Author's response to reviews

Title: Chemical cystitis due to crystal violet: A case report

Authors:

  Takeshi Hashimoto (ha-tkc@tokyo-med.ac.jp)
  Makoto Oriori (mak_ohori@yahoo.co.jp)
  Takeshi Kashima (takeshikasima922@yahoo.co.jp)
  Hidenobu Yamamoto (customroadbike610@yahoo.co.jp)
  Masaaki Tachbana (tachi@tokyo-med.ac.jp)

Version: 3 Date: 12 April 2013

Author's response to reviews: see over
April 12, 2013

Journal of Medical Case Reports
Editor-in-Chief
Dr. Michael Kidd AM

Dear Dr. Michael Kidd AM

Thank you very much for giving us the opportunity to revise our manuscript entitled “Chemical cystitis due to crystal violet”.

We carefully reviewed the comments by 3 reviewers and answered. We have paid particular attention to reviewer's concerns. We explained the answer in revision letter and changed manuscript. We feel that findings from this case will be of special interest to the readers of Journal of Medical Case Reports. And we must call attention to some gynecologist who uses crystal violet.

We really appreciate it if you could reconsider our manuscript for publication of Journal of Medical Case Reports.

Sincerely yours,

Takeshi Hashimoto, MD
Department of Urology,
Tokyo Medical University,
6-7-1, Nishishinjuku, Shinjuku-ku, Tokyo,
160-0023,
Japan
Tel: +81-3-3342-6111
Fax: +81-3-3344-4813
E-mail address: ha-tkc@tokyo-med.ac.jp
Response to reviewer’s comments

Response to Reviewer 1’s comments
Dear Reviewer 1:

1. Good job, clear exposure but I think that there was no strictly need of all radiological exams.

Thank you for your suggestion. We excluded figure 4.

Response to Reviewer 2’s comments
Dear Reviewer 2

1. Crystal violet has been referred to as A CRYSTAL VIOLET in the opening sentence of abstract. I think it should be just referred as CRYSTAL VIOLET.

Thank you for your comment. As you mentioned we changed the wording in the opening title.

2. If the dye is not used currently, why was it used in the mentioned case??

A gynecologist used to use it for diagnosis of the fistula, and some may continue to use it like our case. Actually, gynecologists in the present case were aware of the complications of the dye but felt OK to use it if it was washed out after the examination.

In Introduction
In addition, there was a time even in Japan when crystal violet was used for diagnosis of vesico-vaginal fistula (VVF). Nowadays, it has been replaced with indigo carmine solution. But some gynecologists from older generation may continue to use it for diagnosis of VVF.

3. Why was the patient not prescribed anticholinergic drugs initially itself in spite of such severe storage symptoms and just managed with NSAIDS and glucocorticoids?
As long as we researched, there were not any reports that indicate that anticholinergic drug was beneficial for chemical cystitis. Further, we believe that we need to be careful to use anticholinergic drugs since it may temporally improve the capacity of the bladder but it also worsen the flow of urination. Because we thought it was important to prevent from developing severe inflammation and from becoming scarred in bladder, we used NSAIDs and glucocorticoid as initial management.

4. How was the bladder capacity measured??

We requested the patient to measure urinary volume by a cap and record in one's bladder diary

5. It would have been better to have an urodynamic study in this patient to further classify the effect on bladder.

We agree with you. We actually recommended it to the patient but she was not willing to do it. It was difficult for us to push her since a catheterization and urodynamic itself may cause a pain in such small bladder.

6. The patient was evaluated with a CT initially and MRI 2 weeks later and again by CT on follow up. I beleive it would have been a good practice to evaluate with a single modality to have a good comparison.

We agree with you that we were better to follow the status by a single modality. We had noticed the importance of MRI to evaluate the level of damage after the initial CT scan
Response to Reviewer 3's comments
Dear Reviewer 3

1) In the Introduction section, the author mentioned that crystal violet has been replaced with indigo carmine in the treatment of oral and vaginal candidiasis or for sterilization. Is this correct?

As you mentioned, these sentences may give a false impression so that we changed the sentences as follows:

In Abstract and Introduction
Because crystal violet is potentially toxic to mucosal membranes, it has been replaced with other disinfectant, and crystal violet is rarely used nowadays.

In Introduction
In addition, there was a time even in Japan when crystal violet was used for diagnosis of vesico-vaginal fistula (VVF). Nowadays, it has been replaced with indigo carmine solution. But some gynecologists from older generation may continue to use it for diagnosis of VVF.

2) The author mentioned that crystal violet is a multinominal reagent, which is a mixed ratio of gentian violet, methyl violet, and Bonney’s blue. However, as Bonney’s blue dye is a 1:1 mixture of brilliant green and crystal violet dissolved in ethanol, the reviewer thinks that it is a different solution from crystal violet itself.

Thank for your important comments. Bonney’s blue dye is not strictly the same with crystal violet. Bonney’s blue dye contains brilliant green with the exception of crystal violet. Therefore we changed the sentences as follows:

In discussion
Crystal violet, as well as gentian violet and methyl violet, belongs to a group of triphenylmethane dyes. Similarly, Bonney’s blue also contains triphenylmethane dyes.

3) Avoid overstating the impact of this case report (i.e., any patient with
chemical-induced cystitis “should be evaluated” for the level of damage in the bladder wall by MRI because the present study did not provide any evidence that MRI should be performed in patients with chemical cystitis. Can authors explain how MRI results can change the treatment strategy for such patients?

Since there are a few options to treat chemocystitis, we were not able to change the strategy of treatment because of the findings on MRI. However, if the symptoms were not improved and MRI showed the damage to the bladder muscle, then we had to consider surgical interventions such as iliovesical plasty, etc. Also, because of no damage to the muscle on MRI, we could recommend to the patient to wait further. Therefore, we feel OK to say that MRI may be useful in the present case while, as the reviewer suggested, we should not overstate the role of MRI. We added the reference 8 to explain the role of MRI.

**In discussion**

In case of radiation hemorrhagic cystitis, a previous study describes bladder change on MRI. The patients with hematuria had bladder wall thickness on T1-weighted images and abnormal high signal intensity in the outer bladder wall on T2-weighted images secondary to chronic inflammation. Therefore, MRI may provide the important information as to the extent of the damage [8].

**In Conclusion**

While chemical cystitis by crystal violet can be conservatively managed with NSAID and glucocorticoid, considering the severe side effects, it would be better not to use it to examine the conditions of disease such as VVF.

4) Crystal violet has been suggested to be a carcinogen in experiments in rodents, and the FDA has also suggested a relationship between crystal violet and bladder cancer. With respect to this information, how do the authors think that this patient should be followed up after the chemical-induced cystitis is healed?

As you pointed, there was a report that gentian violet produced cancerous cells in mice. But as long as we investigate, there were no reports regarding humans that the patients exposed to crystal violet developed to be affected with carcinoma. Meanwhile, we think that it is necessary to follow carefully, with urinalysis and urine cytology.