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Case Report

Intravenous acyclovir causing vesicular eruptions at and away from infusion site in a child

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ABSTRACT

Acyclovir is an antiviral drug used to treat infections caused by Herpes virus. Acyclovir is known to cause systemic and local adverse reactions. Local adverse reactions include inflammatory reactions at infusion site. We case report a child with vesicular eruptions at and away from infusion site due to IV acyclovir. It is quite a rare finding, as only few such cases have been reported till now in literature.

Keywords: Acyclovir, Child, Adverse reaction, Vesicular eruptions, Case report

INTRODUCTION

Acyclovir [9-(2-hydroxyethoxymethyl) guanine] is antiviral drug for treatment of Herpes virus infections.[1] It has both systemic and local adverse effects. Systemic reactions are rarely seen and comprises of nephrotoxicity and neurological complications.[1] While local adverse effects mainly comprises of inflammatory changes, oozing of blood, blistering and peeling of skin at infusion site.[2] Here we present a child with vesicular eruptions due to intravenous (IV) acyclovir, at infusion site as well as away from infusion site. Though vesicular eruptions at infusion site due to IV acyclovir is known adverse effect of drug, eruptions away from infusion site is exceptionally rare and reported in very few studies only.[3,4]

CASE REPORT

A 10-year-old boy was brought to hospital with chief complaints of fever for two days and seizure few hours back. On examination he was comatose, had poor spontaneous breathing efforts and was in shock. Signs of meningeal irritation were present. He was admitted in pediatric intensive care unit. In view of short history and clinical examination suggestive of meningitis, presumptive diagnosis of viral meningoencephalitis was made and was treated accordingly. He was put on ventilator, given fluid boluses, started on ionotropes, IV antiepileptic (Phenytoin), empirical broad-spectrum antibiotics (Meropenam, vancomycin) and IV acyclovir (30 mg/kg/day). However, after first dose of IV acyclovir infusion, he developed blisters around infusion site on dorsum of his right hand (Figure 1). Considering possibility of local extravasation of acyclovir, it was restarted at other intravenous site (right foot). However, he developed distant blisters on right leg and left ear (Figure 2 and 3). There were no petechial or purpural rashes anywhere in body. There was no spontaneous bleeding. There was no history of use of acyclovir in any form previously. After 2 days of above-mentioned treatment, patient showed clinical improvement. Patient had eye opening to pain, and had few spontaneous breaths also. Aspirate from blisters was sent for microscopy and culture. Results were sterile fluid without any bacterial/ viral growth. Biopsy of lesions could not be done due to technical issues. Patient blood culture grew *Klebsiella Pneumoniae* with extended spectrum beta lactamase positive and sensitive to colistin. However, as culture was not taken with strict asepsis, probability of contamination was also suspected. His complete blood

count also showed leukocytosis with neutrophilia, platelet counts were within normal limits. Though lumbar puncture cytology, biochemical was normal with sterile culture report. In view of blood reports and adverse reactions to acyclovir, IV acyclovir was discontinued and colistin was added. Rest of supportive treatment, antibiotics and anti-epileptics was continued. After discontinuing acyclovir there were no more vesicular eruptions. However, patient general condition worsened. He again lapsed into coma. His blood tests were repeated and thorough clinical evaluation was done to find cause of deterioration, which inconclusive. As patient had initially improved on acyclovir, patient was restarted on IV acyclovir, this time with four times dilution and double rate of infusion. No adverse drug reaction observed this time. Later on, patient MRI also revealed findings suggestive of Herpes encephalitis. Blisters due to IV acyclovir healed by scarring (Figure 4). As other causes that could cause blisters were ruled out and temporal association of appearance of blisters and starting acyclovir infusion was present, acyclovir was presumed to cause blisters as adverse drug reaction. This association supported by applying Naranjo algorithm, which yielded "probable "adverse reaction score of 6 (Tables 1 and 2).[5]

Figure 1: Vesicular eruption and necrosis around infusion site.

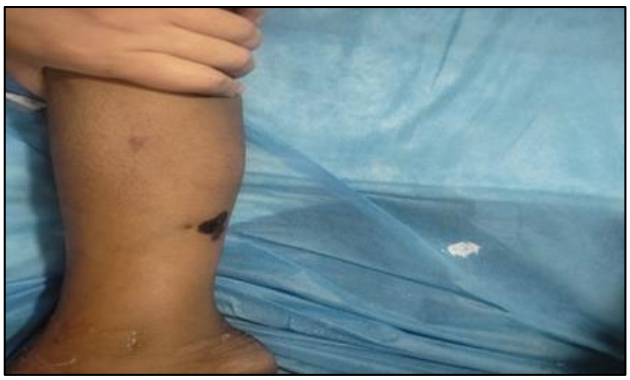

Figure 2: Distant vesicular eruption on leg.

Figure 3: Distant vesicular eruptions on patient's ear.

Figure 4: Lesions healing by scarring.

Table 1: Application of Naranjo algorithm questions score.

Questions	Yes	No	Don't know/not done	Score
Are there previous conclusive reports on this reaction?	+1	0	0	+1
Did the adverse event appear after the suspected drug was given?	+2	-1	0	+2
Did the adverse reaction improve when the drug was discontinued or specific antagonist was given?	+1	0	0	+1
Did the adverse reaction appear when the drug was re-administered?	+2	-1	0	-1
Are there alternative causes that could have caused the reaction?	-1	+2	0	+2
Did the reaction re-appear when a placebo was given?	-1	+ 1	0	0
Was the drug detected in any body fluid in toxic concentrations?	+1	0	0	0
Was the reaction more severe when the dose was increased or less severe when dose was decreased?	+1	0	0	0
Did the patient have similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
Was the adverse event confirmed by any objective evidence?	+1	0	0	+1

Total score-6

Table 2: Scoring based on Naranjo algorithm.

Scoring	ADR
≥9	Definite ADR
5-8	Probable ADR
1-4	Possible ADR
0	Doubtful ADR

ADR-Adverse drug reaction.

DISCUSSION

Acyclovir is an antiviral drug and guanine analogue used for treatment of Herpes simplex and Varicella zoster virus infection.[1] Herpes simplex infection can cause Herpes labialis, genital herpes, ocular herpes and herpes meningoencephalitis. Acyclovir is available in form of intravenous drugs, tablets, eye ointments and skin creams.[6] Acyclovir has both local and systemic side effects.[1,2] Local side effects include inflammation at site of infusion.[2] However, till now only two cases of vesicular eruption at and away from infusion site have been reported, one was adult while other was pediatric age group.[3,4] Despite several theories proposed that include hypersensitivity, extravasation of drug, still mechanism of these vesicular eruptions as adverse drug reaction to acyclovir is not clear. Interestingly, in our case after increasing duration and dilution of IV acyclovir infusion, no adverse drug reaction was seen. This finding is different from previous case report where increasing diluent in IV acyclovir infusion could not prevent adverse drug reaction.[2]

CONCLUSION

In patients receiving IV acyclovir with vesicular lesion at and away from infusion site, adverse drug reaction due to acyclovir should be considered as one of differential diagnosis. Increasing duration and dilution of infusion can be considered in patients where discontinuation of drug is more harmful than possibility of adverse drug reaction. More studies are needed to understand mechanism of this adverse drug reaction to acyclovir. Though we had not studied effect of increasing acyclovir dose on adverse reaction in our case, further such studies can be done in future.

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