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SODIUM VALPROATE INDUCED CATARACT: A CASE REPORT

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ABSTRACT Valproic acid (VPA) is used for the treatment of epileptic seizures. Here we report, a case of cataract following sodium valproate administration for treatment of epileptic seizures. A 25 year female patient presented to ophthalmology out-patient department (OPD) with complaints of poor vision in both eyes. She was diagnosed as a patient of bilateral subcapsular cataract. She was on sodium valproate therapy for treatment of epileptic seizures for past 6 years. According to the Naranjo's scale, the effect of sodium valproate in our patient was scored 6 indicating a probable likelihood of causing cataract. It was a probable cause of cataract according to World Health Organization (WHO) causality scale. She underwent surgical treatment for cataract.

KEYWORDS : Valproic acid (VPA), Cataract, Naranjo's probability scale.

INTRODUCTION

Valproic acid is used for the treatment of epileptic seizures, depression, migraine headaches and manic depression or bipolar disorder.[1] There has been case report of bilateral congenital cataracts in a child out of 37 children after exposure of VPA during pregnancy.[2] VPA is never prescribed in pregnancy in United States and Canada due to teratogenic effects known foetal valproate syndrome.[3] The features of foetal valproate syndrome include infraorbital groove, epicanthic folds, medial deficiency of eyebrows, shallow nasal bridge, short nose with trigoncephaly, anteverted nares and tall forehead. Glover et al also reported high incidence of early onset myopia in foetal valproate syndrome.[2] VPA acts by prolonging inactivation of voltage-activated Na^+ channels and reduction of T-type Ca^{2+} currents in thalamic neurons. Valproate can stimulate the activity of GABA synthetic enzyme, glutamic acid decarboxylase and inhibit GABA metabolizing enzymes, GABA transaminase and succinic semialdehyde dehydrogenase.[1] Valproic acid remains a popular drug due to its proven efficacy and its low cost. It shows efficacy with favorable safety profile and relatively low drug–drug interaction.[4] The National Institutes of Health warns about the risk of serious damage to liver and pancreas associated with the use of this drug. The most common early symptoms of toxicity include anorexia, nausea, vomiting, and ultimately somnolence which may be accompanied by increased convulsions. Other ADRs associated with its use include drowsiness, dizziness, headache, diarrhea, changes in appetite, heartburn, weight changes, back pain, agitation, abnormal thinking, uncontrollable shaking, loss of coordination, blurred or double vision, ringing in the ears, sore throat and hair loss. Severe ADRs include unusual bleeding, fever, rash, confusion, difficulty breathing, weakness in the joints, depression and suicidal thoughts.[1] So, this case report highlights cataract occurring as result of using valproate and therefore treating physicians should be aware of it.

CASE REPORT

The patient was 25-year-old female who had been treated with sodium valproate for 6 years for treatment of epileptic seizures. Seizures appeared at 19 years of age and sodium valproate was administered as per body weight. Presently she was taking 500 mg twice-daily dose of sodium valproate. Early examinations by an ophthalmologist showed no congenital cataracts. She complained of painless gradual diminution in vision of both eyes for last one year and she reported ophthalmology OPD of J.N. Medical College& Hospital, AMU, Aligarh in February 2016. Her visual acuity was 1/60 in both eyes. Intraocular pressure was 18mm Hg (right eye) and 16 mm Hg (left eye) by non-contact tonometer. Slit-lamp microscopy revealed totally white opacity in both eyes. Cataract was mature with entire lens opaque in both eyes. A B-scan ultrasonography of both eye showed cataractous lens (as shown in figures). Funduscopy showed faint red glow in both eyes and no fundus details were seen. Electrocardiography was normal. Hematological and serological results including blood sugar fasting and post prandial, serum calcium, liver and kidney function were within normal limits. There was no history of hypertension, diabetes mellitus and asthma. There was no past history of eye trauma and glaucoma. The patient had paralytic poliomyelitis right lower limb from the age of six months. There was no family history of glaucoma and cataract. There was no use of any other medications. She underwent bilateral cataract extractions by phaco-emulsification and posterior chamber intraocular lens (PCIOL) implantations. Her visual acuity after PCIOL was 6/6 in both eyes.

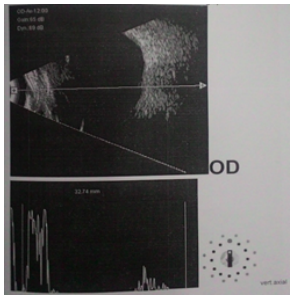

Figure 1: A B-scan ultrasonography of right eye showing cataractous lens

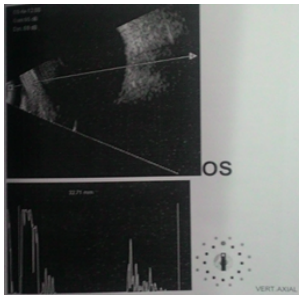

Figure 2: A B-scan ultrasonography of left eye showing cataractous lens

DISCUSSION

Cataract is clouding of lens in the eye leading to decrease in vision. It can affect one or both eyes. Often it develops slowly. Symptoms include blurring of vision, halos around light, trouble with bright lights, and trouble seeing at night.[6] Cataract is responsible for 50% cases of blindness and 33% of visual impairment worldwide. Most common cause of cataract is due to aging, but may also develop due to trauma, radiation exposure, be present from birth, or occur following eye surgery for other problems.[6] Risk factors include diabetes, smoking tobacco, prolonged exposure to sunlight and alcohol. Visual abnormalities associated with valproic acid include diplopia, blurred vision and nystagmus.[5] So it is important to identify other visual abnormalities associated with valproic acid. In this case, the sequence of development of cataract after long term

therapy of sodium valproate for treatment of epileptic seizures and absence of any evidence of other cause, strongly suggest that sodium valproate may have played role in the development of cataract. According to the Naranjo's probability scale the effect of sodium valproate in the patient was scored 6 indicating probable likelihood of causing cataract and also it was probable cause of cataract according to World Health Organization (WHO)causality scale.[7] Palsamy P et al[8] and Shinohara T et al[9] hypothesizes possible sequential events as possible mechanism of VPA induced cataract "VPA induced endoplasmic reticulum (ER) stress mediated unfolded protein response (UPR) activation, reactive oxygen species(ROS) overproduction, ER-Ca^{2+} release, and suppression of Nrf2/Keap1 dependent antioxidant protection by Kelch-like ECH-associated protein 1 (Keap1) promoter demethylation by altering the expression levels of active and passive DNA demethylation pathway enzymes, and finally death in human lens epithelial cells."Psychiatrists should be aware that sodium valproate, which is commonly used for absence seizures and manic depressive psychosis may cause cataract, especially when given for long duration. Regular ophthalmic evaluation should be done during long term therapy with sodium valproate so as to prevent development of cataract and its complications.

REFERENCES

1. McNamara JO. Pharmacotherapy of the epileptics. In: Hardman JG, Limbird LE, Gilman AG, editors. Goodman & Gilman's editors. The Pharmacological Basis of Therapeutics. New York: McGraw Hill Medical; 2011: 583-607.
2. Glover SJ, Quinn AG, Barter P, Hart J, Moore SJ, Dean JC, Turnpenny PD. Ophthalmic findings in fetal anticonvulsant syndrome(s). Ophthalmology. 2002;109:942–947.
3. Wlodarczyk BJ, Palacios AM, George TM, Finnell RH. Antiepileptic drugs and pregnancy outcomes. Am.J. Med. Genet. 2012;158A:2071–2090. [PMC free article] [Pub.Med]]
4. Jankovic SM, Dostic M. Choice of antiepileptic drugs for the elderly: possible drug interactions and adverse effects. Expert Opin Drug Metab Toxicol 2012;8: 81–91.
5. National Institutes of Health. Valproic Acid: Medline Plus Drug Information [Internet]. 2016. Available from: http://www.nlm.nih.gov/medlineplus/druginfo/meds/a682412.html.
6. Contributors W. Cataract [Internet]. Wikipedia, The Free Encyclopedia. 2016 [cited 25 January 2016]. Available from: https://en.wikipedia.org/w/index.php?title=Cataract&oldid=699051544.
7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
8. Palsamy P, Bidasee KR and Shinohara T, Valproic acid suppresses Nrf2/Keap 1 dependent antioxidant protection through induction of endoplasmic reticulum stress and keap1 promoter DNA demethylation in human epithelial cells, Exp Eye tres, 2015, 121, 26-34.
9. Shinohara T, Periyasamy, Bidasee K, Ayaki M and Rajan E, Epilepsy cataract: Valproic acid suppresses the Nrf2 dependent stress/antioxidant protection, Investigative Ophthalmology & Visual, 2013, 54, 59-48.