Case Rep Oncol 2018;11:164-167

DOI: 10.1159/000487390 Published online: March 15, 2018 © 2018 The Author(s) Published by S. Karger AG, Basel www.karger.com/cro



This article is licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC) (http://www.karger.com/Services/OpenAccessLicense). Usage and distribution for commercial purposes requires written permission.

**Case Report** 

# Fluorescent Light-Guided Cystoscopy with 5-ALA Aids in Accurate Surgical Margin Detection for TURBO: A Case Report

Daiji Takamoto<sup>a</sup> Takashi Kawahara<sup>a</sup> Shinji Ohtake<sup>b</sup> Taku Mochizuki<sup>a</sup> Shinnosuke Kuroda<sup>a</sup> Noboru Nakaigawa<sup>b</sup> Koji Izumi<sup>a</sup> Yasuhide Miyoshi<sup>a</sup> Kazuhide Makiyama<sup>b</sup> Masahiro Yao<sup>b</sup> Tomoe Sawazumi<sup>c</sup> Yoshiaki Inayama<sup>c</sup> Junichi Ohta<sup>d</sup> Hiroji Uemura<sup>a</sup>

<sup>a</sup>Departments of Urology and Renal Transplantation, Yokohama City University Medical Center, Yokohama, Japan; <sup>b</sup>Department of Urology, Yokohama City University Graduate School of Medicine, Yokohama, Japan; <sup>c</sup>Department of Diagnostic Pathology, Yokohama City University Medical Center, Yokohama, Japan; <sup>d</sup>Department of Urology, Yokohama Municipal Hospital, Yokohama, Japan

#### Keywords

Fluorescent light-guided cystoscopy · 5-ALA · TURBO · TUR-Bt

#### Abstract

Recent studies have revealed that transurethral resection in one piece (TURBO) has several benefits over standard transurethral resection of bladder tumor (TUR-Bt), including a higher rate of containing the bladder muscle tissue and single-block resection. Five-aminolevulinic acid (5-ALA) was approved for the detection of bladder tumor treated with TUR-Bt. A 71-year-old male patient who received right nephroureterectomy developed bladder tumor recurrence on routine cystoscopy follow-up. We planned TURBO using fluorescent light-guided cystoscopy with 5-ALA. We herein report a case of bladder tumor successfully treated with TURBO using fluorescent light-guided cystoscopy with 5-ALA. We herein report a case of bladder tumor successfully treated with TURBO using fluorescent light-guided cystoscopy with 5-ALA to detect the tumor surgical margin.

Published by S. Karger AG, Basel



Takashi Kawahara, MD, PhD Departments of Urology and Renal Transplantation Yokohama City University Medical Center 4-57 Urafune-cho, Minami-ku, Yokohama, Kanagawa 232-0024 (Japan) E-Mail kawahara@yokohama-cu.ac.jp

| Case Rep Oncol 2018;11:164–167 |   |  |
|--------------------------------|---|--|
| DOI: 10.1159/000487390         | $\ensuremath{\mathbb{C}}$ 2018 The Author(s). Published by S. Karger AG, Basel www.karger.com/cro |  |

Takamoto et al.: Fluorescent Light-Guided Cystoscopy with 5-ALA Aids in Accurate Surgical Margin Detection for TURBO: A Case Report

#### Introduction

Recent studies have shown that transurethral resection in one piece (TURBO) has several benefits over standard transurethral resection of bladder tumor (TUR-Bt), including a higher rate of containing the bladder muscle tissue and single-block resection [1, 2]. Because of its single-block resection characteristic, TURBO requires the establishment of margins before tumor resection. Establishing margins has historically depended on the clinician's experience. Tumor margins are easy to detect in most papillary tumors. However, in some tumors, such as broad-base tumors, the line of the bladder tumor is difficult to detect. Fiveaminolevulinic acid (5-ALA) was approved for use in December 2017 in Japan for the detection of bladder tumors treated with TUR-Bt [3].

We herein report a case of bladder tumor successfully treated with TURBO using fluorescent light-guided cystoscopy with 5-ALA to detect the tumor surgical margin.

#### **Case Presentation**

A 71-year-old male patient who received right nephroureterectomy developed bladder tumor recurrence on routine cystoscopy follow-up. We planned TURBO using fluorescent light-guided cystoscopy with 5-ALA. The patient was administered 5-ALA (ALAGLIO; Chugai Pharmaceutical Co., Tokyo, Japan) according to protocol 4 h prior to TURBO. A laser device was used (Aladuck LS-DLED; SBI Pharmaceuticals, Tokyo, Japan). Before setting the margins for TURBO, we checked the fluorescent lighting of the tumor. The tumor margin was easily detected by fluorescence (Fig. 1). TURBO was then performed without any complications. The final pathological diagnosis was pathological Ta, and the tumor was resected without a positive surgical margin.

#### Discussion

Fluorescent light-guided cystoscopy with 5-ALA has shown good efficacy for TUR-Bt [4]. Using photodynamic diagnostic (PDD) cystoscopy has been found to increase the CIS detection to 91–97% compared with 23–68% with white light [5]. Kata et al. [6] reported that PDD using 5-ALA detected CIS in 12 of 13 cases. Hermann et al. [7] showed that PDD decreased the amount of residual tumor not only in cases of CIS but also in those of Ta and T1 bladder carcinoma.

Urinary bladder cancer is one of the most commonly diagnosed malignancies [8]. Twothirds to three-fourths of patients with bladder tumors initially present with non-muscleinvasive (pTa or pT1) disease that can often be treated with conservative approaches. However, many patients suffer from recurrence, occasionally with grade and/or stage progression [9]. For bladder carcinoma, complete resection is important to control the disease and avoid recurrence of bladder cancer.

In the present case, we established the surgical margins using 5-ALA in order to ensure complete resection of the tumor. TURBO exposed the muscle tissue layer at the bottom of the bladder tumor. TURBO also helped us achieve an accurate pathological diagnosis, as an electric knife is rarely needed in such cases [1].

5-ALA has also proven to be a useful tool for detecting tumors of gastric cancer and glioblastoma [10, 11]. 5-ALA is an intrinsic amino acid intimately involved with heme synthesis

### KARGER

| Case Rep Oncol 2018;11:164–167 |   |
|--------------------------------|---|
| DOI: 10.1159/000487390         | $\ensuremath{\mathbb{C}}$ 2018 The Author(s). Published by S. Karger AG, Basel www.karger.com/cro |
|                                |   |

Takamoto et al.: Fluorescent Light-Guided Cystoscopy with 5-ALA Aids in Accurate Surgical Margin Detection for TURBO: A Case Report

in nucleated cells. Because cancer cells exhibit changes in enzymatic activity in the heme synthetic pathway, the exogenous administration of 5-ALA causes the intracellular accumulation of the heme precursor protoporphyrin IX (PpIX) in cancer cells. Importantly, PpIX emits red light upon excitation with 405-nm blue-violet light, whereas 5-ALA is not fluorescent [12]. Via these mechanisms, establishing the surgical margins using 5-ALA in the first step of TURBO helped achieve accurate resection.

These findings show that 5-ALA detects surgical margins more accurately than white light, resulting in complete surgical resection with the TURBO technique.

#### Conclusion

We herein report a case of bladder tumor successfully treated with TURBO using fluorescent light-guided cystoscopy with 5-ALA to detect the tumor surgical margin.

#### **Statement of Ethics**

Written informed consent was obtained from the patient. Due to ethical restrictions, the raw data underlying this paper are available upon request to the corresponding author.

#### **Disclosure Statement**

The authors declare no conflicts of interest

#### **Funding Sources**

This study was supported by KAKENHI grants (16K20152) from the Ministry of Education, Culture, Sports, Science and Technology of Japan and a grant for the 2016–2017 Research Development Fund (No. WJ2810) of Yokohama City University.

#### **Author Contributions**

Conceived and designed the experiments: D.T., T.K., S.O., N.N., J.O., H.U. Analyzed the data: D.T., T.K., T.S., Y.I. Performed the experiments: D.T., T.K., S.O., T.M., S.K., N.N., K.I., Y.M., K.M., M.Y., H.U. Wrote the paper: D.T., T.K.

#### References

- 1 Ukai R, Hashimoto K, Iwasa T, Nakayama H. Transurethral resection in one piece (TURBO) is an accurate tool for pathological staging of bladder tumor. Int J Urol. 2010 Aug;17(8):708–14.
- 2 Miyamoto H. Clinical benefits of frozen section assessment during urological surgery: does it contribute to improving surgical margin status and patient outcomes as previously thought? Int J Urol. 2017 Jan;24(1): 25–31.
- 3 Inoue K. 5-Aminolevulinic acid-mediated photodynamic therapy for bladder cancer. Int J Urol. 2017 Feb; 24(2):97–101.



| Case Rep Oncol 2018;11:164–167 |   |
|--------------------------------|---|
| DOI: 10.1159/000487390         | © 2018 The Author(s). Published by S. Karger AG, Basel www.karger.com/cro |
|                                |   |

Takamoto et al.: Fluorescent Light-Guided Cystoscopy with 5-ALA Aids in Accurate Surgical Margin Detection for TURBO: A Case Report

- 4 Tran K, Severn M. Blue Light Cystoscopy in Patients with Suspected Non-Muscle Invasive Bladder Carcinoma: A Review of Clinical Utility. In: CADTH Rapid Response Reports. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017.
- 5 Casey RG, Catto JW, Cheng L, Cookson MS, Herr H, Shariat S et al. Diagnosis and management of urothelial carcinoma in situ of the lower urinary tract: a systematic review. Eur Urol. 2015 May;67(5):876–88.
- 6 Kata SG, Zreik A, Ahmad S, Chłosta P, Aboumarzouk O. Concurrent bladder cancer in patients undergoing photodynamic diagnostic ureterorenoscopy: how many lesions do we miss under white light cystoscopy? Cent European J Urol. 2016;69(4):334–40.
- 7 Hermann GG, Mogensen K, Carlsson S, Marcussen N, Duun S. Fluorescence-guided transurethral resection of bladder tumours reduces bladder tumour recurrence due to less residual tumour tissue in Ta/T1 patients: a randomized two-centre study. BJU Int. 2011 Oct;108(8 Pt 2):E297–303.
- 8 Kobatake K, Hayashi T, Black PC, Goto K, Sentani K, Kaneko M et al. Chronic kidney disease as a risk factor for recurrence and progression in patients with primary non-muscle-invasive bladder cancer. Int J Urol. 2017 Aug;24(8):594–600.
- 9 Shimizu F, Muto S, Taguri M, Ieda T, Tsujimura A, Sakamoto Y et al. Effectiveness of platinum-based adjuvant chemotherapy for muscle-invasive bladder cancer: A weighted propensity score analysis. Int J Urol. 2017 May;24(5):367–72.
- 10 Koizumi N, Harada Y, Minamikawa T, Tanaka H, Otsuji E, Takamatsu T. Recent advances in photodynamic diagnosis of gastric cancer using 5-aminolevulinic acid. World J Gastroenterol. 2016 Jan;22(3):1289–96.
- 11 Stummer W, Novotny A, Stepp H, Goetz C, Bise K, Reulen HJ. Fluorescence-guided resection of glioblastoma multiforme by using 5-aminolevulinic acid-induced porphyrins: a prospective study in 52 consecutive patients. J Neurosurg. 2000 Dec;93(6):1003–13.
- 12 Bedwell J, MacRobert AJ, Phillips D, Bown SG. Fluorescence distribution and photodynamic effect of ALAinduced PP IX in the DMH rat colonic tumour model. Br J Cancer. 1992 Jun;65(6):818–24.



**Fig. 1. a** White light image of the tumor. **b**, **c** Fluorescent light-guided cystoscopy with 5-ALA. **d–f** The resection line was determined by fluorescent light-guided cystoscopy.

#### 167

### KARGER