International Journal of Advanced Research and Review

www.ijarr.in

A RARE IDIOSYNCRATIC REACTION TO PHENYTOIN AND CARBAMAZEPINE – CASE REPORT

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ABSTRACT

Phenytoin and carbamazepine are the most widely used antiepileptics. This case report is about rare idiosyncratic complication of long term use of phenytoin and carbamazepine induced myelosuppression in tertiary care hospital, Vijayapur, Karnataka. We report a case of an 18-year-old female patient, known case of seizure disorder for 6years for which she was on phenytoin and carbamazepine. The patient presented with complaints of nasal bleeding and fever. Peripheral smear showing Pancytopenia (severe normocytic normochromic anemia with neutropenic leucopenia). Bone tissue biopsy report showed Hypo cellular marrow suggestive of Aplastic anemia. CT brain showing Leptomeningeal enhancement in parasagittal region of left parietal lobe – suggestive of focal meningitis the patient was treated with broad-spectrum antibiotics, antifungal, granulocyte colony stimulating factor, cyclosporine, and blood transfusion. Even after best efforts the patient's condition worsened and collapsed. So the life-threatening complication like myelosuppression should be diagnosed early and appropriate management is the key in such complications. Reporting of such cases is necessary to create awareness among the clinicians.

Keywords: Phenytoin, Carbamazepine, Myelosuppression

INTRODUCTION

Phenytoin and Carbamazepine are most prescribed for seizure disorder as monotherapy as well as combined therapy since decade[1]. Some of the idiosyncratic adverse reactions include gingival hyperplasia, skin rashes, agranulocytosis, and myelosuppression etc[2].

The prevalence of aplastic anemia appears to be 1in 200,000 in those patients treated with carbamazepine monotherapy[3]. Myelosuppression is commonly observed adverse effects following cytotoxic chemotherapy. Drug-induced myelosuppression due to non-cytotoxic agents like phenytoin, carbamazepine are very rare, unpredictable and life-threatening as it increases the risk of infection[4,5,6].

This study reports a rare case of myelosuppression associated with long term use of phonation and carbamazepine.

CASE REPORT

An 18 year old female referred from the civil hospital, Vijayapura to tertiary care hospital, Vijayapur in view of fever since 1 month and persistent nasal bleed since 7 days. The patient was a known case of seizure disorder for 6 years, on tablet phenytoin 100 mg BD and tablet carbamazepine 200 mg BD. On examination, patient had pallor and nasal pack in situ, soaking present. Gingival hyperplasia present. There was no h/o trauma, rash, hematuria or blood in stools. Patient was afebrile and vitals were normal. She was not a known case of hypertension, diabetes mellitus and tuberculosis.

On first day , Patient WBC was 540 cells/cmm, neutrophils are 1.8%, lymphocytes 96.3%, hemoglobin -4.5gm%, platelets – 5000/cmm, INR -1.13, serum bilirubin – 0.5 mg/dl, Reticulocyte production index (RPI) -0.002%, peripheral smear was showing Pancytopenia (severe normocytic normochromic anemia) with neutropenic leucopenia). Her Serum bilirubin (total) -2.6mg/dl, conjugated bilirubin -2.1mg/dl unconjugated bilirubin -0.5 mg/dl, SGOT – 73 Units/L, SGPT – 263Units/L. HIV Rapid, HbsAg (spot test), HCV(spot test), Hepatitis A virus (spot test) were all negative. The patient was treated empirically with broad spectrum antibiotics, antifungals, antacids, Iv fluids, and Inj. tranexamic acid, Inj. Vitamin k, Inj levetiracetam and phenytoin, and carbamazepine were stopped.

On the third day, the patient had nasal bleeding, Inj. tranexamic acid IV stat given; adrenaline-soaked nasal packs had been put. 1 unit blood transfusion done. BP was 106/56mmhg, GC was fair. Fundoscopy showed bilateral anemic retinopathy. Bone marrow biopsy and aspiration done, aspiration was dry and tissue biopsy report showed Hypocellular marrow suggestive of Aplastic anemia. So, Granulocyte colony-stimulating factor was added to treatment.

On the fifth day, the patient was drowsy. WBC was 380 cells/cmm, neutrophils are 2.6%, lymphocytes 97.4%, hemoglobin -3.3 gm%, platelets – 19000/cmm .The patient developed high-grade fever associated with chills recorded temp was106F. Blood culture isolated E coli and antibiotics were escalated according to culture and sensitivity. CT brain contrast done showed Leptomeningial enhancement in parasagittal region of left parietal lobe – suggestive of focal meningitis. Blood Phenytoin levels were <0.5 microgram/ml. Tab. Cyclosporine added.

On the next day, the patient was febrile recorded temp -104F, she continued to be drowsy. Patient became breathless; saturation dropped to 70 % @ room air, Supportive care was given. Patient was tachypneic, pulse was feeble, BP was 50 systolic, b/l crackles on auscultation. Vitals were deteriorating, patient was intubated and put on mechanical ventilator, ionotropic support was given. Even after the best efforts the patient collapsed.

DISCUSSION

Phenytoin is widely prescribed for treatment and control of generalized tonic clonic, complex partial and psychomotor seizures. Carbamazepine is the drug of choice for patients with partial seizure[7]. Non cytotoxic agents like phenytoin, carbamazepine rarely causes myelosuppression. These types of myelosuppression which are usually not anticipated, are idiosyncratic(type B) and needs more attention and are unlike the dose dependent effects of cytotoxic chemotherapeutic agents which are predictable and amounts to type A myelosuppression that are reversible at clinical dosages. Early diagnosis, hygiene, isolation, and proper hydration is

the key in such cases. Broad-spectrum antibiotics, antifungals covering is a must. A Few case studies suggest the use of Granulocyte colony stimulating factor is effective in drug-induced agranulocytosis[8,9]. For prolonged, drug-induced myelosuppression treatment options may include therapeutic immunosuppression using high dose corticosteroids, cyclosporine or bone marrow transplantation4,5.

CONCLUSION

Even though Phenytoin and carbamazepine are amongst the most commonly used anticonvulsants, it's crucial to keep in mind about their life-threatening rare idiosyncratic reaction i.e myelosuppression. Cautious use of these drugs, early diagnosis, timely discontinuation of the drug and proper management is the mainstay treatment in drug-induced myelosuppression. So the cases which are suspected to be drug-induced myelosuppression, especially type b reactions to phonation, carbamazepine should be reported to regulatory authorities to create awareness among the clinicians.

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