Detection of the Communication Site by Indocyanine Green Adsorbed to Human Serum Albumin Fluorescence During Surgery for a Pleuroperitoneal Communication

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Research Article
Keywords: pleuropitoneal communication, ICG:HSA, indocyanine green

DOI: https://doi.org/10.21203/rs.3.rs-537617/v1

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Abstract

A pleuroperitoneal communication is a serious complication for patients undergoing continuous ambulatory peritoneal dialysis (CAPD). Video-assisted thoracoscopic surgery is performed using indocyanine green adsorbed to human serum albumin fluorescence to identify the communication because human serum albumin reinforces fluorescence images. A patient diagnosed with a pleuroperitoneal communication was referred to our department and underwent surgery. To detect the communication, a dialysate mixture that contained indocyanine green and human serum albumin was injected from the CAPD catheter. Real-time fluorescence images were able to clearly show a bleb-like lesion with a near-infrared spectroscopy camera, and the site was repaired. The patient had no recurrence at one-year follow-up. This method might be good method for pleuroperitoneal communication surgery.

Introduction

The first case of pleuroperitoneal communication (PPC) was reported in 1967 by Edward [1]. Although approximately 50% of patients need to convert to hemodialysis, most patients still need to continue CAPD for social reasons [2]. As the surgical procedures to treat PPC, resection, direct suturing, and reinforcement of the responsible lesion of the diaphragm are performed. For PPC surgery, identification and closure of the communication site is important. Herein, we report a PPC case with VATS in which indocyanine green (ICG)-adsorbed human serum albumin (ICG:HSA) fluorescence and it was able to clearly show a bleb-like lesion and repair communication site. This method might become useful method for pleuroperitoneal communication surgery.

Case Report

A 52-year-old woman was referred to our department for treatment of continuous ambulatory peritoneal dialysis (CAPD)-induced hydrothorax. The patient had chronic renal failure due to chain deposition disease and was started on CAPD one month before being referred. The amounts of CAPD effluent were in negative balance after each injection. Though she had no symptoms during CAPD, a chest X-ray after CAPD showed right hydrothorax. Peritoneal radioscintigraphy using Tc-99m macro-aggregated albumin containing human serum albumin 2.1 mg showed a communication between the peritoneal cavity and the pleural cavity 26 minutes after starting CAPD. (Fig. 1) Because of the patient's desire to continue CAPD for occupational reasons, she underwent surgical intervention to close the communication site using VATS. To accurately identify the communication site, VATS with ICG:HSA fluorescence was performed. Written, informed consent to use ICG:HSA was obtained from the patient before surgery. The operation was performed under general anesthesia with the patient in the left decubitus position. One port (7th intercostal) and one window of 6 cm (5th intercostal) were made. Through the CAPD catheter, 1500 ml of dialysate mixture containing 50 mg of indocyanine green (Daiichi Sankyo, Tokyo, Japan) mixed with 50 ml of 20% albumin (Nihon Pharmaceutical, Tokyo, Japan) were injected. The final concentration of ICG:HSA was 41 μM. To identify the site of communication, the diaphragm was observed with a near-infrared spectroscopy (NIR) thoracoscope (1588 AIM Thoracoscope; Stryker, Tokyo,
Japan). Then, 15 minutes after the injection, green fluorescent dye was seen to seep out from the diaphragm when it was pushed caudally (Fig. 2). A few minutes later, a thinner part of the diaphragm with bleb-like lesions was stained with green. However, 30 minutes after filling the intraperitoneal cavity with the CAPD mixture, no leakage was seen from the peritoneal cavity to the pleural cavity.

After marking the communication sites with crystal violet pen, the dialysate mixture was collected into the CAPD bag. Then, horizontal mattress sutures with 2 – 0 VICRYL Plus (ETHICON, Inc., somerville, NJ, USA) were placed. After closure, ICG:HSA solution was re-injected from the CAPD bag to the peritoneum to check residual leakage. No major leakage was found, except for slight seepage at the needle hole. Then, the diaphragm was covered with oxidized regenerated cellulose (SURGICEL absorbable hemostat, Jonson and Jonson, Tokyo, Japan) and fibrin glue (Beriplast P, CSL Behring, Tokyo, Japan). The patient resumed CAPD 14 days later, and no recurrence of the right hydrothorax was observed for 12 months after the operation.

Discussion

The first case of PPC was reported in 1967 by Edwards [1]. Although approximately 50% of patients need to convert to hemodialysis, most patients still need to continue CAPD for social reasons [2], and they require non-surgical or surgical treatment. As the surgical procedures to treat PPC, resection, direct suturing, and reinforcement of the responsible lesion of the diaphragm are performed, and these techniques are used either singly or in combination. In 1996, Di Bisceglie reported the first case of VATS for a PPC [3]. For identification of the communication between the peritoneal and pleural cavities, scintigraphy, the dye method (indigo carmine [6] and ICG [7]), and the CO₂ method [8] have been reported.

In our previous case, we used indigo carmine to identify the communicating lesion of the diaphragm [9]. However, a small lesion was difficult to detect because of poor visibility so we think ICG-HSA method is good for detecting the communication site. ICG is a water-soluble amphiphilic molecule with a molecular weight of 774.96 Da. Its hydrodynamic diameter is 1.2 nm, rendering it an excellent vascular and lymphatic contrast agent if injected intravenously and into the lymphatic system (for example by subcutaneous injection), respectively. After intravenous injection, 95% of ICG will bind to serum macromolecules such as albumin and lipoprotein [10], generating fluorescence in the near-infrared (center wavelength of 845 nm) with illumination by light of wavelength of 750–800 nm as the excitation light. In blood vessels, ICG binds lipoprotein in the blood and is easy to detect with an NIR camera.

Previous preclinical and clinical work has demonstrated that adsorption of ICG to human serum albumin increases the fluorescence intensity compared with ICG alone [11, 12]. In the present study, fluorescence was not detected without albumin, but it was well detected with a small amount of albumin (Fig. 3). Kawakita first reported the use of ICG fluorescence imaging combined with pneumoperitoneum for the detection of a diaphragmatic defect in a patient with hepatic hydrothorax [13]. Hepatic ascites often contains a high level of albumin, and it may adsorb ICG, but, in the peritoneal cavity, the amount of
albumin or lipoprotein is usually extremely low. Therefore, we used a dialysate mixture with ICG:HSA, as reported by Troyan and Mieog [12, 14]. ICG:HSA has about sixfold higher fluorescence intensity than ICG alone at a fluorophore concentration of 30μM in phosphate-buffered saline[11].

There are at least two advantages of the ICG:HSA fluorescence method during VATS. First, this method can easily identify not only leakage sites but also thinner parts of the diaphragm. Second, the fluorescence color facilitates finding the communication from the peritoneum to the pleura.

**Limitations**

As expected, there are limitations of this method. There was a difference between the preoperative scintigraphy and intraoperative ICG fluorescence method findings. Initially, during surgery, intrathoracic pressure is not negative because of one-lung ventilation. Second, the intraoperative position of the patient was usually the lateral decubitus position, and abdominal pressure was not affected. These factors might cause a difference in the findings between before and during surgery. Third, ICG toxicity is low, but it does contain sodium iodide. Therefore, it should be used with caution in patients with a history of allergy to iodides. Moreover, albumin is a blood product and administration should be minimized in terms of diminishing use. In case of hepatic hydrothorax, communication sites may identify with ICG alone because ascites contains large amount of albumin [13, 15].

**Conclusion**

Real-time ICG:HSA fluorescence images were obtained intraoperatively using an NIR camera to detect the thinner part and bleb-like lesions of the diaphragm. This method is considered suitable and might become standard for PPC management during VATS.

**Declarations**

**Authors’ Contributions** D.K. T.S. T.T. and I.F. were involved in conceptualisation, case data compilation and analysis. D.K. and C.Y.S. wrote the manuscript. I.F., S.K., T.F., R.M., N.N. and S.K. did proof reading of the manuscript. All authors read and approved the final version of the manuscript to be submitted.

**Data Availability** Not applicable.

**Compliance with Ethical Standards**

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Ethical Approval** The study was conducted in accordance with the ethical standards of the institute and with the 1964 Helsinki declaration and its later amendments.

**Consent to Participate** Written informed consent was obtained from the patient included in this study.
Consent for Publication Written informed consent was obtained from the patient for publication in a scientific journal.

Code Availability Not applicable.

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Figures

**Figure 1**

Imaging findings. A. Chest X-ray of a 52-year-old woman with chronic renal failure. The chest X-ray shows a right hydrothorax. B. Chest 99mTc-macro-aggregated albumin (99mTc-MAA) radionuclide imaging of the patient. 99mTc-MAA was administered into the peritoneal cavity with dialysate, and 26-28 minutes later, leakage of the dialysate into the right pleural cavity is detected.
Figure 2

Detection and closure of the diaphragm with the ICG fluorescence method. A. First, the thinner part of the diaphragm is stained. B. Then, a bleb-like lesion of the diaphragm is stained, but no leakage from the peritoneum to the pleura is seen. C. Marking the thinner part of the diaphragm with a crystal violet pen. Arrowhead shows a bleb-like lesion. D. Re-injected dialysate mixture shows slight leakage through the needle hole, but no other leakage is seen.

Figure 3

Luminous differentiation of CAPD mixture by 20% albumin. CAPD liquid 7.5 ml and ICG 0.25 mg were mixed. Albumin is added at different concentrations. A. A photograph of primary imaging. B. ICG
fluorescence imaging technique shows no signal without albumin, but a bright signal with a small amount of albumin.