Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Anesthesiology

Unexpected Intraocular Inflammation Following the Use of Anti-Adhesion Agents, Mediclore® - A Case Report

In-Jung Jun[1], Jong Won Chae[2], Mi Hwa Chung[2], Eun Mi Choi[2*]

[1]Department of Anesthesiology and Pain Medicine, Inje University Sanggye Paik Hospital, Seoul, Republic of Korea
[2]Department of Anesthesiology and Pain Medicine, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea

DOI: 10.36347/sjmcr.2024.v12i02.014 | **Received:** 03.01.2023 | **Accepted:** 12.02.2024 | **Published:** 15.02.2024

***Corresponding author:** Eun Mi Choi
Department of Anesthesiology and Pain Medicine, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea

Abstract **Case Series**

Several cases of unexpected intraocular inflammation have been reported following the use of anti-adhesion agents, including Mediclore®. However, anti-adhesion agents are now used in many surgeries because of their effectiveness in preventing postoperative adhesions. Awareness of the relationship between postoperative intraocular inflammation and anti-adhesion agents is important to avoid unnecessary evaluations. Two women experienced congestion and pain in both eyes after undergoing gynecological surgery using robotic and laparoscopic techniques under general anesthesia. They were diagnosed with anterior uveitis and episcleritis, and the cause was considered to be an anti-adhesion agent after excluding other factors and ophthalmic examinations. Here, we report two cases of intraocular inflammation after surgery and describe the clinical importance of anterior uveitis and episcleritis.

Keywords: anti-adhesion agents, Mediclore®, anterior uveitis and episcleritis.

INTRODUCTION

Various complications related to the surgical procedure and medications can occur after surgery under general anesthesia. Unexpected intraocular inflammation can occur after the use of anti-adhesion agents. Previous studies have reported that anti-adhesion agents and intraocular inflammation seem to be related [1, 2]. Mediclore®, an anti-adhesive agent, is effective in preventing postoperative adhesions and is utilized not only in gynecological surgeries but also in various other procedures. Among the components of Mediclore®, chitosan is associated with a potential risk of adverse effects in individuals with shellfish allergies [1, 3]. However, our patient, who had no known allergies, including crustaceans, experienced ocular congestion and pain in both eyes after undergoing gynecological surgery with robotic and laparoscopic techniques under general anesthesia. We identified the cause of intraocular inflammation by excluding other factors and performing an ophthalmic examination. It is important to be aware of the relation of postoperative intraocular inflammation and anti-adhesion agents to avoid unnecessary evaluation. Although there have been several reports on the relationship between intraocular inflammation and anti-adhesion agents, these agents are now used in many surgeries. Here, we report two cases of intraocular inflammation after surgery and describe the clinical importance of anterior uveitis and episcleritis.

CASE REPORT 1

Written informed consent was obtained from the patient before publication of this case report.

A 43-year-old woman weighing 53 kg and 155 cm in height was admitted to the gynecology department for a robot-assisted laparoscopic hysterectomy. The patient was diagnosed with a uterine 6 cm myoma and had symptoms such as urinary frequency, lower abdominal pain, and heavy menstrual bleeding. She had no known underlying health conditions and had undergone right breast papilloma removal in 2012 and 2020 under general anesthesia without any complications.

Upon admission, the patients' laboratory tests showed no abnormalities. The patient had no known allergies, including those to crustaceans. As a preoperative treatment, the prophylactic antibiotic cefuroxime (750 mg) was administered intravenously (IV), and premedication with glycopyrrolate (0.2 mg)

and midazolam (2.0 mg) was administered by intramuscular injection. Upon arrival in the operating room, the patient's initial vital signs were stable. To induce anesthesia, the patient was administered propofol (90 mg) and rocuronium (40 mg IV). After endotracheal intubation, ventilation was controlled to maintain end-tidal CO_2 ($ETCO_2$) between 30 and 40 mmHg. Anesthesia was maintained with sevoflurane 1.5-2.5 v% to maintain the bispectral index within the 40-60 range, and remifentanil and rocuronium were also infused continuously. The patients' eyes were closed with silicone tape to prevent ophthalmic complications. The surgery began with a small incision below the belly button, and a trocar was inserted into the incision site. A steep Trendelenburg position was implemented, and a carbon dioxide pneumoperitoneum was formed for surgical exposure. A robot-assisted hysterectomy was performed. Approximately 30 minutes before the end of the surgery, an anti-adhesion agent (Mediclore®, 5ml) was applied to the intraabdominal surgical site to prevent adhesions. After surgery, pyridostigmine (20 mg) and glycopyrrolate (0.4 mg IV) were administered to reverse muscle relaxation for extubation. The patient's peak inspiratory pressure (PIP) was maintained below 25 mmHg, and vital signs were stable during the surgery. The surgery lasted for 120 minutes and the estimated blood loss was 100 ml. The patient's condition remained stable, and the surgery was successfully completed without any major issues.

After surgery, the patient was observed in the recovery room for 30 minutes. Vital signs were stable, and for pain control, fentanyl (50 mcg IV) was administered. Subsequently, a continuous intravenous patient-controlled analgesia (IV PCA) system consisting of fentanyl and ramosetron was administered for continuous pain management. The patient was transferred to the ward for further care. Approximately 8 hours after surgery, the patient complained of bilateral eye redness and experienced varied symptoms such as stinging, itching, pain, and blurred vision. Prednisolone 1% eye drops and homatropine hydrobromide eye drops were applied to the eyes for treatment. Four days later, bilateral eye redness improved, but blurred vision persisted. For the ophthalmological evaluation, the patient underwent a comprehensive eye evaluation, including visual acuity, intraocular pressure (IOP) measurement, slit-lamp biomicroscopy, fundus examination, and optical coherence tomography. Based on these examinations, no abnormalities in visual acuity, IOP, or fundus of the eye were noted. However, conjunctival injection was observed in both eyes, along with inflammatory cells in the anterior chamber. Consequently, the patient was diagnosed with anterior uveitis, and treatment with prednisolone eye drops four times a day was recommended. Outpatient follow-up was performed and patient' symptoms were improved within a week.

CASE REPORT 2

Written informed consent was obtained from the patient before publication of this case report.

A 32-year-old woman weighing 58 kg and 154 cm height was admitted to the gynecology department for laparoscopic bilateral ovarian cystectomy under general anesthesia. She had no known underlying health conditions or allergies. She had cesarean sections in 2016 and 2017 under general anesthesia. No notable complications or comorbidities were noted in her medical history.

As in Case 1, the patient was prepared for preoperative evaluation, prophylactic antibiotics, and premedication. Upon arrival in the operating room, the patient's initial vital signs were stable. After the induction of general anesthesia, silicone tape was applied to the patient's eyes to prevent ophthalmic complications. The Trendelenburg position was used, and a carbon dioxide pneumoperitoneum was created to expose the surgical area. A laparoscopic right ovarian wedge resection and left ovarian drilling were performed. Before the end of the surgery, an anti-adhesion agent (Mediclore®, 5 ml) was applied to the surgical site to prevent adhesions. During surgery, the patient's PIP was maintained at < 25 mmHg. The surgery lasted for 90 minutes, and the patient's condition remained stable throughout the procedure and in the recovery room after surgery.

A day after surgery, the patient experienced symptoms of bilateral eye redness, pain, and blurred vision. The patient consulted an ophthalmologist during hospitalization. Visual acuity and IOP were measured, and fundus photography was performed. The ophthalmologist diagnosed episcleritis and anterior uveitis in both eyes and recommended moxifloxacin, 0.1% fluorometholone, and bromfenac eye drops. On the third day after surgery, the symptoms in both eyes had significantly improved, and the patient was discharged.

DISCUSSION

Our patient experienced bilateral eye redness, pain, and blurred vision after undergoing gynecological surgery using robotic and laparoscopic techniques under general anesthesia. The patient was diagnosed with anterior uveitis and episcleritis on ophthalmic examination.

After surgeries are performed under general anesthesia, various complications related to the surgical procedure and medications can occur, affecting the circulatory, respiratory, and other systems. Unexpected postoperative intraocular inflammation can be triggered by various reasons.

During robotic and laparoscopic surgeries, carbon dioxide pneumoperitoneum leads to an increase

in the IOP due to decreased venous return and increased episcleral venous pressure. Additionally, the use of the steep Trendelenburg position results in a greater increase in IOP due to increased PIP and choroidal vasodilation due to increased $ETCO_2$. Subsequently, these factors lead to an increase in intracranial pressure (ICP) and IOP, which can cause conjunctival swelling and injection [4-6]. In our cases, the patients' vital signs, PIP, and $ETCO_2$ were maintained within the normal range during surgery, and the duration of total anesthesia was within 2 hours. Therefore, it was considered that the patients' ICP and IOP did not increase, causing ocular complications due to pneumoperitoneum and the steep Trendelenburg position. Additionally, the patients were diagnosed with uveitis and episcleritis, which differ from conjunctival swelling and injection due to increasing IOP and ICP.

Another reason for the red eyes and pain could be direct trauma to the eye during the perioperative period. However, unilateral rather than bilateral eyes tended to be affected.

Systemic reactions to various medications can cause intraocular inflammation. The uvea is the middle layer of the eye, and because of the abundant blood flow, it tends to be the primary site of inflammatory reactions in the eye, leading to uveitis. Intraocular inflammation can be in the form of uveitis and rarely presents as episcleritis or scleritis, similar to our patients. Although the pathophysiology of non-infectious uveitis remains unclear, the involvement of genetic predisposition and environmental factors has been proposed. Several previous studies have reported that various drugs are related to anterior non-infectious uveitis, known as drug-induced uveitis (DIU), by immune complex deposition in the uveal tissue or immune reactions to antigens [7-9]. Various drugs, such as systemic drugs, NSAIDs, and some vaccines, cause uveitis via systemic, topical, and intravitreal routes. In our cases, the use of the anti-adhesive agent Mediclore® during the intraoperative period seemed to be associated with the occurrence of anterior uveitis related to an immune disorder.

Postoperative tissue adhesion can lead to various complications, such as bowel obstruction and pain. Strategies to prevent this include minimizing tissue manipulation during surgery, using anticoagulants and anti-inflammatory agents, and employing various forms of anti-adhesive agents like films, solutions, and gels [3].

Anti-adhesive agents commonly used include Mediclore®, Guardix®, Hibarry®, and Medicurtain®. Mediclore® is a biocompatible, temperature-sensitive sol-gel type composed of poloxamer, gelatin, and chitosan. This agent is effective in preventing postoperative adhesions and is utilized not only in gynecological surgeries but also in various procedures such as implant-based breast reconstruction, endonasal dacryocystorhinostomy, total knee arthroplasty, and transurethral resection of the prostate [10, 11].

Among the components of Mediclore®, chitosan is a substance derived from the shells of crustaceans. Thus, there is a potential risk of adverse effects for individuals with shellfish allergies. Additionally, the fact that the processing of chitosan can result in the production of diglycolic acid, which has the property of dilating blood vessels, is known. This characteristic could potentially lead to ocular congestion. Gelatin, including animal collagen, is also a component of anti-adhesion agents. A previous animal study reported that collagen from animals can cause intraocular inflammation and relapsing polychondritis via an immune reaction. Our patients had no known allergies, including crustaceans. Therefore, gelatin of an anti-adhesion agent cannot be excluded as a cause of the intraocular inflammation in our patients [12, 13].

A previous study reported the occurrence of ocular congestion and intraocular inflammation after the use of Mediclore® [1]. The authors retrospectively analyzed 2,694 patients who used anti-adhesion agents during various surgeries and found that 0.51% of the patients received treatment for eye congestion and pain. Ocular symptoms occurred on average 1.5 days after surgery, and anterior chamber cells were observed, similar to our patients.

Many anti-adhesive agents, including Mediclore®, are now used in various surgeries due to their effectiveness in preventing postoperative adhesions. In cases of ocular symptoms, the medical team should evaluate the relationship between anti-adhesion agents and intraocular inflammation by ophthalmic examination. Identification of offending agent of uveitis is important to stop additional administration of the agent. If prompt treatment is administered, drug-induced uveitis usually resolves without major sequelae. Antibiotic, NSAID, and steroid eye solutions, oral NSAID, and prednisolone can be used for the symptomatic treatment of uveitis. Intravitreal triamcinolone acetonide, or anti-vascular endothelial growth factor, is also used to treat noninfectious uveitis [9].

In our cases, the anti-adhesion agent Mediclore® used during intraoperative period was considered responsible for the occurrence of ocular inflammation related to an immune disorder. Awareness of the relationship between postoperative intraocular inflammation and antiadhesion agents is important to avoid unnecessary evaluations, especially in patients with previous uveitis. Based on immunogenetics, further research is necessary to identify the underlying pathology between intraocular inflammation and the antiadhesive agent Mediclore®.

Notes
Funding: None

Conflicts of Interest: No potential conflict of interest relevant to this article was reported.

Data Availability Statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Conceptualization: Jong won Chae. Writing - original draft: In-Jung Jun. Writing - review & editing: Jong won Chae, In-Jung Jun. Investigation: Eun Mi Choi. Resources: Jong won Chae. Supervision: Mi Hwa Chung, Eun Mi Choi. Validation: In-Jung Jun.

REFERENCES

1. Lim, J. W., Lim, J. H., Kim, C. Z., Lee, S. U., & Lee, S. J. (2022). Intraocular Inflammation after Use of Anti-adhesion Agents. *Journal of Retina*, *7*(1), 16-20.
2. Yu, M. M., Jiang, T. F., Wang, Y. H., Wang, D. Y., & Lv, Z. H. (2013). Identification and analysis of an impurity inducing clinical adverse effect in anti-adhesion carboxymethyl chitosan products. *Journal of pharmaceutical and biomedical analysis*, *85*, 21-27.
3. Park, J., Kang, H., Choi, Y. S., Suh, S. W., Hong, S. A., Choi, G. J., & Sim, W. J. (2022). Prevention of Intra-Abdominal Adhesions Using the Combination of Mediclore® and a Statin. *European Surgical Research*, *63*(3), 123-131.
4. Ripa, M., Schipa, C., Kopsacheilis, N., Nomikarios, M., Perrotta, G., De Rosa, C., ... & Motta, L. (2022). The impact of steep trendelenburg position on intraocular pressure. *Journal of Clinical Medicine*, *11*(10), 2844.
5. Grosso, A., Scozzari, G., Bert, F., Mabilia, M. A., Siliquini, R., & Morino, M. (2013). Intraocular pressure variation during colorectal laparoscopic surgery: standard pneumoperitoneum leads to reversible elevation in intraocular pressure. *Surgical endoscopy*, *27*, 3370-3376.
6. Awad, H., Santilli, S., Ohr, M., Roth, A., Yan, W., Fernandez, S., ... & Patel, V. (2009). The effects of steep trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesthesia & Analgesia*, *109*(2), 473-478.
7. Takeuchi, M., Mizuki, N., & Ohno, S. (2021). Pathogenesis of non-infectious uveitis elucidated by recent genetic findings. *Frontiers in immunology*, *12*, 640473.
8. Babu, K., Konana, V. K., Ganesh, S. K., Patnaik, G., Chan, N. S., Chee, S. P., ... & Zierhut, M. (2020). Viral anterior uveitis. *Indian journal of ophthalmology*, *68*(9), 1764-1773.
9. Agarwal, M., Majumder, P. D., Babu, K., Konana, V. K., Goyal, M., Touhami, S., ... & Bodaghi, B. (2020). Drug-induced uveitis: A review. *Indian journal of ophthalmology*, *68*(9), 1799-1807.
10. Hong, K. Y., Kim, I. K., Sakong, Y., Park, B. Y., & Jin, U. S. (2023). Effects of an Antiadhesive Agent on Capsule Formation in Implant-Based Breast Reconstruction: A Randomized Controlled Trial. *Plastic and Reconstructive Surgery*, *151*(4), 717-726.
11. Shin, H. Y., Paik, J. S., & Yang, S. W. (2018). Clinical results of anti-adhesion adjuvants after endonasal dacryocystorhinostomy. *Korean Journal of Ophthalmology*, *32*(6), 433-437.
12. Yang, H., Peng, L., Jian, M., & Qin, L. (2014). Clinical analysis of 15 patients with relapsing auricular polychondritis. *European Archives of Oto-Rhino-Laryngology*, *271*, 473-476.
13. Mccune, W. J., Schiller, A. L., Dynesius-Trentham, R. A., & Trentham, D. E. (1982). Type II collagen—induced auricular chondritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *25*(3), 266-273.