Case Report

A novel method of using indocyanine green fluorescence technique for nephron-sparing surgery

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ABSTRACT

Two complex small renal masses were operated using a novel method of utilising indocyanine green fluorescence for nephron-sparing surgery (NSS), overcoming its current limitations of short duration of effect and non-enhancement of the tumor. The dye was emulsified with ethiodized oil and a 1:1 mixture was administered on the morning of the surgery using superselective cannulation of the direct tumoral blood supply. The fluorescence could be used throughout the entire course of the surgery irrespective of arterial clamping, allowing quick tumor identification, edge marking, and near-enucleation over enucleoresection. This novel method has the potential to aid the surgeon during various critical steps of NSS.

INTRODUCTION

Saving the nephrons is the prime goal of all nephron-sparing surgeries (NSSs). Many maneuvers have been tried in this respect such as unclamped NSS, early declamping, enucleation, and single-layer renorrhaphy. Similarly, preoperative and intraoperative aids such as three-dimensional (3D) rendering, 3D modeling, ultrasonography, and firefly™ imaging with indocyanine dye have also shown some promise.[1] However, indocyanine is limited by its property of primarily enhancing the normal renal parenchyma,[2] whereby its utility is limited to ensuring a rim of normal parenchyma over the tumor or defining the zone of perfusion. Moreover, the transient nature of its effect, with quick wash-out into the biliary system, further limits its usability. We present a novel way of using the indocyanine green firefly™ technique by binding it with Ethiodized Oil (Lipiodol®). In effect, the dye now binds to and preferentially enhances the tumor, and also remains actively useful during the entire course of surgery irrespective of the arterial clamp, potentially enabling superior tumor identification, tumor edge marking, splicing, and performing enucleation over enucleoresection.

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CASE REPORT

Two high complexity small renal masses were operated upon using this novel method. Robotic NSS was performed using the daVinci Xi® robotic system (Intuitive Surgicals, USA).

A 48-year-old woman was diagnosed with right upper polar renal mass on the ultrasound abdomen obtained for epigastric pain and discomfort. A completely endophytic 3.8 cm × 3.7 cm renal mass was confirmed on the contrast enhanced computed tomography [Figure 1]. In view of high complexity (renal score 9) and wide anticipated contact surface area of the resection margins, we planned injecting indocyanine green mixed with Ethiodized Oil into the tumor selectively on the morning of the surgery. A separate signed informed consent was obtained specifically for the angiography procedure. Superselective cannulation of the artery supplying the tumor was achieved through the

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right common femoral arterial access using microcatheter. Reconstituted indocyanine green (2.5 mL of 1 mg/mL in distilled water) and Ethiodized Oil (2.5 mL) were mixed to form an emulsion and then injected slowly. A postinjection run showed good ethiodized oil deposition in the upper pole mass. The patient was then immediately shifted to the operation theatre for robotic NSS.

After taking control of the hilar vessels, tumor margins were marked with the aid of fluorescence, supplemented by intraoperative ultrasonography. Super-selective clamping was performed, clamping only the upper polar vessel as suggested by the angiography. The renal vein was left unclamped. Tumor enucleation could be performed along with excision of a minimal amount of surrounding normal renal parenchyma [Figure 2]. The warm ischemia time was 13 min and the renorrhaphy was performed in two layers using the sliding clip technique for cinching. The estimated blood loss was 180 cc. The postoperative period was uneventful and she was discharged on day 2. The final histopathology showed clear cell carcinoma, Grade 2 with succinate dehydrogenase B positivity in the tumor cells. At 3 months' follow-up, the patient is asymptomatic.

Another 49-year-old male presenting with right renal tumor underwent Robotic NSS with a similar use of indocyanine green technique and had warm ischemia time of 11 min, blood loss of 130 cc, no complications and negative surgical margins.

DISCUSSION

Indocyanine green is a water soluble, nontoxic fluorophore that remains intravascular as it binds quickly to the plasma lipoproteins and gets rapidly excreted as such without metabolism, almost exclusively through the biliary system.[3] The near-infrared light, that emanates from the dye, is able to penetrate tissues for few mm. Selective intra-arterial injection of the dye has thus been used to define perfusion during the surgery. Besides, the renal arteries being end-arteries, this method may be used to define super-selective perfusion zones as well.[4] By combining the indocyanine with ethiodized oil, binding of the dye to the tumoral tissue can be achieved through direct transarterial delivery. Such an approach has been used for hepatic cancers enabling precise hepatectomy by saving as much normal parenchyma as possible under real-time fluorescence with high success rates.[5]

We used a similar strategy and mixed the lipiodol® with indocyanine green to reverse the enhancement to the tumor tissues rather than the normal parenchyma by virtue of its binding to the tumor. After some time, the dye remains bound only to the tumor tissues while it clears off from the surrounding normal tissues creating background contrast through fluorescence in the near infrared light. Major advantage of this technique is that the tumor remains fluorescent through the entire course of the surgery, irrespective of the arterial clamp status. We were able to demonstrate selective retention of the dye in the tumor during the surgery even 4-hrs after the injection. The margins of the tumor correlated exactly as demonstrated by the intraoperative ultrasonography and the resection could be completed using the principle of enucleation rather than resection. The fluorescence was well distributed all over the tumorous tissue in the resected specimen and evaded the normal rim of parenchyma [Figure 2].

This point of technique represents a novel way of using the indocyanine green dye for partial nephrectomy and may be a useful adjunct for completely endophytic tumors or where enucleation may be preferred over resection. The use of superselective technique limits the dose of lipiodol® required, thus reducing the chances of systemic toxicity. Max safe dose of Ethiodized Oil that can be used is 20-cc. Lipiodol® is an oil-based contrast medium which can be used as an emulsifier for drug delivery due to its tumor binding property, while simultaneously retaining the radiopacity allowing intra-arterial direct delivery. The lipid component of Lipiodol® is also primarily excreted through the biliary route while its iodine component is excreted through urinary excretion after catabolism. Overdosing may have potential risks of peripheral oil embolism, allergic reaction, and pneumonitis related to the toxic unbound free fatty acids. More detailed bio-chemical studies may be required to ascertain if the size of the emulsion droplets can have an impact on the uptake of the dye or the drug by the tumor or toxicity of the drug.

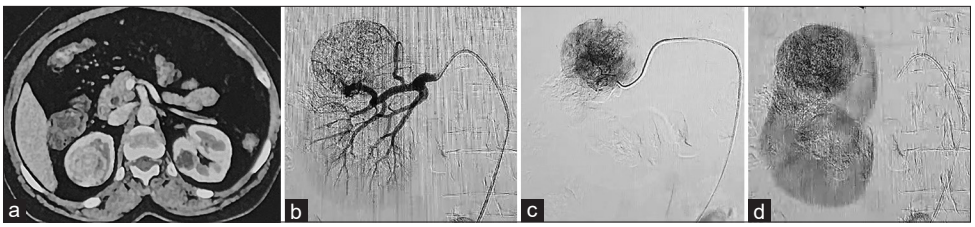

Figure 1: (a) Contrast computed tomography scan axial image showing the right upper pole mass which is entirely endophytic (b) Preoperative digital subtraction angiogram image showing the tumor being supplied through two upper pole arterial branches (c) Indocyanine and Ethiodized Oil mixture was injected superselectively into the branch vessels supplying directly to the tumor (d) Postinjection run of the main renal artery showing Ethiodized Oil deposition in the upper pole mass, whereas the rest of kidney shows normal nephrogram

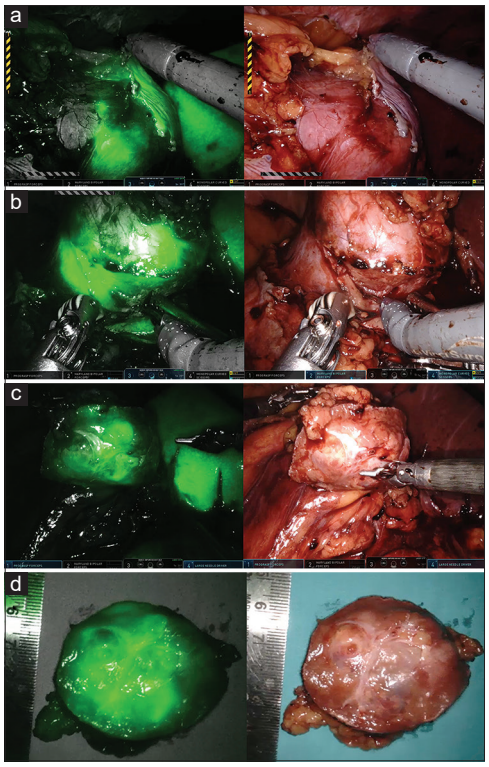

Figure 2: Corresponding firefly and white light images showing (a) Green fluorescent tumor visible from the surface while the rest of the tissues appear black as the dye had already been flushed out and excreted via the biliary system. Fluorescence from the liver can be seen in the background. (b) Tumor resection was performed with intermittent switching between the white and the near infra-red light. (c) Completely excised specimen showing the persistent glow from indocyanine dye bound to deep-seated tumor. (d) Final image of the specimen

Need for angiography for such novel use, potentially comes with the additional risk of contrast-induced nephropathy in some cases. This technique is primarily for cases which may be potentially T3a and have a high nephrometry score. More controlled studies with larger number of patients may better define the role of this novel mode of use of indocyanine green for NSS. However, angiography in such complex cases also adds the benefit of providing the best-detailed roadmap of the arterial tree, as exemplified from our first case where we used superselective clamping only, rendering warm ischemia time majorly inconsequential. In some cases, one may not find a single artery supplying the tumor and multiple superselective injections can be made in such cases.

CONCLUSIONS

This study demonstrates the feasibility of superselective use of indocyanine green fluorescence mixed with ethiodized oil for NSS. This technique has the potential to aid the surgeon during the various critical steps of surgery.

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