ABSTRACT

Posterior Reversible Encephalopathy Syndrome is a clinic-radiological entity presenting with headache, seizures, visual alterations etc. with transient lesions on neuroimaging. There are various conditions like toxemia in pregnancy, toxic agents, post-transplantation, infections, autoimmune diseases etc. which can cause this syndrome. Here we present case report of a 10 years old child suffering from acute lymphoblastic leukemia who developed posterior reversible encephalopathy syndrome after methotrexate therapy. Prompt diagnosis of posterior reversible encephalopathy syndrome is utmost important to avoid delay in therapy and complications.

KEYWORDS: childhood ALL, methotrexate, posterior reversible encephalopathy syndrome.

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) was first described and reported by Hinchey et al in 1996. PRES is a clinic-radiological entity presenting with headaches, nausea, vomiting, impaired consciousness, seizure activity, visual abnormality, focal neurological deficit and hypertension with varying incidence in different reported case series and radiologically characterized by presence of vasogenic oedema with four radiologic patterns including holohemispheric watershed pattern, superior frontal sulcus pattern, dominant parietal-occipital pattern, partial or asymmetric expression of the primary patterns. Common conditions at risk of PRES include toxemia in pregnancy (preeclampsia/eclampsia), post-transplantation (allogenic bone marrow transplantation, solid organ transplantation), immune suppression (cyclosporine, Tacrolimus, infection/sepsis/shock, autoimmune diseases, post cancer chemotherapy and many other conditions. Cancer chemotherapeutic agents lead to PRES include combination chemotherapy with alkylating agents (cisplatin, oxplatin, carboplatin), anti-metabolites (gencitabine, cytarabine, methotrexate), mitotic inhibitors (vincristine, irinotecan hydrochloride), L-asparaginase, vincristine, bevacizumab, rituximab, interferon-alpha etc. There were two possible contradictory hypothesis about pathogenesis of PRES - a) cerebral hyperperfusion exceeding the capacity for autoregulation of perfusion pressure results in vasogenic edema, b) cerebral hypoperfusion causing disruption of the blood-brain barrier and leads to vasogenic edema.

CASE REPORT

A 10 years old male child was presented with high grade intermittent fever and joint pain for last two and half months with history of gum bleeding 2 months back and diagnosed as a case of CALLA positive B- acute lymphoblastic leukemia (B-ALL), standard risk group. He was started on chemotherapy according to BFM-90 protocol. On day 14 of induction phase A chemotherapy, he was given intrathecal methotrexate. On day 15, he developed sudden bilateral loss of vision and one episode of focal tonic clonic seizure with secondary generalization. On examination, blood pressure was 140/90 mm of Hg. Serum sodium, potassium, calcium, phosphate levels were within normal limit. Computed tomography of brain was normal. Magnetic resonance imaging (MRI) of brain [figure 1] revealed multifocal areas of hyper-intense lesions on T2 weighted images & fluid-attenuated inversion recovery (FLAIR) sequences with no contrast enhancement in T1-weighted sequences involving both the parietal lobe, right temporal cortex, and central part of Pons. Cerebrospinal fluid study was normal. He was managed with intravenous phenytoin followed by oral levetiracetam. Second dose of intrathecal methotrexate was withheld and rest of the chemotherapy was continued. Repeat MRI after 11 days showed the lesions were completely resolved except altered signal intensity seen within the central part of the Pons [figure 2]. Diagnosis of post-chemotherapy (methotrexate) posterior reversible encephalopathy syndrome was made. After completion of phase A induction chemotherapy, his bone marrow was in
remission and phase B induction chemotherapy was completed. He is now on consolidation phase of chemotherapy.

LEGEND FOR FIGURES

Figure 1: Magnetic resonance imaging (MRI) of brain in a patient with posterior reversible encephalopathy syndrome (PRES). Fluid-attenuated inversion recovery (FLAIR) sequences showing high-intense lesions involving both parietal lobes, right temporal cortex, and central part of Pons.

Figure 2: Repeat MRI after 11 days showed the lesions completely resolved except altered signal intensity seen in the central part of the Pons.

DISCUSSION

PRES is well documented in childhood cancer, most commonly seen in Acute Lymphoblastic Leukaemia (ALL) (55%). Hypertension is most common association and seizure being one of the most common presentations. PRES in childhood cancer may be due to infection, metabolic abnormalities, central nervous system (CNS) involvement by malignancy, methotrexate encephalopathy and stroke. In our patient we had ruled out metabolic derangements, infection and CNS involvement by malignancy. So chemotherapy related toxicity was one possible explanation of PRES. In a study by Parasole R et al, 10 out of 253 (4%) children with ALL, enrolled for therapy, developed PRES. Dicuonzo F et al reported intrathecal methotrexate induced PRES in a 15 year old girl with ALL. Our patient was receiving vincristine, daunomycin, L-asparaginase as per BFM 90 protocol and also received one dose of intrathecal methotrexate on 14 days, one day before developing PRES. In the study of 115 cases (109 patients) by Fugate JE et al, most common abnormality on neuro-imaging (by MRI) in PRES is edema involving the white matter of parieto–occipital regions (94%), followed by the frontal lobe (77%), temporal lobe (64%), and cerebellum. Follow-up imaging often show evidence of radiologic improvement, partial or complete. In our case the MRI showed involvement of bilateral parietal lobe, right temporal lobe, and central part of Pons. Repeat MRI after 11 days showed lesions were completely resolved except central part of Pons. The management of PRES includes control of hypertension, removal of offending agents and anticonvulsant therapy in cases with seizures. We managed our case with anti-convulsant therapy, withhold the second dose of intrathecal methotrexate and delayed other chemotherapy schedule for 1 week. Patient was responded to therapy and our patient was recovered without any further complications. The etiology of PRES in our case was thought to be chemotherapeutic agents, particularly intrathecal methotrexate, as we were able to continue other chemotherapeutic agents after one week without reappearance of PRES symptoms or any further complications.

CONCLUSIONS

PRES in childhood leukemia though very rare, it is well documented. High index of suspicion and early neuroimaging is utmost important to diagnose such cases to avoid complications and delay in chemotherapy protocol.

REFERENCES


