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A case report on Acyclovir induced thrombocytopenia

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ABSTRACT

Acyclovir an antiviral drug widely used to treat Herpes simplex virus, Varicella zoster virus and some Epstein barr virus mediated infections. Acyclovir is also effective in patients of immune deficitstatus. Acyclovir is generally well tolerated and has minimal adverse drug reactions. Common adverse effects include rashes, sweating, headache, stinging sensation and emesis. Here we report a case of Acyclovir induced thrombocytopenia developed due to constant use of oral formulation. In this case, patient was diagnosed with Disciform keratitis and was treated with Acyclovir and corticosteroids. Thrombocytopeniawas confirmed based on laboratory test reports. Although Acyclovir induced thrombocytopenia is rare &can be managed by discontinuing the drug. In this case, it was managed by altering the route of administration from oral to topical route because in some cases even only withdrawal of suspected offending agent may not correct thrombocytopenia due to presence of certain underlying etiologies. Thus proper diagnosis should be made before coming to a conclusion and such reporting should be encouraged.

INTRODUCTION

Acyclovir (acycloguanosine) is a synthetic purine nucleoside analogue, 9 - [(2 hydroxyethoxy) methylguanine] [1]. It is clinically active against Herpes Simplex Virus [HSV], Varicella Zoster Virus [VZV] and some Epstein Barr Virus mediated infections. Acyclovir is effective in patients with normal as well as deficit immune status. Mechanism of antiviral action results from inhibition of viral DNA replication[2].Acyclovir diffuses readily into most tissues and body fluids and can also achieve levels in the cerebrospinal fluid sufficient to inhibit most pathogens[3]. It is mainly excreted in urine and indicated in Herpes Simplex Infections (Immuno-compromised Patients, Genitalis, Encephalitis and Neonatal Herpes Simplex Virus Infection) and Varicella-Zoster Infections in immuno-compromised patients[4]. Oral dose in HSV is 200mg, five times a day for 5 days and for VZV is 800mg, 5 times a day for 7 days. Acyclovir is generally well tolerated and has minimal adverse drug reactions[5]. Common adverse effects include; stinging & burning sensation after each topical application. Headache, nausea, malaise, rashes, sweating, emesis with oral formulation[4]. Reversible neurological manifestations (tremors, lethargy, disorientation, hallucinations, convulsions and coma) have been described to higher doses [1]. In addition to common adverse events, following events have been identified during post approval use, as they are reported voluntarily from a population of unknown size, thus estimation of frequency cannot be made. These events have been chosen for inclusion due to either their seriousness, frequency of reporting, potential casual connection to Acyclovir, or a combination of these factors. Observed adverse events include; anemia, leukocytoclasticvasculitis, leukopenia, lymphadenopathy and thrombocytopenia [6]. Disciform keratitis is a cell mediated immune response to corneal endothelial tissue that presents with diffuse stromal edema mainly caused by HSZ and HZV. This condition responds remarkably well to Acyclovir and topical corticosteroids with restoration of endothelial function and resolution of corneal edema. Here we report a case of Acyclovir induced thrombocytopenia in a Disciform Keratitis patient [7].

CASE REPORT

A 9 years old male child weighing 27kg was admitted in department of pediatrics on 8-9-15 for bilateral undescended testes, he was referred from a private hospital where he was admitted with Disciform Keratitis (17-8-15) and was on following drugs:

1. Tab. Acyclovir-200mg 5 times/ day.
2. Predforte (Prednisolone 1%) eye drops 6 times/day (1 drop every 4 hours).
3. Homide (Homatropine 2%) (5ml) eye drops 2 times/ day.

His past history reveals that 2 months before admission to Private Hospital he was diagnosed with Disciform Keratitis and was on Tab. Acyclovir& Prednisolone eye drops. Table 1 shows

Table 1. : Past diagnostic test results:

Parameters	Normal ranges	20/8	21/8	24/8	25/8	27/8	28/8	31/8	2/9
Hemoglobin	11.5- 15.5 (gm/dl)	11.8	11.8	12	12.2	12.1	12.1	12	11.8
RBC	4-5.2 (million/cumm)	5.3	5.2	5.4	5.4	5.4	5.4	5.2	5.3
WBC	4000- 12,000(cells/cumm)	8,700	7,600	6,500	8,500	7,200	7,800	9,300	9,700
Neutrophils	31-61 %	62%	53%	50%	48%	58%	45%	60%	50%
Lymphocytes	28- 48 %	27%	34%	40%	40%	38%	35%	35%	33%
Eosinophils	**0-2 %**	**5%**	**8%**	**8%**	**10%**	**2%**	**15%**	**3%**	**10%**
Monocytes	0-8 %	6%	5%	2%	2%	2%	5%	2%	7%
Basophils	0-4 %	0%	0%	0%	0%	0%	0%	0%	0%
Platelets	**1.5-4.5 (lakhs/cumm)**	**0.37**	**0.48**	**0.45**	**0.33**	**0.24**	**0.35**	**0.28**	**0.5**

Impression: Thrombocytopenia with mild eosinophilia

Table 2. : Present diagnostic test results

Parameters	Normal ranges	9-9-15	12-9-15
Hemoglobin	11.5-15.5 gm%	8 gm%	9.5 gm%
WBC	4000-1200 cells/cumm	2000 cells/cumm	4,500 cells/cumm
Polymorphs	31-61%	65%	56%
Lymphocytes	28-48%	25%	35%
Eosinophils	**0-2%**	**5%**	**7%**
Monocytes	0-8%	5%	2%
Blood smear		Anisocytosis, few microcytes, tear drop cells, target cells.	Anisocytosis, normocytic hypochromic anemia, microcytes, mild eosinophilia.
Platelets	**1.5-4.5 lakh/cumm**	**Reduced**	**1.25 lakh/cumm**
Blood sugar	<200 mg%	104 mg%	-
Sr. Creatinine	0.6- 1.2 mg%	0.6 mg%	-
Blood urea	15-40 mg%	23 mg%	-

his past diagnostic tests i.e., from 20-8-15 to 2-9-15.

On examination patient was found to be conscious and coherent, afebrile, cardiovascular sound S1 & S2 heard, bilateral air entry was normal & no abnormal sound was present on respiratory examination, per abdomen was soft. Upon admission he was prescribed with

1. Tab. Paracetamol - ½ tab, SOS(each tab=500 mg).
2. Tab. B Complex OD.

On day 2 (9-9-15) child was referred to ophthalmologist, on examination by ophthalmologist revealed;corneal Disciform Keratitis in right eye with mildly dilated pupil and was prescribed with Acyclovir eye ointment 5times/day, Predforte (Prednisolone) eye drops 4 times/day and Atropine eye ointment 2 times/day and was advised for Complete Blood Picture (CBP) which was repeated on day 5 (12-9-15), results are shown in Table 2.

Same treatment was continued upto 7th day (10-9-15 to 14-9-15). Treatment was stopped for 1 week, as the child need to undergo surgery (22-9-15) for bilateral undescended testes and was prescribed with:

1. Inj.Taxim(Cefotaxime)1gm, IV, BD
2. Syp. Combiflam(Ibuprofen + Paracetamol) 5ml, TID for 5 days

Later patient was discharged on 22nd day (28-9-15) with following medicine for 7 days:

1. Neosporin ointment- 2-3 times a day.
2. Syp. Combiflam 5ml, TID.

DISCUSSION

Acyclovir induced thrombocytopenia is a rare clinical condition and has reported only in few earlier observed cases[8]. Thrombocytopenia a common hematological manifestation may be due to a wide variety of etiologies like; hematologic malignancies, infectious disease (dengue), thrombotic micro-angiopathies, autoimmune disorders and adverse effect of many drugs[9].

Management of drug induced thrombocytopenia required early and prompt identification of offending agent followed by withdrawal or discontinuation of drug or even change of route may improve the condition with regular monitoring of platelet count[10]. In this case Acyclovir induced thrombocytopenia was identified long after initial administration of the drug. These conditions may mislead the clinician regarding identification of offending agent. A thorough medical and medication history is maximum important to diagnose the exact cause[11]. In some cases even only withdrawal of suspected offending agent may not correct the thrombocytopenia due to presence of certain underlying etiologies. Thus proper diagnosis should be made before impending to a conclusion[12,13].

In this case thrombocytopenia was managed by altering the route of administration; oral to topical route. This condition supports the case plan by altering route of drug when drug discontinuation is not possible because of its effect[14,15].

Clinical pharmacist must play an imperative role in identification and reporting of various adverse events associated with drug, as it is an important component of monitoring and evaluation various activities performed in hospitals. A productive hospital based reporting program can be helpful in providing valuable information regarding potential problems of drug usage in an organization. Reporting and publishing rare adverse drug events will create responsiveness among healthcare professional for proper care process. Through these efforts, problems can be identified and resolved, which results in continuous improvement of patient care [16].

CONCLUSION

Drug induced rare clinical complication must be identified and managed accordingly and reporting of such events needs to be improved by clinician to create awareness.

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Patient informed consent:

Informed consent was obtained from the guardian or the patient for publishing the case. A copy of informed consent is available with corresponding author for further requirements.

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