Pediatrics & Therapeutics
ISSN: 2161-0665

Lorenzo et al., Pediatr Ther 2016, 6:2
DOI: 10.4172/2161-0665.1000287

Case Report Open Access

Acyclovir Crystalluria: A Rare Secondary Effect of a Common Drug

Claudia Sánchez-Villares Lorenzo*, Sheila De Pedro, Ana Isabel Benito and Carla Criado

Department of Pediatrics, University Hospital of Salamanca, Spain

***Corresponding author:** Claudia Sánchez-Villares Lorenzo, Department of Pediatrics, University Hospital of Salamanca, Spain, Tel: 34-605-57-64-10; E-mail: claudiasanchezvillares@hotmail.com

Rec date: Apr 19, 2016, **Acc date:** May 19, 2016, **Pub date:** May 23, 2016

Abstract

Acyclovir is a highly active antiviral drug that acts against the herpes simplex virus (HSV). Among its secondary effects, we can observe rare cases of crystalluria, which can be associated or not associated to renal failure. We present the case of a healthy lactating 13-month-old baby girl with gingivostomatitis, who 48 hours after the start of treatment with this drug showed a change in the color of her urine, which was associated with the appearance of crystals in the sediment. This finding was associated with the prescription of Acyclovir, because it has been described in the literature, and no other ascribable causes could be found. Crystalluria is a rare adverse effect that has been reported generally in adult immunosuppressed patients. We have only been able to find one case that could be compared to ours, in an immunocompetent pediatric patient in which a momentary treatment was implemented to treat a herpetic infection.

Keywords: Crystalluria; Acyclovir; Gingivostomatitis

Introduction

Acyclovir is an antiviral drug which is mainly active against herpes simplex and varicella zoster virus [1]. During childhood, its most common use focuses on prophylaxis or treatment of these viruses in immunosuppressed patients. However, it is also prescribed in the daily practice, albeit less commonly, so as to limit the clinical evolution of herpetic gingivostomatitis and herpes zoster. Cephalalgia, malaise and digestive symptoms are regarded as the most common secondary effects of its oral administration [2]. Crystalluria is considered a rare secondary effect, even less so in healthy children, which in some cases may lead to acute renal failure [3]. We present the case of a healthy lactating girl in which acyclovir caused the appearance of crystalluria.

Clinical Case

The patient is a lactating girl of 13 months of age who is admitted with fever and aphthous ulcers of 48 hours of evolution, with intense pain and hyporexia. The examination revealed multiple ulcers on the oral cavity, apart from edema and significant gingival hyperemia. The patient is clinically diagnosed with herpetic gingivostomatitis and is treated with oral acyclovir (15 mg/kg/dose every 6 hours), topical sodium lidocaine and metamizole for pain control.

48 hours later, the patient is readmitted as an emergency with the urine dyed an intense orange colour for 4 hours prior to consultation. In the examination, oral lesions are still present, accompanied by candidiasis. Standard urine analysis and analysis of urine sediment with a catheter are performed, and the pathological colour of urine is verified (Figure 1). Also, glycosuria (50 mg/dl), proteinuria (25 mg/dl), signs of hemoglobin, and leukocyte esterases (+) are observed. The sediment reveals abundant crystals which might be related to some drug (Figure 2). Therefore, administration of the antiviral drug is interrupted and the patient is scheduled for assessment and study after 24 hours.

Figure 1: Orange color of urine.

The blood analysis shows normal ranges for creatinine and urea (0.23 mg/dl and 22 mg/dl respectively), and the ionogram and venous blood gasometry are also normal. The glomerular filtration estimation was normal (Gao 104.56 ml/min/1.73 m^2 and Schwartz 119.41 ml/min/1.73 m^2). Proteinuria still remains (20 mg/dl) with a protein/creatinine ration of 0.36 mg/mg and a microalbuminuria/creatinine ratio of 0.56 mg/mg. Crystals are no longer visible, but the urine shows a moderate presence of squamous cells.

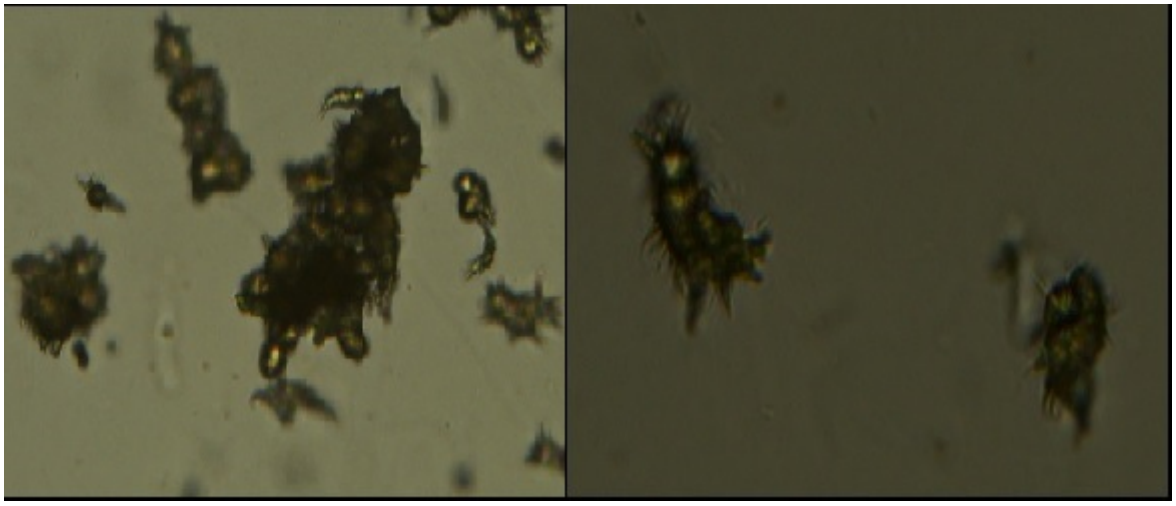

Figure 2: Acyclovir crystals in urine sediment.

Discussion

Herpetic gingivostomatitis is one of the most common forms of primary herpes simplex virus infection during childhood [4]. It is characterized by gingival edema and erythema and very painful mouth ulcers, and it is accompanied by general symptoms such as fever or anorexia. It has an essentially clinical diagnosis [5,6], and that was the case for our patient, who presented with many oral aphthous ulcers together with fever, malaise and anorexia.

The treatment focuses on keeping the patient hydrated and controlling the pain. It has been shown that topical acyclovir has no beneficial effects. Therefore, whenever it is prescribed, an oral administration is indicated for immunocompetent children when the aphthous ulcers have an evolution of less than 72-96 hours, which would reduce their duration [6-8]. 15 mg/kg/dose 4 times a day is recommended for 5-7 days [1,6]. In our case, in which the patient was a healthy lactating girl with symptoms of 48 hours of evolution, treatment with acyclovir started after oral tolerance was verified.

Acyclovir crystalluria is considered a rare adverse effect which is more commonly described if there is intravenous administration. However, it may also be associated with oral administration [9]. It is more common in immunosuppressed patients, probably due to the fact that acyclovir is more widely indicated in this patient group [10-12]. In the presence of acyclovir, kidney failure may be induced by the intratubular precipitation of crystals [13]. However, this situation does not always take place, and several cases of isolated crystalluria have been described. The urine analysis may reveal one or more of the following: crystals, hematuria, pyuria, glycosuria, mild proteinuria, increased density or decreased pH. Crystals may be needle-shaped and birefringent when seen through a polarized light microscope [3,6,12].

Mason et al. [10] reported the case of a 60-year-old man who was an HIV carried and had altered levels of consciousness, who was treated empirically with acyclovir. Two hours after starting the endovenous treatment, a change in the colour of his urine was observed (cloudy and whitish), associated with a worsening of his renal function, which was resolved after intensifying the intravenous hydration. Lyon et al. [3] published a similar case, in which a 53-year-old woman who was also immunocompromised due to an oncological process showed crystalluria after starting treatment with acyclovir, with cloudy and yellow urine. She did not show a deterioration of her renal function. It is difficult to find in the current literature a case of acyclovir crystalluria in a pediatric patient. We have to go back to 1986, when an article was published by Potter et al. [11] in which there are two cases, a 7-year-old girl affected by lymphoblastic leukemia, and therefore in a state of immunosuppression; and another 12-year-old girl under treatment for herpetic encephalitis which eventually caused her death. This last case is the most similar to our patient, who was also healthy beforehand, and in which crystalluria did not affect the renal function.

There are risk factors which promote the appearance of crystalluria, such as dehydration, an underlying renal condition and changes in the urine pH [6,11]. Therefore intravenous or oral rehydration is recommended, as well as withdrawal of the drug. It is generally a transient situation with complete recovery. In our patient, a healthy lactating baby, the risk factor which may have triggered crystalluria is a certain degree of dehydration due to hyporexia. As is described in the literature, 72 hours after the removal of the drug, the urine had gone back to normal and the girl was asymptomatic.

The crystals presenting our patient were not the characteristics described in the literature (needle- shaped and birefringent when seen through a polarized light microscope), however, she was not taking any other drug, and after remove of acyclovir, they disappeared in the urine, so crystals are likely secondary to treatment with acyclovir. To reach a definitive diagnosis, it would have to expose the patient back to acyclovir and display the same crystals in urine.

Conclusion

Acyclovir crystalluria is a rare condition which is generally described in immunosuppressed adult patients. It can lead to transient renal failure, and therefore it shall be taken into account whenever there are macroscopic alterations of urine or analytical data suggesting renal involvement. The peculiarity of the case in our study is due to the detection of crystalluria without renal involvement in a pediatric patient with no relevant previous history, which is a rarely described situation in the recent literature.

References

1. Comité de Medicamentos de la Asociación Española de Pediatría (2007) Pediamécum.
2. Zachary KC (2014) Acyclovir: An overview.
3. Lyon A, Mansoor A, Trotter M (2002) Urinary Gems: Acyclovir Crystalluria. Arch Pathol Lab Med 126: 753-754.
4. Kolokotronis A, Doumas S (2006) Herpes simplex virus infection, with particular reference to the progression and complications of primary herpetic gingivostomatitis. Clin Microbiol Infect 12: 202-211.
5. González MI (2014) Infecciones por virus del herpes simple 1 y 2. Cruz Tratado de Pediatría p: 885-891.
6. Keels MA, Clements DA (2014) Herpetic gingivostomatitis in young children.
7. Nasser M, Fedorowicz Z, Khoshnevisan MH, Tabarestani SM (2008) Acyclovir for treating primary herpetic gingivostomatitis. Cochrane Database Syst Rev 8: CD006700.
8. Hudson B, Powell C (2009) Towards evidence based medicine for paediatricians. Does oral acyclovir improve clinical outcome in immunocompetent children with primary herpes simplex gingivostomatitis? Arch Dis Child 94: 165-167.
9. Lam NN, Weir MA, Yao Z, Blake PG, Beyea MM, et al. (2013) Risk of Acute Kidney Injury from Oral Acyclovir: A Population-based Study. Am J Kidney Dis 61: 723-729.
10. Swayer MH, Webb DE, Balow JE, Straus SE (1988) Acyclovir-induced renal failure. Clinical course and histology. Am J Med 84: 1067-1071.
11. Mason WJ, Nickols HH (2008) Crystalluria from Acyclovir Use. N Engl J Med 358: e14.
12. Potter JL, Krill CE (1986) Acyclovir crystalluria. Pediatr Infect Dis 5: 710-712.
13. Parazella MA (2014) Crystal-induced acute kidney injury (acute renal failure).