Urology Case Reports 12 (2017) 37–38

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

Anaphylactic Shock After Intravenous Administration of Indocyanine Green During Robotic Partial Nephrectomy

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ARTICLE INFO

Article history:
Received 10 January 2017
Accepted 6 February 2017

Keywords:
Indocyanine green
Anaphylactic shock
Robotic surgery

ABSTRACT

Indocyanine Green (ICG) is frequently used during urologic robotic procedures and is generally considered to be safe. However, there are reported cases of severe complications from ICG when used for non-urologic purposes. We present the first case to our knowledge of anaphylactic shock in response to intravenous ICG during a robotic partial nephrectomy.

Introduction

ICG, a sterile US Food and Drug Administration-approved water-soluble dye, is a popular diagnostic reagent that has been in clinical use for the examination of hepatic function, ophthalmic angiography, cardiac output and circulating blood volume. With the advent of robotic-assisted laparoscopic surgery and near-infrared fluorescence (NIRF) lenses, ICG has found several applications in Urologic surgery including ureteral identification, differentiation of tumors from normal parenchyma and as a lymphangiography agent.

Intravenous (IV) ICG has had a long record of safety for over 50 years with previous reports of mostly low-grade complications.[1,2] We report the first case of anaphylactic shock following IV administration of ICG during a robotic-assisted partial nephrectomy.

Case presentation

A 53-year-old, 90-kg male was incidentally diagnosed with a left interpolar 2.2 cm × 2.3 cm × 2.2 cm renal mass (cT1a, Stage 1) on imaging following a penetrating abdominal trauma. Patient denied any constitutional symptoms (fevers, night sweats or weight loss) and had no pertinent physical exam findings.

Past medical history was significant for coronary artery disease with prior myocardial infarction, hypertension, and insulin-dependent diabetes mellitus. He had no prior anesthetic complications, nor allergies to food, iodinated contrast, or medications. He demonstrated good performance status and cardiopulmonary evaluation revealed normal findings. A beta-blocker was started 1 week prior to surgery.

The patient underwent uneventful anesthesia induction, and the case proceeded with a robotic-assisted transperitoneal approach. Prior to clamping the renal hilum, IV mannitol 12.5 g and ICG 5 mg were given. Shortly after, the patient developed increased peak airway pressures, severe hypotension and ventricular tachycardia. The ET tube and depth of anesthesia were confirmed. Epinephrine and phenylephrine were administered and IV fluids were increased. After the patient failed to respond, the robot was undocked and the patient repositioned supine. A weak pulse was palpated and chest compressions were initiated. The patient underwent successful cardioversion with return to sinus rhythm and an improvement in hypotension. After the patient stabilized for an appropriate period, the operation was completed without further issue (estimated blood loss was 100 mL and 5 L IV fluid administered with warm ischemia time of 28 min). Serologic tests including cardiac enzymes and C3/IgE were within normal limits. However, serum tryptase was elevated at 56.7 μg/L (reference < 10.9 μg/L). The remaining course was uneventful and the patient was discharged on post-operative day two. Final pathology revealed a pT1aNxMxR0 clear cell renal cell carcinoma, Fuhrman grade three.

Abbreviations: IV, intravenous; ICG, indocyanine green; NIRF, near-infrared fluorescence.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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http://dx.doi.org/10.1016/j.eucr.2017.02.006

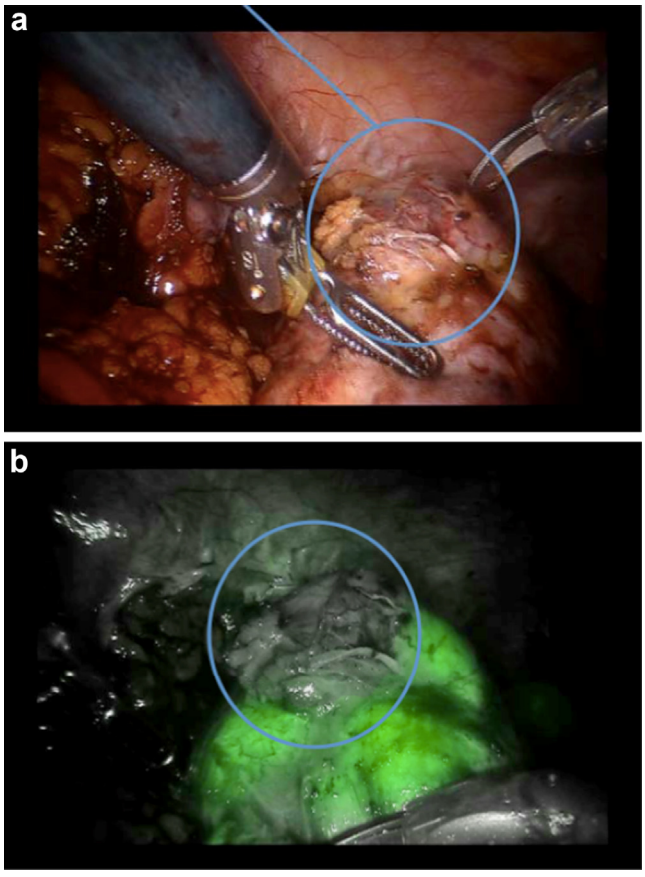

Figure 1. (a) Exophytic tumor in white light mode. (b) Exophytic tumor in fluorescence mode.

Discussion

ICG ($C_{43}H_{47}N_2NaO_6S_2$) is a sterile, water-soluble, tricarbocyanine dye that fluoresces bright green when viewed under near-infrared light (700–1000 nm). Following IV injection, ICG is rapidly bound to plasma protein, of which albumin is the principle carrier (95%). It is then taken almost exclusively by the hepatic parenchymal cells and is secreted entirely into the bile (half-life of three to 4 min).

Although it requires a separate NIRF visualization system due to emission out of the visible spectrum, infrared fluorescence enables deeper tissue penetration and allows visualization even in a bloody operative field. This technology has been applied to robotic partial nephrectomy, to differentiate tumor from normal parenchyma. It has been hypothesized that normal kidney tissue fluoresces green, while the tumor commonly remains hypo-fluorescent, thereby aiding tumor excision (Fig. 1a and b). There have been numerous other novel uses of ICG within urologic robotic surgery. However despite its common use, most urologists are not well versed in the potential adverse effects of ICG.

ICG has generally been considered safe and accepted as having a low incidence of morbidity. Hope-Ross et al prospectively evaluated complications from IV ICG use for video angiography in 1226 patients (1923 cases).[1] Incidence of mild, moderate, and severe complications were 0.15%, 0.2%, and 0.05% respectively. However, while severe complications were rare, two of these were deaths attributed to anaphylaxis. Obana et al similarly reported on a large series of IV or intradermal ICG video angiography cases (3774 cases performed on 2820 patients).[2] Incidence of adverse reaction was only 0.34%, the majority of which were mild. However, two patients experienced hypotension. Notably the dose of ICG varied from 25 to 75 mg, which is much higher than the typically used for robotic surgery. Bjerregaard et al described two cases of severe hypotension following IV ICG administered (5 mg and 2.5 mg respectively) during neurovascular procedures.[3]

We describe, the first of our knowledge, a case of a life-threatening anaphylaxis following IV ICG during a robotic urologic surgery. We believe our case to be consistent with an anaphylactic response to ICG for several reasons. First, the timing of the patient's acute changes following IV ICG corroborates a medication response. Second, while there are other causes of increased peak airway pressures, our patient developed a rapid constellation of findings including hypotension and ventricular tachycardia. Also, the position of the endotracheal tube and appropriate depth of anesthesia were confirmed. The patient was also placed supine and the abdomen was desufflated in the event that the surgical positioning or pneumoperitoneum were contributing to isolated bronchospasm. There was also no significant blood loss to account for the acute changes. Third, the markedly increased postoperative serum tryptase level, a serum protease secreted by mast cells used to assess for anaphylaxis,[4] supports the diagnosis of anaphylaxis.

It has been proposed that systemic reactions from ICG may be attributable to the iodide component.[3] However, the physiology of these reactions remain unknown as cases of adverse events have been documented in iodide-free preparations of ICG.[5] Further, ICG has been used safely in patients with recorded iodine allergies. In addition, there is no known dose threshold below for an ICG adverse reaction as seen in our case in which a single small dose (5 mg IV) was given. As the mechanism behind ICG reactions remains unknown, currently there is no way to predict who will experience an ICG-related complication. Skin or low dose IV testing for ICG allergy has not proven useful.[5]

Conclusion

We report the first episode of anaphylactic response to ICG in the contemporary robotic surgical era. While ICG-related complications are rare, the vulnerable population remains unknown and Urologists should be familiar with this complication.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

No acknowledgements.

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