

## Case Report

# Parathyroid adenoma with intraoperative indocyanine green localization: a case report

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## ABSTRACT

Intra operative identification of parathyroid glands poses a major difficulty while performing parathyroidectomy or total thyroidectomy, due to the close resemblance with fatty tissues and risk of hypocalcemia. To minimize these complications and to enhance the chances of accurate clinical identification, a number of techniques have been developed and tested along the years. One such novel technique that has been developed is the use of indocyanine green (ICG) and near infrared fluorescence imaging. Per operative ICG fluorescence aids in the accurate identification of the glandular tissue and targeted resection of the same. The following case report is that of a 65-year-old male who was evaluated for hip pain and found to have parathyroid adenoma of the right gland and how intra operative ICG administration aided us in the accurate identification and resection of the gland.

**Keywords:** ICG fluorescence, Parathyroid localization, Parathyroidectomy, Intraoperative imaging

## INTRODUCTION

The visual similarity between parathyroid glands and nearby adipose tissue makes their identification during surgery technically demanding. The standard practice to identify parathyroid glands has been visual inspection and careful palpation, with an aim to preserve the blood supply of the parathyroids.<sup>1</sup>

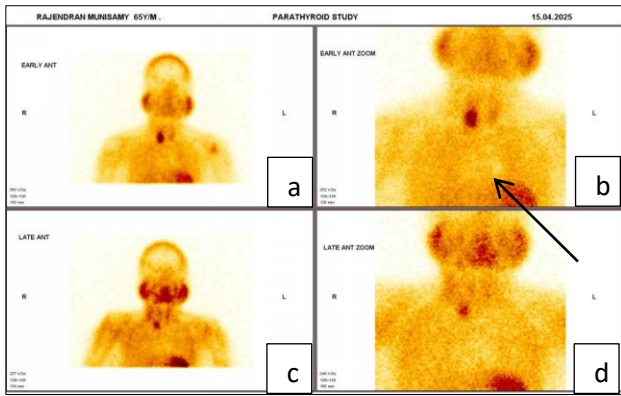
The two alternative invasive methods include: frozen section analysis and 'float and sink' technique. However, both these techniques compromise the structural integrity of the parathyroid gland and maybe sometimes associated with transient hypocalcemia.<sup>2</sup> While visual inspection and palpation remain the primary methods for identifying parathyroid glands (PGs), various alternative techniques have been explored for gland visualization and assessment of vascularity. However, many of these methods offer limited effectiveness or are no longer in clinical use. As a result, a consistent and non-invasive intraoperative approach for accurately detecting and evaluating PG perfusion is lacking.

To address this challenge, a number of techniques have emerged including ICG fluorescence, auto-fluorescence and intra operative PTH assessment. Near-infrared (NIR) fluorescence imaging using indocyanine green (ICG) has emerged as a promising modality for enhancing intraoperative localization and preservation of the parathyroid glands.<sup>3,4</sup> Pathological parathyroid glands show enhanced ICG accumulation, leading to increased fluorescence intensity when compared to nearby tissues, the exact mechanism is not known.<sup>5</sup>

## CASE REPORT

A 65-year-old male was evaluated with complaints of persistent hip ache and was found to have lytic lesions of the hip joint along with an elevated serum calcium level of 13 mg/dl and serum parathyroid hormone (PTH) of 805 pg/ml.

On clinical examination, a vague mass was palpable in the right para tracheal region that moved with deglutition.



**Figure 1 (a-d): Increased sestamibi intake in right parathyroid gland. Arrow indicates enlarged right parathyroid gland.**

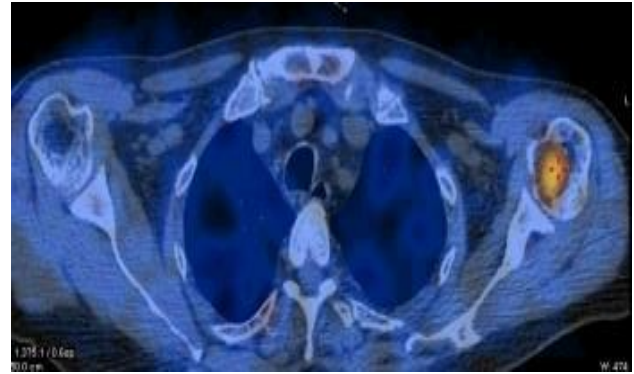
Positron emission tomography/computed tomography (PET CT) done revealed right para tracheal lesion abutting the inferior pole of right lobe of thyroid gland with subcentimetric mediastinal nodes and multiple lytic lesions involving the axial and appendicular skeleton. <sup>99m</sup>Tc-Sestamibi SPECT-CT showed a tracer-avid soft tissue lesion posterior and inferior to the right thyroid lobe, suggestive of a parathyroid adenoma or carcinoma. A lytic lesion with soft tissue extension and cortical breach was noted in the left humeral head, along with multiple expansile skeletal lesions lacking significant tracer uptake.

VLS done revealed bilateral normal vocal cords. Endocrinologist opinion was obtained and he was treated with IV fluids to maintain adequate hydration, diuretics and injection calcitonin. His serum calcium levels were monitored serially. After discussing with the multidisciplinary team, patient was planned for excision of the parathyroid mass.

Patient was operated in supine position with neck in extension under general anesthesia. Standard Kocher's incision was made and upper and lower flaps elevated. A 3×3 cm mass was seen arising from the right inferior parathyroid gland adherent to the right lobe of thyroid and carotid sheath posteriorly. ICG dye was diluted with 5 ml of sterile water and initially administered to look for any anaphylactic reaction and later administered completely. Fluorescence was detected 2 min later using Stryker SPY camera that uses near infrared technology (Figures 2 and 3).

The abnormal gland showed fluorescence compared to the surrounding thyroid tissue that ruled out any gross involvement of right lobe of thyroid and carotid sheath. The other parathyroid glands visualised were normal. The diseased gland was removed and sent for post-operative histopathology.

Post operatively his serum calcium levels were monitored.



**Figure 2: Increased sestamibi intake in lytic lesion of left humerus.**



**Figure 3: Right inferior parathyroid adenoma.**

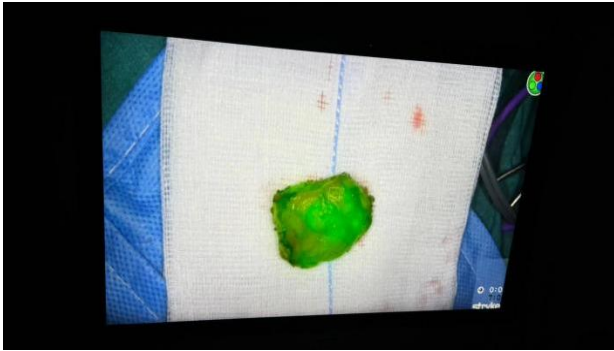
**Table 1: Serum calcium levels.**

Post op day	Serum calcium levels	Intervention
1	8.3	Oral calcium and vit D
2	6.9	IV calcium gluconate
3	8.1	Oral calcium and vit D

Patient was discharged with oral calcium and calcitriol supplementation and his serum calcium levels were monitored during the post-operative follow up visits. Histopathology report was consistent with parathyroid adenoma.



**Figure 4: ICG fluorescence.**



**Figure 5: Specimen fluorescence.**

## DISCUSSION

Hyperparathyroidism (HPT) refers to excess synthesis and secretion of the parathyroid hormone. Depending on the causative factor, it can be primary, secondary or tertiary.<sup>6</sup> Primary hyperparathyroidism refers to the autonomous over production of PTH by one or more abnormal parathyroid glands and the spectrum varies from parathyroid adenoma, accounting for about 80-85% of the cases followed by parathyroid hyperplasia amounting to 10-15% and rarely carcinoma in 1-2% of the general population.<sup>7</sup> The Indian incidence of primary hyperparathyroidism stands at 2.5/1000 population with a greater preponderance in females (females: males - 3: 1).<sup>8</sup> Solitary glandular variant is more commonly observed and is usually asymptomatic at the time of presentation.<sup>9</sup> The incidence tends to increase with rising age, most common age group being 50-60 years. Given the rarity of the condition amongst South Indians and its presentation, a high degree of clinical suspicion is a pre requisite to the diagnosis of this relatively rare clinical condition.

Excess PTH secretion results in hypercalcemia, which when coupled with loss of negative feedback mechanism, leads to abnormally high serum calcium levels and continued resorption of calcium from bones. Osteoporosis and pathological fractures are the most common presenting feature in patients with parathyroid adenoma/hyperplasia. Renal abnormalities arise from deposition of calcium salts in renal parenchyma, which can ultimately impair renal function. The symptom complex of hyperparathyroidism is collectively addressed as “stones, bones, moans and abdominal groans” representing renal stones, osteoporosis with pathological fractures, depression and pancreatitis, respectively.<sup>10</sup>

The diagnosis of parathyroid adenoma relies on a combination of clinical features and corroborative laboratory investigations. Key biochemical markers typically include elevated serum calcium and PTH levels. However, these parameters may occasionally vary. A characteristic profile often includes raised PTH, hypercalcemia, low serum phosphate, and increased urinary calcium excretion.<sup>11</sup> Approximately 50% of patients with primary hyperparathyroidism (PHPT) exhibit

hypophosphatemia, and about 60% demonstrate elevated 24-hour urinary calcium levels.<sup>12</sup>

Surgical removal of the parathyroid gland has seen a paradigm shift from total parathyroidectomy with auto transplantation to focused minimally invasive parathyroidectomy. Earlier, due to non-availability of localisation techniques, surgeons conventionally removed all four glands and re implanted a part of the healthy gland into the forearm or sternocleidomastoid. This radical surgery was associated with higher risk of complications such as persistent hypocalcemia. In order to overcome this, focused parathyroidectomy was suggested as an alternative in patients with single gland disease. However, accurate localisation of the abnormal gland was a pre requisite to perform focused parathyroidectomy.

Localisations techniques used can be widely divided into preoperative and intra-operative. Pre-operatively, USG of the neck can be performed to identify the location of the adenoma. However, USG had a sensitivity of only 64.3%, which was considerably less and made it difficult in performing minimal access parathyroidectomies.<sup>13</sup> Hence, the 99 m-Tc Sestamibi scans were used for localisation with a sensitivity of 83.3%.<sup>13</sup>

99 m-Tc Sestamibi (aka MIBI), is a radiopharmaceutical lipophilic cationic tracer. It has a greater affinity for tissues with high mitochondrial content and negative plasma membrane potential and hence tissues with high metabolic activity and blood flow show increased uptake.<sup>14</sup> 99m Tc-Sestamibi SPECT-CT combines functional imaging of the gland with anatomical details. SPECT provides 3D imaging for depth; CT adds precise anatomical localization. These are visualised as ‘hot spots’.

Intra-operative identification techniques are broadly classified into invasive and non-invasive techniques. The invasive techniques include frozen section analysis and ‘float and sink’ method. Non-invasive techniques include ICG fluorescence using near infrared spectroscopy and autofluorescence of parathyroid gland.

ICG is a biologically inert, water-soluble dye rapidly binds to plasma lipoproteins and remains confined to the vascular compartment. It is cleared exclusively via the hepatobiliary system due to the first-pass metabolism.<sup>15</sup> With a short plasma half-life of around  $3.4 \pm 0.7$  minutes, ICG can be administered multiple times during a single operative procedure. These pharmacokinetic features make it an excellent agent for intraoperative angiography and fluorescence-guided identification of vascularized tissues. ICG fluorescence is observed at 800 nm with maximum absorption at 805 nm. Oxyphil cells of parathyroid gland have a high mitochondrial content which is responsible for the increased uptake and fluorescence.

It also has the advantage of selective accumulation in abnormal parathyroid gland at a greater concentration,



which is responsible for the higher intensity of contrast. This technique is of particular importance especially while dealing with ectopic parathyroid glands located within the carotid sheath or mediastinum and in cases of redo surgeries. ICG contains 5% sodium iodine which can lead to urticarial and anaphylactic reactions. In rare cases, it can also induce 'black thyroid' phenomenon, causing pigmentation of the thyroid gland.

An alternative to ICG fluorescence is utilisation of the auto-fluorescence property of parathyroid gland. Parathyroid glands have shown to emit near infrared auto fluorescence in 785-820 nm range when stimulated with light in the 700-800 nm wavelength. Parathyroid autofluorescence remains detectable irrespective of the gland's vascularity and can still be observed even after the gland has been surgically excised. Even though it is a dye less technique, AF is strictly a localisation tool only, it doesn't differentiate between normal and abnormal gland. There can also be interference from the background thyroid fluorescence, decreasing the chances of accurate localisation of the gland.

In spite of the constant struggle faced in identification and localisation of parathyroid gland during thyroidectomies/parathyroidectomies, there is no single available protocol to be followed intra operatively. Although pre and intra operative PTH assessment can act as an adjunct in detecting removal of the abnormal gland, it is a time-consuming method making it difficult for the surgeon and the patient.

Even though ICG fluorescence technique uses an external dye, it allows visualisation of the gland in real time, to distinguish between normal and abnormal glands by difference in uptake intensity, and preservation of vascularity of the gland during surgery.

In spite of these advantages, the dosage and use of ICG for intra operative parathyroid localisation has not yet been standardised.<sup>17</sup>

## CONCLUSION

Intraoperative localization of parathyroid glands continues to pose significant challenges, particularly in cases involving ectopic or adherent lesions. This case highlights the effective use of ICG fluorescence imaging as a valuable adjunct for real-time identification and guided excision of parathyroid adenomas. ICG not only facilitated accurate localization but also aided in preserving the surrounding structures by clearly delineating the vascular anatomy. While conventional imaging and visual inspection remain foundational, the integration of ICG-enhanced near-infrared fluorescence offers a promising step forward in achieving precision and minimizing complications during parathyroid surgery. However, larger studies are needed to establish standardized protocols regarding dosage, timing, and safety to enable its routine use in endocrine surgery.

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