Case Report

Successful mesna intra catheter treatment in hemorrhagic cystitis post chemotherapy patients

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ABSTRACT

Background: Cyclophosphamide and ifosfamide are an alkylating antineoplastic agents for chemotherapy with common side effect such as hemorrhagic cystitis. Various treatments have been reported, but there is still no gold standard of therapy. The treatment of chemical hemorrhagic cystitis from chemotherapeutics focuses on prevention and then expectant management of hemorrhagic cystitis

Aim: To demonstrate that mesna can be used to treat hemorrhagic cyctitic after chemothreraphy

Method: All the data was collected from the electronic medical record. We report two cases of HC, the difficulty of the management and a brief review of the literature the management and the prevention.

Case Description: Two pediatric patients who still suffered cyctitic hemmorhagic even after receiving infusions and intravenous 2-mercaptoethane sulfonate sodium (mesna) pre-treatment of cyclophosphamide and ifosfamide then treated successfully after intravenous and intravesical mesna.
Conclusion: Mesna might be usefull for the treatment of hemorrhagic cystitis that already occurred after chemotheraphy, but futher investigations should be demontrated.

Keywords: alkylating agent, hemorrhagic cystitis, 2-mercaptoethane sulfonate sodium, cyclophosphamide, ifosfamide

INTRODUCTION

Cyclophosphamide and ifosfamide are commonly used alkylating antineoplastic agents for chemotherapy with common side effect hemorrhagic cystitis (HC) in children. The incidence rates are 7% until 70%.[1] Acrolein are the urinary metabolite of cyclophosphamide and ifosfamide. Acroleins believed to be responsible for the HC.[2] The standard treatment for HC still remained unknown. Here we report two cases of HC induced by alkalyting neoplastic agents, the difficulty of the management and a brief review of the literature about the prevention and its management. All the data was collected from the electronic medical record. All the patients were treated successfully after intravenous and intravesical mesna.

CASE REPORT 1

A seven years old boy with diagnose of forth grade osteosarcoma came to the hospital for the osteosarcoma chemotheraphy. Then he received mesna, cyclophosphamide, etoposide, carboplatin and leucogen. He received cyclophosphamide cumulative dose more than 3000 mg/m2/day for the first two days. On the fifth day of admission, after finishing the chemotherapy cycle he complained about dysuria and redness in his urine. He got his urine checked and the result is erytrocyte >70/hpf and blood 3 RBCs. He never experiance this before. Then he got mesna intravenous 1200 mg and mesna intracatheter 200 mg every twelve hours for his hematuria. He also got his complete blood examination and the result was anemia, neutropenia and thrombocytopenia. Then he got platelet transfusion for his trombocytopneia. He stil got mesna intracatheter treatment. The colour of his urine began to become clearer on the 14th day of the treatment. He also got his renal fumction test and

ultrasonography of his renal. Both of the result of the test showed normal renal function. After 18 days of mesna intravenous and intracatheter treatment his urin become clear. Then he got discharge with no longer complained about hematuria nor dysuria.

Picture 1

CASE REPORT 2

A two years old boy with diagnose of rhabdomyosarcoma. He started his first chemoththeraphy that include ifosfamide, vincristine and dactinomycin in his regiment. He received ifosfamide cumulative dose 3000 mg/m2/day for the first two days. After finishing his first cycle of chemotheraphy he started to complained about dysuria, then we performed abdominal ultrasound to the patient. The result is a full bladder. After we performed urine catheter, we found the urine was mixed with blood. We perform red blood cell transfusion to the patient and mesna intracatheter 200 mg every twelve hours for 7 days for the hemorrhagic cystitis. After 7 days of mesna intracatheter the urine become clear.

DISCUSSION

Cyclophosphamide is commonly used for the treatment of solid tumors and B cell malignancy.[3] Adverse effects of cyclophosphamide therapy such as bone marrow suppression, hemorrhagic cystitis, alopecia, pulmonary fibrosis, infertility and carcinogenesis.[4] The incidence of hemorrhagic cystitis may develope in 20-25% in patients who received a high-dose cyclophosphamide. Patient who received ifosfamide may also have a greater possibility to produce HC due to a high doses that administered. Higher doses of ifosfamide may cause higher amounts of acrolein that cause the HC.[2] In the absence of adequate uroprotection, HC become dose limiting. Because of the direct contact with the acrolein, the uroepithelial will get edema, ulceration, hemorrhage and necrosis.[5] Ifosfamide will be converted to the urotoxic metabolite and the accumulation of the metabolte in uroepithelial tissues will lead to HC. The treatments for HC had developed varied such as administration of large volume of i.v. fluid to promote diuresis, continuous 24 hours mesna infusion, urinary catheterization or combination any of the above.[6]

Grading system for severity of hemorrghagic cystitis has been varying from no symptom to massive macroscopic hematuria.[7]

Grade	Symptoms
0	No symptom of bladder irritability or hemorrhage
I	Microscopic haematuria
II	Macroscopic haematuria
III	Macroscopic haematuria with small clots
IV	Massive macroscopic hematuria requiring instrumentation for clot evacuation and/ or causing urinary obstruction

Table 1 Grading of hemorrhagic cystitis

The first case received intravenous cyclophosphamide 2500 mg daily for two days in the hospital for his osteosarcoma chemotherapy and also mesna for preventing the hemorragic cystitis, but after finishing his chemotherapy cycle he complained about dysuria and redness in his urine. During a nearly 1 month hospital stay he received intravenous mesna and intracatheter mesna two times a day for 18 days and a platelet transfusion, and the hematuria gradually subsided. After he got discharged, he never had any complained about hematuria or dysuria.

The second case received ifosfamide 1750 mg for two days in the hospital and also mesna for preventing hemorragiccystitis. Three days after receiving ifosfamide he complained about dysuria and after using catheter we found cystitis hemmoragic in his urine.

The treatment of chemical cystitis from chemotherapeutics focuses on prevention and then expectant management of hemorrhagic cystitis. All patient who are to undergo infusions of cyclophosplamide and ifosfamide therapy received pre- and post treatment oral or intravenous 2-mercaptoethane sulfonate sodium (mesna). Mesna will get filtered through the kidneys and will be excreted into urine where it can directly bind and neutralize the acrolein. Current management of hemorrhagic cystitis caused by radiation or chemotherapeutics involves numerous interventions with degrees of efficacy. Commonly, manual irrigation by urinary catheterization is administered. The bladder irrigant usually normal saline, reduce bleeding by removing urokinase, an anticoagulant substance secreted into the urine by the kidney. Hyperbaric oxygen has been shown to have efficacy in the treatment of patients who failed other management. [2]

CONCLUSION

Cyclophosphamide and ifosfamide (alkylating antineoplastic agents) induced hemorrhagic cystitis is one of a severe complication which can cause a significant morbidity. Various treatments have been reported, however there is still no standard of therapy for this complication. In this cases mesna can be used for the treatment if the hemorrhagic cystitis is already occurred but futher research should be demontrated.

REFERENCES

1. Wang CC, Weng T, Lu MY, Yang RS, Lin KH, Wu MH, et all. Hemorrhagic cystitis in children treated with alkylating agent cyclophosphamide: The experience of a medical center in Taiwan. J Formos Med Assoc. 2015; 114: 691-7.
2. Payne H, Adamson A, Bahl A, Borwell J, Dodds D, Heath H, et all. Chemical and radioation induced hemorrhagic cystitis: current treatment and challenges. BJU Int. 2013; 122: 885-97.
3. Korkmaz A, Topal T, Oter S. Pathophysiological aspects of cyclophosphamide and ifosfamide induced hemorrhagic cystitis; implication of reactive oxygen and nitrogen species as well as PARP activation. Cell boil toxicol. 2007; 23: 303-12.
4. Varma PP, Subba DB, Madhoosudanan P. Cyclophosphamide induced haemorrhagic cystitis. MJAFI. 1998; 54: 59.
5. Vieira MM, Brito GAC, Filho JNB, Macedo FYB, Nery EA, et all. Use of dexamethasone with mesna for prevention of ifosfamide-induced hemorrhagic cystitis. International Journal of Urology; 2003:595-602.
6. Saito Y, Kumamoto T, Makino Y, Tamai I, Ogawa C, et all. A retrospective study of treatment and prophylaxis of ifosfamide induced hemorrhagic cystitis in pediatric and adolescent and young adult (AYA) patients with solid tumors. Jpn j Clin Oncol.2016;46:856-61.
7. Manikandan R, Kumar S, Dorairajan LN. Hemorrhagic cystitis: a challenge to the urologist. Indian J Urol. 2010; 26: 159-166.
8. Haldar S, Dru C, Bhowmick NA. Mechanism of hemorrhagic cystitis. Am J Clin Exp urol. 2014; 2: 199-208.