrophages.

Diagnosis procedure for Macrophage Activating Syndrome (MAS):

Bone Marrow Examination
Ferritin levels
CRP and ESR.

Treatment for Macrophage Activating Syndrome (MAS):

Steroid therapy
Anakinra (Interleukin antagonists)

2.Case Report

A 10-year-old male child having body weight of 27 kgs developmentally normal presented on 24th Feb 2022 with low grade fever on and off for 3 months, not associated with chills and rigors. History of increased fatigability for 3 months and loss of appetite for 1½ month, history of weight loss for 1½ month (2 kg reduced in one month) and no history of swelling in the body, no history of bleeding manifestation, previous blood transfusion, vomiting, abdominal pain, rash, joint pain, breathing difficulty, haematuria, and no history of contact with tuberculosis.

His history shows no medical and surgical history with proper immunization history completed up to date and no family history for the same.

General examination shows no Cyanosis, oral cavity or normal, bilateral non-significant multiple cervical lymphadenopathies of Lymph nodes, no pallor, no clubbing, no icterus. Pulse shows 102/min, temperature shows 98.4°F, respiratory rate shows 24/min.

CNS shows no focal neurological deficit, genitals are normal, CVS shows s1 and s2 are heard normal and no murmurs. RS shows bilateral air entry equal and normal vesicular breath sounds.

Haematological reports showed pancytopenia (HB=b-6.9gm/TC-1970/Platelets-34000). Peripheral blood smear was unremarkable. In view that pancytopenia, haematologist opinion was sought and done bone marrow aspiration which revealed hypocellular marrow with no atypical lymphocytes ruling out the possibility of leukaemia. PRBC CT was done due to persistent fever, which revealed significant cervical, supraclavicular, mediastinal, bilateral hilar, axillary, inguinal nodes and abdominopelvic lymph nodes with hepatosplenomegaly and bulky pancreas. Hence lymphoma was suspected, and cervical node biopsy was done which showed only reactive pattern, ruling out lymphoma.

He was started with broad spectrum antibiotics on 24th Feb 2022 (Piperacillin and tazobactam-2.7g of Piperacillin) and given for 7 days and stopped as cultures were sterile. As he had persistent fever spikes, further investigations were done to look for evidence of other common infection like malaria, scrub typhus, infectious mononucleosis, brucellosis, CMV and dengue which were all negative. A diagnosis of MISC was also suspected as his covid antibody was positive but ruled out as his CRP and other inflammatory markers were negative. ECHO was done to rule out endocarditis and to look for any coronary artery involvement and it was negative.

Autoimmune work up was done on 2nd March 2022, and he was tested positive for Anti-Nuclear antibodies (ANA) (strongly positive), Anti double stranded DNA (Anti ds DNA), low C3 and C4 levels, direst coomb's test was positive, urine spot protein creatinine ratio was in nephrotic range. Hence the diagnosis of systemic lupus erythematous (SLE) with lupus nephritis was made. As per rheumatologist advice he was started on pulse therapy, Inj. Methylprednisolone 800mgIntravenous continuous infusion (30mg/kg) was given for 3 days followed by tapering dose of steroids and Right Cervical lymph node Biopsy was done.

He developed severe abdomen pain on day 4 (5th March 2022) of pulse steroid with elevated serum amylase and lipase which was suggestive of SLE induced acute pancreatitis confirmed by USG abdomen. Hence gastroenterologist opinion was sought and was managed conservatively. Inj. Pantoprazole 30mg twice daily intravenously was added. His Hb levels (HB=b-6.9gm) falls below the reference range and potassium, calcium

levels also fall. Significantly Tab. Folic acid 5 mg once daily, Tab. Urdodeoxycholic acid 150 mg BD, Cholecalciferol 60000IU sachets once in a week, Tab. spirnolactone25 mg BD, Lactulose solution 7.5 ml once in a day at bedtime and Multi vitamin syrup was given, and it enhances child physiology as well.

He had urine protein of 2+ with plenty of RBC, low C3, C4 level in the background of ANA and dsDNA positivity suggestive of lupus nephritis, hence he was given premedication as Inj. Ondansetron 4mg Intravenously followed by 1st dose of Cyclophosphamide 500 mg in 200 ml ½ NS over 2 hours with Mesna 180 mg on 6/3/2022.

On day 6 (7th March 2022) of starting steroids, he was developed multiple episodes of seizures with elevated blood pressure, hence he was shifted to PICU and managed with anti-hypertensives (Inj. Labetalol 20 mg infusion was started, and Inj. Clonidine 100 mcgTDS intravenously and later changed to oral antihypertensives, Tab. Metoprolol 25 mg TDS and Tab. Nifedipine 15 mg QID) and seizure drugs (Inj. Fosphenytoin 100 mg BD intravenously, Inj. Lacosam 50 mg BD intravenously and Inj. Levetiracetam 500mg BD intravenously). MRI brain done on 8/3/2022 had features of PRES. On 11.3.22 child had recurrence of seizures with hypertension, so labetalol infusion restarted, Tab. Prazosin 2.5mg TDS was added, and other antihypertensive doses escalated. His blood pressure was kept under control with adequate anti-hypertensive coverage.

Blood investigations showed worsening of pancytopenia with increasing Ferritin levels up to 10000 with low C-Reactive Protein (CRP) and Erythrocyte's sedimentation Rate (ESR), multi organ involvement in the form of hepatitis and serositis hence MAS considered. So, Methyl prednisolone dose was increased to 20mg/Kg followed by 10mg/Kg for 3 days and Tab. Cyclosporin 25mg BD was added. Since he had recurrence of seizures with hypertension, multi-disciplinary meeting involving pediatric intensivist, primary pediatrician, nephrologist, and rheumatologist made a decision to reduce the dose of methyl prednisolone, increase the dose of cyclosporine and to add Anakinra 100 mg (given for 7 days) and Tab. Hydroxychloroquine 200mg OD. In view of persistent pancytopenia with worsening counts, increase in Ferritin and persistence of altered sensorium despite adequate BP control, possibility of worsening MAS was considered and managed with plasma exchange and given 5 cycles.

Post plasma exchange, child remained stable with control of hypertension and improvement of blood counts. Anti-hypertensives were gradually decreased after shifting out of ICU. Anti-epileptics (Tab. Levetiracetam 500mg BD and Tab. Lacosamide 50mg BD) were changed to oral. He was found to have hyperkalemia drug induced; hence Calcium polystyrene sulphonate 7.5g twice daily orally was added along with low potassium diet. As the blood pressure was under control with metoprolol and nifedipine.

On Right cervical lymph node biopsy and Bone marrow aspiration was done Inj. Rituximab 300 mg in 300 ml NS over 8 hours of continuous intravenous infusion as 1st dose was given on 28/3/2022 in view of persistent proteinuria to which he tolerated well. His renal parameters were normal throughout the hospitalization.

Inj. Rituximab 300 mg in 300 ml NS over 8 hours as final dose was given on 4th April 2022 and hence is being discharged with an advice of follow up as outpatient was advised.

3.Discussion

In patients with systemic lupus erythematous especially lupus nephritis Anti-malarial play a major role. Hydroxy chloroquine settles down the lupus nephritis among the SLE individuals. Better therapeutic outcome and lower mortality rates are associated with reduced hypertension, thrombosis, and an infection. Previous case reports also convey the same treatment strategy for SLE[1]. In anterior hypothalamus thermoregulatory is present and it regulates the body temperature. This response to stimulation of pyrogenic cytokines. The activated macrophages and monocytes procure factors namely Interleukin-1, Interleukin-6, Tumor Necrosing Factor, TNF-α, TNF-ɤ, TNF-β. Among them IL-1 is responsible for susceptibility to SLE in Asian and European population. Anakinra is IL-1 receptor antagonist in auto inflammatory disease, and it provide better clinical outcomes and well serological improvements. Case reports also suggests that anakinra having huge advantages over other medications in the treatment of recurrent fever in SLE[2]. Though steroids having strong anti-inflammatory action used worldwide for SLE conditions comes under autoimmune diseases. Here also steroids state a strong response among treatment outcomes[3]. Like previous case reports cyclophosphamide well involved in treating SLE and patient responds well for Cyclophosphamide therapy[4]. It is a traditional and golden approach in treating SLE. According to the treatment guidelines cyclosporin a potent immunosuppressant found to have safest drug among all and patient too responds with this therapy in this case[5, 6]. Rituximab having some better outcomes in lupus nephritis and in this case, it worked as well and expected therapeutic outcome occurred with depreciation of proteins that bound in the urine called protienurea[7, 8, 9]. Steroid pulse therapy will be effective in macrophages activating syndrome and hence the patient was treated with methylprednisolone as 30mg/kg regarding pulse therapy and then tapering the dose of methylprednisolone followed by oral steroid therapy[10]. Posterior reversible encephalopathy syndrome will cause hypertension along with seizures. So that labetalol infusion was started along with fosphenytoin therapy so that the child was under control with seizures and hypertension. Previous reports conveys the above statements that are very responsive among seizure with hypertension[11, 12, 13].

4.Conclusion

Systemic lupus erythematous (SLE) is one of the most life-threatening diseases among populations especially in children and woman. Although earlier diagnosis can recover patient through the treatment guidelines having

for SLE. Most of the cases were responds to steroid therapy and immunosuppressants like Cyclosporine, Cyclophosphamide with certain adverse effects hence it cannot used for long duration. RTX also hold a fine role in the treatment of lupus nephritis with the degree of cycles of doses which depend upon the patient physiological and biochemical parameters. Steroids, immunosuppressants along with antimalaria drug like hydroxychloroquine will be well beneficial treatment among SLE and the complications occurred. Thus, adding vitamin supplements and iron supplementswill be more effective in the treatment adherence of SLE. Moreover SLE will be treatable when it diagnosed earlier as possible with the proper treatment strategies that followed in this case as well

Reference

[1] Sisó A, Ramos-Casals M, Bové A, Brito-Zerón P, Soria N, Muñoz S, Testi A, Plaza J, Sentís J, Coca A. Previous antimalarial therapy in patients diagnosed with lupus nephritis: influence on outcomes and survival. Lupus.2008 Apr; 17 (4): 281-8.
[2] Dein E, Ingolia A, Connolly C, Manno R, Timlin H. Anakinra for recurrent fevers in systemic lupus erythematosus. Cureus.2018 Dec 27; 10 (12).
[3] Kondo M, Matsushima Y, Iida S, Umaoka A, Nakanishi T, Habe K, Yamanaka K. Successful treatment with oral steroid and hydroxychloroquine in a patient with systemic lupus erythematosus upon COVID-19 infection: A case report with detailed laboratory data. Clinical case reports.2021 Aug; 9 (8)
[4] Petri M. Cyclophosphamide: new approaches for systemic lupus erythematosus. Lupus.2004 May; 13 (5): 366-71.
[5] Griffiths B, Emery P. The treatment of lupus with cyclosporin A. Lupus.2001 Mar; 10 (3): 165-70.
[6] Tarr T, Zeher M, Szegedi G, Kiss E. Ciclosporin A kezeléssel szerzett tapasztalataink szisztémás lupus erythematosusban [Clinical experiences with cyclosporin A in patients with systemic lupus erythematosus]. Orv Hetil.2005 Dec 4; 146 (49): 2485-9. Hungarian. PMID: 16398313.
[7] Sinha R, Agrawal N, Xue Y, Chanchlani R, Pradhan S, Raina R, Marks SD. Use of rituximab in paediatric nephrology. Archives of disease in childhood.2021 Nov 1; 106 (11): 1058-65.
[8] Basu B, Roy B, Babu BG. Efficacy and safety of rituximab in comparison with common induction therapies in pediatric active lupus nephritis. Pediatric Nephrology.2017 Jun; 32 (6): 1013-21.
[9] Stolyar L, Lahita RG, Panush RS. Rituximab use as induction therapy for lupus nephritis: a systematic review. Lupus.2020 Jul; 29 (8): 892-912.
[10] Boom V, Anton J, Lahdenne P, Quartier P, Ravelli A, Wulffraat NM, Vastert SJ. Evidence-based diagnosis and treatment of macrophage activation syndrome in systemic juvenile idiopathic arthritis. Pediatric Rheumatology.2015 Dec; 13 (1): 1-3.
[11] Rijal JP, Giri S, Dawadi S, Dahal KV. Posterior reversible encephalopathy syndrome (PRES) in a patient with late postpartum eclampsia. Case Reports.2014 Feb 27; 2014: bcr2013203162.
[12] Rijal JP, Giri S, Dawadi S, Dahal KV. Posterior reversible encephalopathy syndrome (PRES) in a patient with late postpartum eclampsia. Case Reports.2014 Feb 27; 2014: bcr2013203162.
[13] Rijal JP, Giri S, Dawadi S, Dahal KV. Posterior reversible encephalopathy syndrome (PRES) in a patient with late postpartum eclampsia. Case Reports.2014 Feb 27; 2014: bcr2013203162.
[14] Washio, M., Kiyohara, C., Ohta, A. Epidemiology of Systemic Lupus Erythematosus. In: Lionaki, S., editor. Lupus-New Advances and Challenges [Internet]. London: IntechOpen; 2019 [cited 2022 Apr 24]. Available from: https://www.intechopen.com/chapters/65635 doi: 10.5772/intechopen.84146
[15] Eddy AA, Symons JM. Nephrotic syndrome in childhood. The lancet.2003 Aug 23; 362 (9384): 629-39

Acknowledgement

We would like to express our sincere thanks towards the Department of Pediatrics for helping us by providing all the data's necessary to incorporate in this case report.

Declarations

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required