Editorial

Resection of ectopic parathyroid adenomas within the carotid sheath—can fluorescence help the surgeon?

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Parathyroid adenomas account for most cases of primary hyperparathyroidism (PHPT), with approximately 6–16% of adenomas occurring in ectopic sites (1-3). Ectopic glands occur because of aberrant parathyroid gland migration along the path of embryologic descent. As a result of their broad localization and small size, ectopic adenomas account for a significant proportion of failed primary surgery in patients with PHPT. Most notably, those localized within the carotid sheath, though rare, pose a particularly challenging task for surgeons.

Treatment of hyperparathyroidism caused by ectopic adenomas thus requires a precise pre- and perioperative strategy. Many techniques have been developed to assist in minimally-invasive parathyroidectomy, such as indocyanine green (ICG) fluorescence imaging (4,5). ICG fluorescence of the parathyroid glands is an innovative imaging tool that has the potential to help surgeons reduce the risk of treatment failure, but the use of this technique during resection of adenomas within the carotid sheath has not been demonstrated.

What further benefits can the surgeon expect from intraoperative ICG fluorescence? In the manuscript of *Gland Surgery*, Rupp *et al.* shed light on this topic. They present the case of a 75-year-old woman diagnosed with PHPT due to a parathyroid adenoma localized to the left carotid sheath (6). Localization of an ectopic inferior parathyroid gland adenoma within the left posterior carotid sheath of the patient was confirmed using single photon emission computed tomography/computed tomography (SPECT/CT) and ultrasound. Upon minimally-invasive parathyroidectomy via transverse cervical incision, ICG fluorescence enabled intraoperative visualization of the adenoma and ensured no fluorescing parathyroid tissue remained after surgery. The authors also noted an unremarkable post-operative recovery of the patient. This is the first published case report of ICG use to aide minimally-invasive parathyroidectomy of a carotid sheath parathyroid adenoma, preventing failed primary resection and intraoperative complications. Prior to this study, several groups have reported cases of failed primary surgery of ectopic tissues later found to be localized to the carotid sheath. Sanders *et al.* describe the case of a failed initial parathyroidectomy with subsequent high-resolution imaging confirming the presence of ectopic tissue within the carotid sheath (7). Similarly, Chopra *et al.* present a case of failed initial surgery after preoperative imaging had failed to reveal the pathological tissue which was later localized posterior to the right common carotid artery (8). In another case that our group reported recently, preoperative ultrasound, technetium-99 m-sestamibi scintigraphy, three cervical explorations and one thoracoscopic thymectomy were unable to reveal the presence of an intra-vagal parathyroid adenoma. The parathyroid adenoma was only successfully identified after contrast-enhanced ^{18}F-fluorocholine-positron emission tomography (PET)-CT (9). These cases highlight the diagnostic and surgical complexity that carotid sheath parathyroid adenomas can pose, where preoperative localization is clearly necessary but may not be sufficient to identify the pathological tissue.

The case report in this study highlights the clinical utility and benefits of ICG fluorescence as an intraoperative modality during parathyroidectomy. Despite the availability of pre-operative imaging that allows precise localization of parathyroid adenomas, the search for ectopic glands located in the carotid sheath, whether they are attached (or embedded) to the vagus nerve or not, is challenging by naked eye and requires the dissection of tissue situated in anatomical areas at risk of hemorrhagic or nerve damage complications. Clear identification and precise removal of the pathologic tissue are crucial in such a rare and delicate anatomic location as the carotid sheath. ICG fluorescence provides a reliable tool that can complement naked eye examination, which allows the surgeon to distinguish parathyroid tissue from surrounding structures (especially lymph nodes) and minimizes error.

Use of ICG fluorescence is also simple and safe. ICG is a nontoxic, fluorescent iodide dye that binds to plasma proteins and remains in the bloodstream and circulates only in the intravascular compartment until it is absorbed by the liver and excreted into the bile. It has a short half-life of (3–5 min) that allows for repeated applications, and is eliminated by the liver within 15–20 minutes (10). ICG angiography is used in many areas of surgery to assess the vascularization of operated tissue, such as skin flap or digestive anastomosis (11). Less than 10 years ago, the use of ICG in the field of endocrine surgery to locate the parathyroid glands was described for the first time (12). The perioperative approach of most endocrine surgeons has changed since then as a result of subsequent studies reporting the use of ICG angiography to evaluate the viability of remaining parathyroid tissue and therefore to reduce the rate of hypoparathyroidism after thyroidectomy (5,13-15) and subtotal parathyroidectomy (16).

Though not discussed by the authors, additional perioperative tools for identifying and assessing parathyroid glands exist. Recently, the discovery that parathyroid tissue exhibits a unique autofluorescence signature when excited at the near-infrared (NIR) wavelength of 785 nm (17-22) has led to the introduction of parathyroid autofluorescence as yet another intraoperative optical technology for precise localization of the parathyroid glands. Near-infrared autofluorescence (NIRAF) can be used at any time during surgery and allows the surgeon to see parathyroid tissue before it is visible to the naked eye. However, NIRAF also comes with several limitations, namely the interference from background thyroid fluorescence hindering detection of parathyroid glands and the occurrence of false positives by surrounding tissue, like brown fat. It was also recently reported that parathyroid adenomas exhibit weaker NIRAF intensity than the normal parathyroid gland and contain a cap of more autofluorescent tissue that corresponds to the rim of normal parathyroid tissue (23).

Other perioperative adjuncts to surgery, such as fresh frozen sections or measurement of the intraoperative parathyroid hormone (ioPTH), are already used by most endocrine surgeons (24,25). However, these tools do not allow for real-time intraoperative detection of the parathyroid glands like ICG fluorescence and autofluorescence do.

Altogether, the present study demonstrates the use of ICG fluorescence to guide resection of an ectopic inferior parathyroid gland adenoma located within the left posterior carotid sheath. The case presented is a good example of the appropriate use of ICG for the detection and safe resection of an ectopic adenoma which would have certainly been more difficult without the help of this simple and safe technique. Like ICG fluorescence, autofluorescence imaging holds great promise for real-time identification of ectopic parathyroid adenomas, with the additional advantage over ICG of being a label-free modality.

Although further investigation is needed to elucidate whether these novel approaches can further reduce postoperative failure, this report begins to elucidate the pivotal role that intraoperative imaging can play in successful primary resection of ectopic adenomas at anatomically complex locations like the carotid sheath. Importantly, intraoperative imaging does not and should not replace pre-operative imaging; rather, the combination of both pre-operative localization and intraoperative fluorescence-based imaging to assist surgeons in preventing surgical treatment failure.

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