Acta Scientiae Veterinariae, 2025. 53(Suppl 1): 1012.

CASE REPORT
Pub. 1012

ISSN 1679-9216

Management of Recurrent Skin Dehiscence by Subcutaneous Ureteral Bypass Shunting Port in a Bitch - Efficacy of Doxycycline

Jongchul Yun & Sungin Lee

ABSTRACT

***Background*:** Ureteral obstruction compromises renal function depending on duration, requiring immediate evaluation and renal decompression. Less invasive interventional techniques increasingly supplement traditional surgical treatments. In dogs, double pigtail ureteral stents are commonly used; however, subcutaneous ureteral bypass devices should be treatment options when stents fail due to complications. Doxycycline, a tetracycline antibiotic, has been shown to have anti-inflammatory and immunomodulatory properties by various mechanisms. This report demonstrates the efficacy of doxycycline for managing recurrent skin dehiscence caused by a local immune response to a SUB shunting port in a bitch.
***Case*:** A 10-year-old spayed bitch toy poodle weighing 4.1 kg, was referred for recurrent skin dehiscence at the SUB shunting port placement site. The bitch had been diagnosed with right ureteral obstruction caused by a ureteral calculus 15 months ago, and unilateral SUB placement had been performed. The animal underwent 3 reconstructive surgeries with broad-spectrum antibiotics treatment at the local animal hospital. Despite these interventions, skin dehiscence recurred at the SUB shunting port placement site. On presentation, the shunting port was exposed on the right side of the midline, with a mild exudate around the port. Cytology examination and bacterial culture were negative for infection. Laboratory tests revealed elevated blood urea nitrogen, alkaline phosphatase, C-reactive protein, and monocytosis. Diagnostic imaging showed severely irregular margins of both kidneys, bilateral renal and right ureteral calculi, with the SUB device correctly placed and no evidence of fluid leakage or displacement. Based on the patient's history and these findings, the skin dehiscence was determined to be caused by a local immune response. Treatment with doxycycline, known for its anti-inflammatory and immunomodulatory effects, was selected. SUB replacement with skin debridement was performed under general anesthesia, and doxycycline was administered orally for 4 weeks. At the 3-week post-surgery follow-up, the skin had completely healed, demonstrating the successful treatment outcome. At 3 months post-surgery, no complications were observed, and the overall condition remained stable.
***Discussion*:** To our knowledge, this is the 1st report of recurrent skin dehiscence caused by a subcutaneous ureteral bypass shunting port in dogs. The implantation of medical devices triggers a complex signaling cascade with the host's immune system, resulting in foreign body reactions. The lack of response to previous antibiotic treatments at the local animal hospital, the absence of bacterial infection evidence, and the clinical improvement with doxycycline suggest that the immune and inflammatory response to the medical device was modulated through mechanisms such as matrix metalloproteinase inhibition, decreased pro-inflammatory cytokine levels, and reduced reactive oxygen species. Although these complications with subcutaneous ureteral bypass devices are rare, immune responses should be considered in cases of poor response to treatments. These foreign body reactions are highly complex, and their mechanisms are not fully understood, making diagnosis and treatment challenging. Since the limited therapeutic options available to mitigate these responses with minimal adverse effects, doxycycline presents a viable alternative for managing complications associated with medical devices in dogs.

Keywords: canine, dog, ureteral obstruction, subcutaneous ureteral bypass, skin dehiscence, doxycycline, immunomodulatory agent.

DOI: 10.22456/1679-9216.141728

Received: 20 October 2024 Accepted: 12 December 2024 Published: 8 January 2025

Department of Veterinary Surgery, College of Veterinary Medicine, Chungbuk National University (CBNU), Cheongju, Republic of Korea. CORRESPONDENCE: S. Lee [sunginlee@cbnu.ac.kr]. Department of Veterinary Surgery, College of Veterinary Medicine - CBNU. Chungdae-ro 1, Seowon-gu, Cheongju 28644, Republic of Korea.

INTRODUCTION

Ureteral obstruction impairs renal function, leading to intertubular fibrosis and tubular atrophy depending on the duration, thus requiring prompt evaluation and renal decompression [6]. Traditional surgical treatments (eg, ureterotomy, neoureterocystotomy, pyelotomy, and ureteroureterostomy) are being supplemented by interventional management techniques, which are less invasive and demonstrate effective outcomes [2]. In dogs, double pigtail urethral stents are commonly used; however, if the stent is no longer functional due to complications, subcutaneous ureteral bypass (SUB) devices may be considered [14]. In one study of 9 dogs undergoing SUB placement for benign ureteral obstruction, the placement was successful in 12 renal units with no perioperative or procedure-related deaths. Complications include obstruction with mineral debris, urinary tract infection, and progressive azotemia [13].

Doxycycline - a tetracycline antibiotic - has been shown to modulate various inflammatory pathways, notably by inhibiting matrix metalloproteinases (MMPs) that degrade structural components within the extracellular matrix, produce changes in cellular behavior and modulate subsequent foreign body reaction and wound healing [9].

This case report aims to demonstrate the use of doxycycline as an anti-inflammatory and immunomodulatory agent for recurrent skin dehiscence, presumed to be caused by local immune response to SUB shunting port in a bitch.

CASE

A 10-year-old spayed bitch toy poodle, weighing 4.1 kg, was referred for recurrent skin dehiscence at the SUB shunting port placement site. The bitch had been diagnosed with right ureteral obstruction caused by a ureteral calculus 15 months ago, and unilateral SUB placement had been performed. The animal had undergone 3 reconstructive surgeries at the local animal hospital. Two surgeries included skin debridement and skin closure with broad-spectrum antibiotic treatment for 6 weeks, and one involved replacement of SUB device with broad-spectrum antibiotic treatment for 4 weeks. Despite these interventions, skin dehiscence recurred at the SUB shunting port placement site.

On presentation, the shunting port of the SUB was exposed on the right side of the midline, and a mild exudate was identified around the port (Figure 1A). Cytology examination using a sterilized swab revealed no bacteria, and bacterial culture was negative. Complete blood count and serum biochemistry tests showed normal values for all parameters except elevations in blood urea nitrogen (58.2 mg/dL; Ref.: 7-25 mg/dL), alkaline phosphatase (522 IU/L, Ref.:29-97 IU/L), C-reactive protein (18.14 mg/L; Ref.: 0-10 mg/L), and monocytosis (1.63 k/μL; Ref.:0.16-1.12 k/μL). Abdominal radiography revealed bilateral renal and right ureteral calculi. Abdominal ultrasonography revealed severely irregular margins and a reduced corticomedullary definition with a hyperechoic cortex in both kidneys. The SUB device was correctly placed within the right renal pelvis and bladder, and no fluid was observed in the retroperitoneal cavity. Based on the patient's history and these results, the skin dehiscence was determined to be caused by a local immune response. Treatment was planned to reduce the immune response following SUB replacement surgery. Typically, glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), and anti-fibrotic agents are used to control the immune response. However, due to concerns about delayed skin union, skin atrophy, infection, and renal damage, doxycycline was selected for its potent anti-inflammatory and immunomodulatory effects.

SUB replacement with skin debridement was performed to stabilize the skin at the surgical site. Before surgery, amoxicillin-clavulanate[1] [22 mg/kg] and midazolam[2] [0.2 mg/kg] were administered intravenously. Perioperative analgesia was provided with remifentanil CRI[3] [2.5 μg/kg/h]. The dog was anesthetized and positioned in left lateral recumbency (Figure 2A). The exposed port was cleaned with a 0.5% diluted chlorhexidine solution, and an extended incision was made on the skin around the exposed shunting port. Subcutaneous tissue was removed and debrided (Figure 2B). During the operation, iohexol diluted in lactated Ringer's solution was delivered by using C-arm fluoroscopy with a SUB flushing kit (20-gauge Huber point needle port, 3-way stopcock, T-port connector) to ensure that the device was functioning correctly (Figure 2C). Finally, the shunting port was sutured to the ventral body wall musculature and lavaged with warm, lactated Ringer's solution. The subcutaneous tissue and skin over the port were routinely closed (Figure 2D), and topical lidocaine and bupivacaine were injected into the subcutaneous space around the incision line.

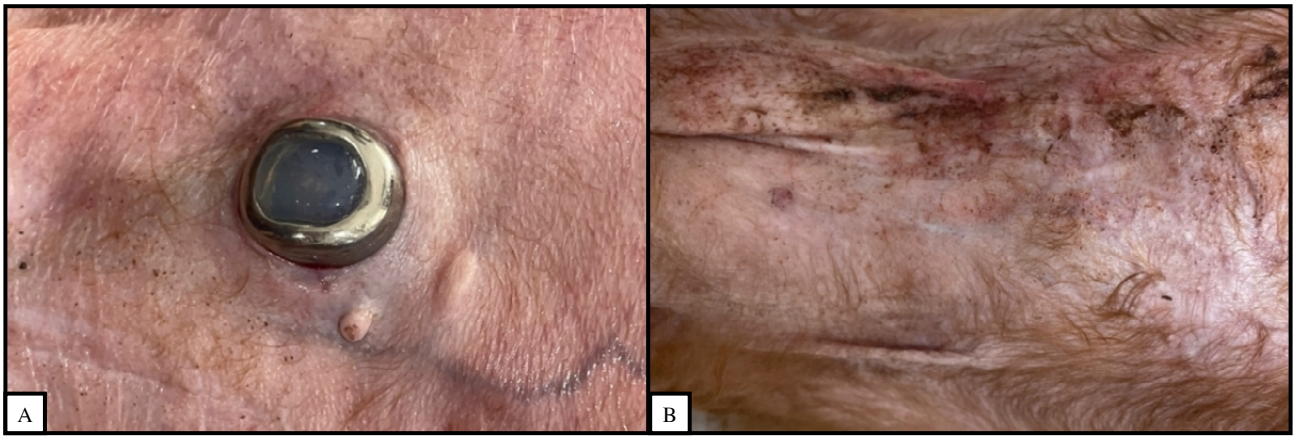

Figure 1. A- The SUB shunting port was exposed on the right side of the midline. B- Three months after the surgery, no complications were identified.

The dog was discharged 1 day after surgery, and doxycycline[4] [5 mg/kg, q12h] was administered orally for 4 weeks. At the 3-week post-surgery follow--up, the skin had completely healed (Figure 1B). After 3 months of the surgery, no complications were identified.

DISCUSSION

This case report demonstrates the efficacy of doxycycline for managing recurrent skin dehiscence caused by SUB shunting port in a dog. In 3 retrospective studies on dogs and cats with SUB devices, no direct skin dehiscence or extrusion of devices was reported at the placement site [3,13,18]. There are only 2 case reports in cats that have documented skin dehiscence and device exposure as complications of SUB placement [7,12]. These complications, although rare, should be considered major due to the risk of infection and the necessity of reoperation. Factors such as biocompatibility, infection, device design, implantation technique, and complex interactions between the biomaterial and host immune system have been suggested as causes of these

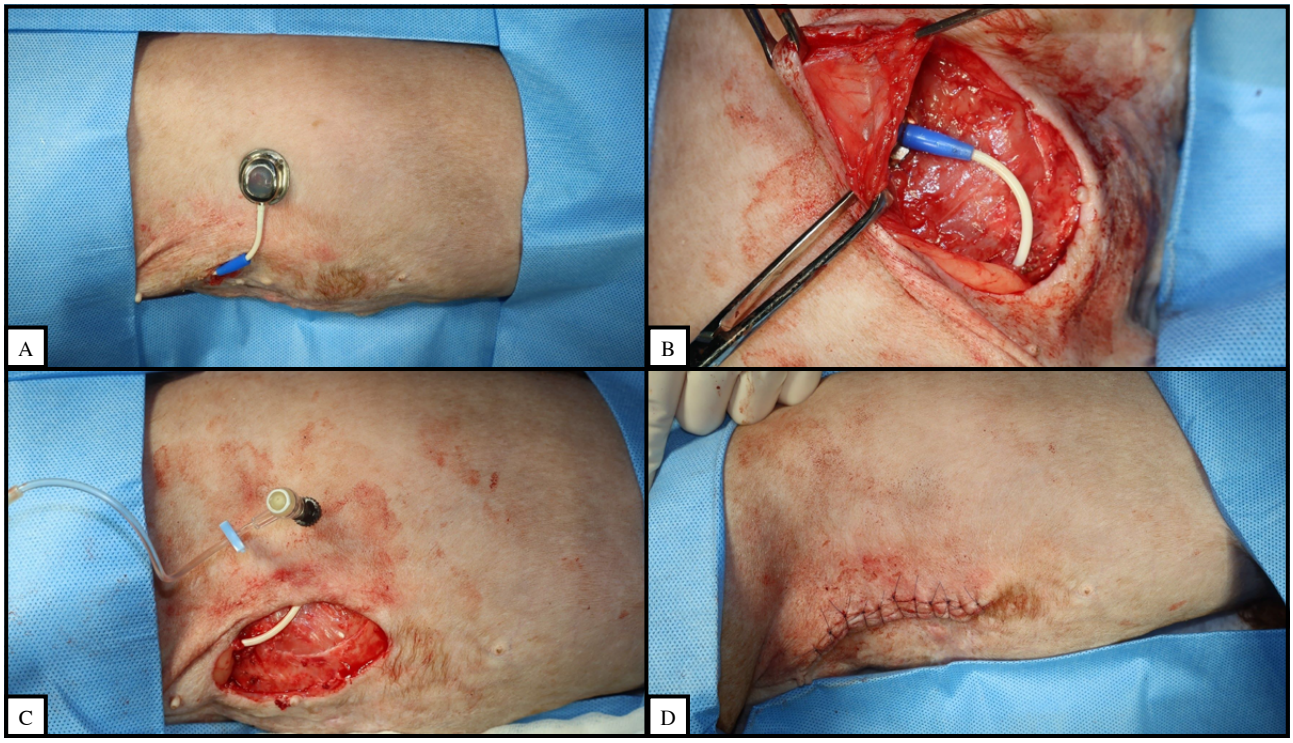

Figure 2. A- The bitch was anesthetized and positioned in left lateral recumbency. B- An extended incision was made in the skin around the exposed shunting port. Removal of subcutaneous tissues and debridement were performed. C- Iohexol diluted in lactated Ringer's solution was delivered using an SUB flushing kit to ensure the device was functioning correctly. D- The shunting port was sutured to the ventral body wall musculature and lavaged with warm lactated Ringer's solution. The subcutaneous tissue and skin over the port were closed routinely.

complications [1,7,11,12,16,20]. In this case, the lack of response to previous surgeries with broad-spectrum antibiotic treatments, the absence of bacterial infection evidence, and the clinical improvement after doxycycline administration suggest that the anti-inflammatory and immunomodulatory properties of doxycycline were significant in managing recurrent dehiscence.

The interaction between implanted medical devices and the skin initiates a complex immune response within 2 weeks, marked by protein adsorption, acute and chronic inflammatory phases, and foreign body reactions [1]. Upon subcutaneous implantation, proteins such as albumin, fibronectin, fibrinogen, and complement absorb onto the implant surface, leading to an acute inflammatory response characterized by the infiltration of neutrophils and macrophages. These immune cells, particularly macrophages, recognize the implant as foreign and induce the formation of foreign body giant cells and the secretion of pro-inflammatory cytokines that perpetuate the inflammatory response [10]. In humans, glucocorticoids, NSAIDs, and anti-fibrotic agents are used as tissue response modifiers to target cellular components of the foreign body reaction and disrupt the cascade of inflammation around an implant [4]. In this case, glucocorticoids were not considered due to the risk of infection, skin atrophy, and delayed wound healing. Additionally, because the patients had abnormal findings in both kidneys, NSAIDs were avoided due to their potential renal toxicity.

Doxycycline has been shown to have beneficial immunomodulatory actions in various inflammatory and immune-mediated conditions, especially on the skin [17,19]. MMPs, particularly MMP-2, MMP-3, MMP-8, MMP-9, and MMP-13, are inhibited by doxycycline, reducing their expression and enzymatic activity [8]. Since MMPs are involved in inflammatory processes and tissue remodeling, doxycycline, as an MMP inhibitor, mitigates inflammatory response to medical devices and promotes tissue healing. Doxycycline also modulates pro-inflammatory cytokines such as IL-6, IL-8, TNF-α, and nitric oxide synthesis - a molecule associated with inflammation and tissue damage [5]. Furthermore, its effect on canine neutrophil function is corroborated, demonstrating that doxycycline significantly diminishes the production of reactive oxygen species and induces neutrophil extracellular trap formation [15]. With these multimodal immunomodulatory activities, doxycycline was considered to have the fewest possible side effects for patients with long-term administration and has shown positive outcomes for the patient.

To our knowledge, this is the 1st report of recurrent skin dehiscence caused by SUB device extrusion in a dog. It highlights the potential of doxycycline as an effective treatment for managing complications associated with medical devices in dogs. Although these complications are rare, immune responses should be considered in cases of poor response to common treatments Given the limited options available to mitigate these responses with minimal adverse side effects, doxycycline should be the therapeutic alternative.

MANUFACTURERS

[1]Kuhnil Pharmaceutical. Co. Ltd. Seoul, Republic of Korea.
[2]Bukwang pharm. Co. Ltd. Seoul, Republic of Korea.
[3]BCWorld Pharm Co. Ltd. Sungnam, Republic of Korea.
[4]YoungPoong Pharmaceutical Co. Ltd. Incheon, Republic of Korea.

Acknowledgments. This work was supported by supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (RS-2023-00253736), and "Regional Innovation Strategy (RIS)" through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (MOE) (2024RIS-001).

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1 **Anderson J.M. & Jiang S. 2017.** Implications of the acute and chronic inflammatory response and the foreign body reaction to the immune response of implanted biomaterials. In: Corradetti B. (Ed). *The Immune Response to Implanted Materials and Devices.* Cham: Springer, pp.17-36. DOI: 10.1007/978-3-319-45433-7_2

2 **Berent A.C. 2011.** Ureteral obstructions in dogs and cats: a review of traditional and new interventional diagnostic and therapeutic options. *Journal of Veterinary Emergency and Critical Care.* 21: 86-103. DOI: 10.1111/j.1476--4431.2011.00628.x

3 **Berent A.C., Weisse C.W., Bagley D.H. & Lamb K. 2018.** Use of a subcutaneous ureteral bypass device for treatment of benign ureteral obstruction in cats: 174 ureters in 134 cats (2009-2015). *Journal of the American Veterinary Medical Association*. 253(10): 1309-1327. DOI: 10.2460/javma.253.10.1309

4 **Chandorkar Y., Ravikumar K. & Basu B. 2019.** The foreign body response demystified. *ACS Biomaterials Science & Engineering*. 5(1): 19-44. DOI: 10.1021/acsbiomaterials.8b00252

5 **Di Caprio R., Lembo S., Di Costanzo L., Balato A. & Monfrecola G. 2015.** Anti-inflammatory properties of low and high doxycycline doses: an *in vitro* study. *Mediators of Inflammation.* 2015: 329418. DOI: 10.1155/2015/329418

6 **Fink R.L.W., Caridis D.T., Chmiel R. & Ryan G. 1980.** Renal impairment and its reversibility following variable periods of complete ureteric obstruction. *Australian and New Zealand Journal of Surgery.* 50: 77-83. DOI: 10.1111/j.1445-2197.1980.tb04502.x

7 **Fouhety A. & Boursier J.F. 2020.** Infection and extrusion of a subcutaneous access port in a cat: a long-term postoperative complication of a subcutaneous ureteral bypass device. *Journal of Feline Medicine and Surgery Open Reports.* 6(1): 2055116920911765. DOI: 10.1177/2055116920911765

8 **Henehan M., Montuno M. & De Benedetto A. 2017.** Doxycycline as an anti-inflammatory agent: updates in dermatology. *Journal of the European Academy of Dermatology and Venereology*. 31: 1800-1808. DOI: 10.1111/jdv.14345

9 **Jones J.A., McNally A.K., Chang D.T., Qin L.A., Meyerson H., Colton E., Kwon I.L.K., Matsuda T. & Anderson J.M. 2008.** Matrix metalloproteinases and their inhibitors in the foreign body reaction on biomaterials. *Journal of Biomedical Materials Research Part A*. 84A: 158-166. DOI: 10.1002/jbm.a.31220

10 **Kastellorizios M., Tipnis N. & Burgess D.J. 2015.** Foreign body reaction to subcutaneous implants. In: Barbosa M.A. & Martins M.C.L. (Eds). *Immune Responses to Biosurfaces. Advances in Experimental Medicine and Biology*. Cham: Springer, pp.93-108. DOI: 10.1007/978-3-319-18603-0_6

11 **Kunda L.D., Stidham K.R., Inserra M.M., Roland P.S., Franklin D. & Roberson Jr. J.B. 2006.** Silicone allergy: a new cause for cochlear implant extrusion and its management. *Otology & Neurotology*. 27(8): 1078-1082. DOI: 10.1097/01.mao.0000235378.64654.4d

12 **Lee S.M. & Tuan J. 2024.** Surgical repositioning with omentalisation of an exposed subcutaneous ureteral bypass shunting port in a cat. *Journal of Feline Medicine and Surgery Open Reports*. 10(1): 20551169241257884. DOI: 10.1177/20551169241257884

13 **Milligan M.L., Berent A.C., Weisse C.W., Lamb K. & Tozier E. 2020.** Outcome of SUB placement for the treatment of benign ureteral obstruction in dogs: nine dogs and 12 renal units (2013 to 2017). *Journal of Small Animal Practice*. 61: 428-435. DOI: 10.1111/jsap.13137

14 **Pavia P.R., Berent A.C., Weisse C.W., Neiman D., Lamb K. & Bagley D. 2018.** Outcome of ureteral stent placement for treatment of benign ureteral obstruction in dogs: 44 cases (2010–2013). *Journal of the American Veterinary Medical Association*. 252(6): 721-731. DOI: 10.2460/javma.252.6.721

15 **Rieder J.C., Steffensen N., Imker R., Lassnig S. & Buhr N. 2024.** The effect of doxycycline on canine neutrophil functions. *Veterinary Immunology and Immunopathology.* 267: 110701. DOI: 10.1016/j.vetimm.2023.110701

16 **Santarpia G., Sarubbi B., D'Alto M., Romeo E. & Calabrò R. 2009.** Extrusion of the device: a rare complication of the pacemaker implantation. *Journal of Cardiovascular Medicine*. 10(4): 330-332. DOI: 10.2459/JCM.0b013e328316bbf8

17 **Sapadin A.N. & Fleischmajer R. 2006.** Tetracyclines: nonantibiotic properties and their clinical implications. *Journal of the American Academy of Dermatology*. 54(2): 258-265. DOI: 10.1016/j.jaad.2005.10.004

18 **Vrijsen E., Devriendt N., Mortier F., Stock E., van Goethem B. & Rooster H. 2021.** Complications and survival after subcutaneous ureteral bypass device placement in 24 cats: a retrospective study (2016–2019). *Journal of Feline Medicine and Surgery*. 23(8): 759-769. DOI: 10.1177/1098612X20975374

19 **Yu Jr. L.P., Smith Jr. G.N., Brandt K.D., Myers S.L., O'Connor B.L. & Brandt D.A. 1992.** Reduction of the severity of canine osteoarthritis by prophylactic treatment with oral doxycycline. *Arthritis & Rheumatism*. 35: 1150-1159. DOI: 10.1002/art.1780351

20 **Zakhar J., Blount T.J., Gehi A.K. & Ferns S.J. 2020.** Un-LINQed: spontaneous extrusion of newer generation implantable loop recorders. *Indian Pacing and Electrophysiology Journal*. 20(5): 189-192. DOI: 10.1016/j.ipej.2020.04.005