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Case Report

Post vaginal hysterectomy serotonin syndrome

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ABSTRACT

Serotonin syndrome is a potentially fatal complication associated with the use of methylene blue dye and antidepressants. Methylene blue is a dye commonly used to visualize structures in OB/GYN surgeries. Due to difficulty in manufacturing other dyes, more physicians will likely have to use methylene blue, thus making the knowledge of its monoamine oxidase inhibition properties even more vital in the prevention of serotonin syndrome complications. Serotonin syndrome is a potentially deadly disease that has a high likelihood of occurring if methylene blue is used concurrently with any type of serotonin modulating agent. While it is listed as a black box warning when used with anti-depressants, it is still relatively rare but should be considered in cases such as these.

Keywords: Methylene blue, Serotonin syndrome

INTRODUCTION

Serotonin syndrome is a potentially fatal complication associated with the use of any Serotonin Receptor Modulator, most commonly SSRI's, SNRI's, SRA's, or MAO-I's.[1] Patients can have varying disease severity and presentations but commonly will present with some combination of hyperthermia, hypertension, hyperreflexia, tachycardia, flushing of the skin and clonus. Methylene blue is a dye commonly used to visualize hard to see structures in OB/GYN surgeries that has MAO-I properties. Due to difficulty in manufacturing other dyes, that do not possess any intrinsic MAO-I qualities, such as indigo carmine, more physicians will likely have to use methylene blue as their default dye at many institutions.[2] Thus, making the knowledge of its monoamine oxidase inhibition properties even more vital in the prevention of serotonin syndrome complications. Serotonin syndrome is a potentially deadly disease that has a high likelihood of occurring if methylene blue is used concurrently with any type of serotonin modulating agent, even in the minuscule amounts used for the contrast dye. While it is listed as a black box warning when used with anti-depressants, it is fairly rare that the methylene blue can induce a serotonin syndrome, but it should always be considered in cases such as this one. The objective of this case report is to raise awareness of the potential for methylene blue to precipitate a serotonin syndrome in patients who may otherwise have had this potential trigger be overlooked.

CASE REPORT

Patient is a 24-year-old G4P3013 with past medical history of depression and HTN and OB/GYN history of cone biopsy, C-section, and VBAC, who came to clinic complaining of pelvic pain of 6 months, with spotting over the past 2 months. Ultrasound showed a small uterus measuring 40×45×34 cm with an irregular globular appearance suggestive of Adenomyosis. Patient preference was for hysterectomy over hormonal options to control the pain. We informed the patient that we would initially attempt it as a vaginal procedure, but with her previous history Ob/GYN, it may be difficult, and that there was potential that we would need to do the procedure with

laparoscopic assistance. Patient was amenable to the risks as they were explained to her and was subsequently scheduled for vaginal hysterectomy.

The patient was placed under general anesthesia, foley catheter inserted, then a weighted speculum was placed and the Deaver grasped the cervix with a tenaculum in the midline. 2 tenaculum had to be used due to the patient's cervix being very bulky. Then infiltrated circumferentially with 0.25% Maracaine with Epi. The cervix was circumcised with the scalpel. A weighted speculum was placed, and the bladder was pushed cephalically. Peritoneal reflection was appreciated and entered sharply. On both sides, the cardinal-uterosacral ligament complex was clamp cut and stick tied, the fundus was then delivered.

Once each pedicle was divided, the uterus was removed. Once hemostasias had occurred, the vaginal cuff was closed by taking the Cardinal-Uterosacral ligament stitch on the left side and driving it from inside-out through the vaginal mucosa and tying it back down, with no blood leakage being noted. Cystoscopy was pre-formed with a 30-degree scope was to visualize the ureters. After this both ureters were visualized peristalsing urine and the bladder was intact with no apparent injuries. The patient was taken to recovery room in stable condition.

While, in recovery room patient became obtunded, tachycardic, and complained of left sided flank pain, and exhibited vertical and horizontal nystagmus in addition to waxing and waning consciousness. Emergent CT was ordered, and while in the scanner the patient became even more lethargic and unresponsive, failing to respond to sternal rub. CT scan showed a small amount of pelvic hemorrhage with no active extravasation. Patient was taken back to operating room and intubated due to progressing loss of consciousness. Stab incisions were made in the umbilicus, and Veress needle introduced pressure of <15 mmHg. A 5 mm Trochar was inserted with camera in situ. Incisions were then made on right and left sides for trochars, which were then inserted. Patient was then placed in Trendlenburg position, and the hemoperitonenum in the pelvis was suctioned out. Small bleeding sites were noted at the left side of the vaginal cuff, and caudal surface of the left ovary, which were then cauterized.

The blood was then irrigated out, and the vaginal cuff was oversewen. Surgiflo hemostatic foam with a dissolving mesh was then applied to area. Because the patient's blood loss between both procedures was not significant enough to explain the patients altered mental status it was decided the best course of action was to leave her intubated, and obtain a head CT. The patient was then taken to the ICU where she was noted to be breathing on her own, so she was subsequently extubated and transferred to the floor. The patient was discharged home on post-op day 2 with no complications.

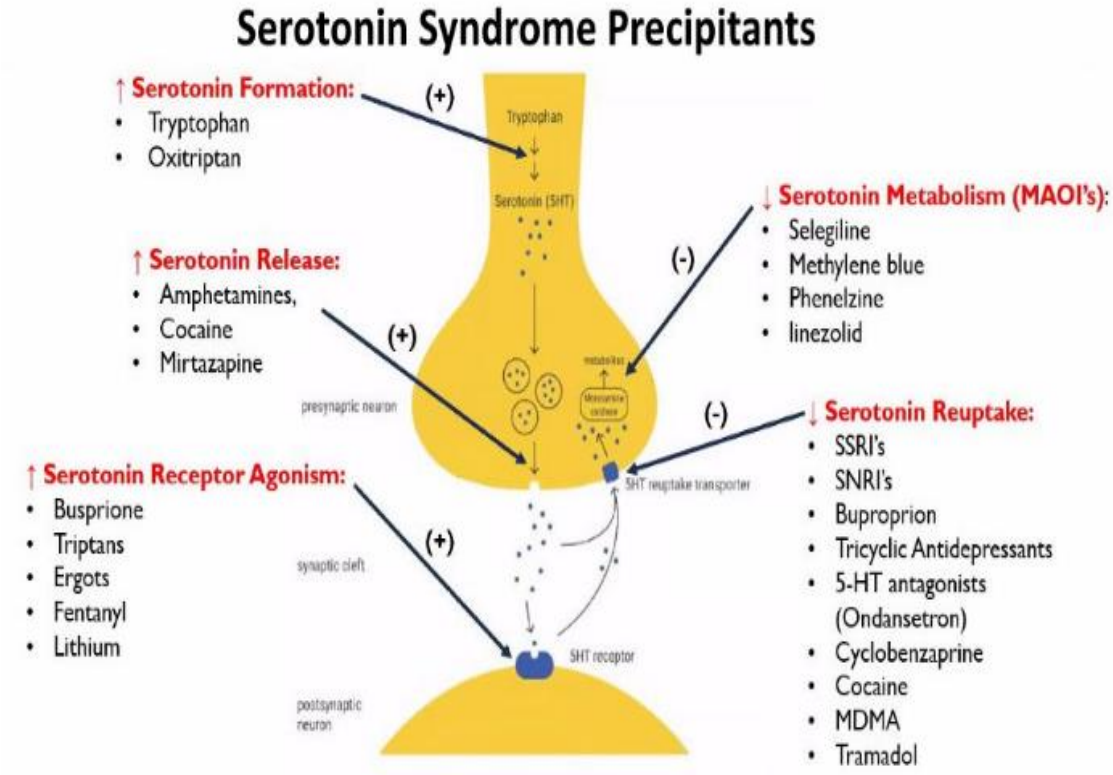

Figure 1: The role methylene blue amongst other serotonin modulators has at the synaptic cleft.

DISCUSSION

Methylene blue induced serotonin syndrome is a rare, but potentially fatal side effect of the marker dye's use in any procedure.[3] While methylene blue by itself has not exhibited any cases of serotonin syndrome, due to it being a strong MAO inhibitor, it carries a significant risk for precipitating a serotonin syndrome when combined with any serotonin reuptake inhibition modulators, such as SSRI's, SNRI's, and even weaker ones such as a tramadol, or a transdermal fentanyl patch.[4] Due to the relative rarity of methylene blue induced serotonin syndrome, symptoms may be mistaken for other disease processes, such as life-threatening haemorrhage or malignant hyperthermia.

In addition to the fact that operative depressant agents may hide symptoms until later on in the disease course, it is important to keep it on your differential, because it does occur in various surgical settings and sites, when evaluating any patient who shows any signs or symptoms of the disease such as spontaneous clonus, tachycardia, hyperreflexia, inducible clonus, or ocular clonus just to name a few.[5] Treatment for mild serotonin syndrome typically starts with stopping the serotonin medication, cooling the body to prevent hyperthermia, and other supportive measures. If the disease is more severe in nature a serotonin receptor antagonist such as cyproheptadine may be indicated.[3]

While discontinuing a serotonin modulating medication and allowing for an appropriate washout period would be ideal, this is not always possible for patients, which makes the use of other marker dyes a potentially more beneficial option. The primary alternative to methylene blue has historically been indigo carmine, which has been successfully used to visualize the ureters and ureteral patency with minimal side effects. Indigo carmine has been in a nationwide shortage due to various issues in production, such as insufficient amounts of raw materials, and issues in manufacturing. Indocyanine green has been used in some cases to examine the ureters when coupled with infrared light.[2]

CONCLUSION

We describe a case of the marker dye methylene blue induced serotonin syndrome in a patient who was receiving a vaginal hysterectomy. Due to difficulty in obtaining other marker dyes, methylene blue is a common dye used at most institutions. It is important to be aware of its monoamine oxidase inhibitory properties, because even in exceedingly small amounts it is able to precipitate a serotonin syndrome in patients receiving any type of serotonin modulation therapy, which can even be life threatening in certain situations.

Methylene blue induced serotonin syndrome is a relatively rare disease presentation, that has very minimal cases reported in the literature. With more and more people in the world receiving serotonin modulating treatment for various diseases, it is important for physicians to be aware of its MAO inhibition properties, so as to avoid precipitating a serotonin syndrome.

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REFERENCES

1. Diaz G. Serotonin Syndrome Drug Precipitants and Pharmacology. 2012. Available at: https://www.grepmed.com. Accessed on 12 July 2014.
2. Drug shortage detail: Indigo carmine injection. ASHP. 2018. Available at: https://www.ashp.org. Accessed on 15 July 2024.
3. Gillman PK. CNS toxicity involving methylene blue: The exemplar for understanding and predicting drug interactions that precipitate serotonin toxicity. Journal of Psychopharmacol. 2010;25(3):429-36.
4. Pedavally S, Fugate JE, Rabinstein AA. Serotonin syndrome in the intensive care unit: Clinical Presentations and precipitating medications. Neurocritical Care. 2013;21(1):108–13.
5. Locke, A. Methylene blue and the risk of serotonin toxicity. Anesthesia Patient Safety Foundation. 2012. Available at: https://www.apsf.org/article/methylene-blue-and-the-risk-of-serotonin-toxicity. Accessed on 30 July 2024.
6. Ng BK, Cameron AJ, Liang R, Rahman H. Serotonin syndrome following methylene blue infusion during parathyroidectomy: A case report and literature review. Canadian J Anesthesia Canadien d'anesthésie. 2008;55(1):36–41.

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