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Annals of Case Reports

Vanella S, et al. Ann Case Report 12: 251.

DOI: 10.29011/2574-7754.100251

Case Report

Minimally Invasive Video-Assisted Total Parathyroidectomy for Secondary Hyperparathyroidism with Superior Mediastinal Ectopic Parathyroid

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Citation: Vanella S, Crocco A, Selvaggiuolo M, Soglia S, Serini M, et al. (2019) Minimally Invasive Video-Assisted Total Parathyroidectomy for Secondary Hyperparathyroidism with Superior Mediastinal Ectopic Parathyroid. Ann Case Report 12: 251. DOI: 10.29011/2574-7754.100251

Received Date: 27 August, 2019; **Accepted Date:** 10 December, 2019; **Published Date:** 15 December, 2019

Abstract

Secondary hyperparathyroidism develops in kidney failure due to a combination of vitamin D deficiency, hypocalcemia and hyperphosphatemia and exists in almost all patients at the time of dialysis beginning. When the level of parathyroid hormone persists over 800 pg/ml for more than 6 months, despite medical therapy, parathyroidectomy should be considered especially if there are concomitant disorders such as persistent hypercalcemia or hyperphosphatemia, tissue or vascular calcification including calciphylaxis and / or worsening of osteodystrophy. Parathyroidectomy is associated with an improvement in survival in dialysis patients and it also improves hypercalcemia, hyperphosphataemia, tissue calcification, bone mineral density and health-related quality of life. Scintigraphy is the most accurate technique for locating abnormal parathyroid glands. Other imaging modalities include ultrasound and CT. An intraoperative rapid PTH test can be performed within minutes to detect any remaining abnormal glands. The main sites of ectopic localizations for the lower parathyroid glands are: intrathymic, anterosuperior mediastinal, intrathyroid, within the thyrothymic ligament, submandibular; for the upper glands: tracheoesophageal, retroesophageal, posterior-superior intrathyroid, mediastinum, in the carotid and paraesophageal sheath. We present a case of secondary hyperparathyroidism with upper mediastinal ectopic parathyroid gland treated with minimally invasive video-assisted parathyroidectomy by transcervical approach.

Keywords: Endoscopic Parathyroidectomy; Mediastinal Ectopic Parathtyroid Gland; Minimally Invasive Video-Assisted Parathyroidectomy (MIVAP); Secondary Hyperparathyroidism

Introduction

Traditional treatment approaches for hyperparathyroidism patients boast excellent cure rates and low complication rates, and include an anterior cervicotomy and Bilateral Neck Exploration (BNE) with intraoperative identification and removal of the pathologic parathyroid gland. The advances in imaging techniques have led to pre-operative localization, which has allowed for minimally invasive targeted surgical approaches in cases of a single adenoma. Imaging with sonography and scintigraphy scans have demonstrated 85% and 90% sensitivities in identifying hyperfunctioning parathyroid glands of patients, respectively [1,2]. Concordant results of both studies correctly identified the single adenoma in 95% of cases. The development of Intraoperative Parathyroid Hormone (ioPTH) has allowed for evaluation of cure upon removal of the suspected gland, with long term cure rates as high as 99% [3,4]. Using these methods, patients with pre-operatively localized glands benefited from a targeted open approach -Open Minimally Invasive Parathyroidectomy (OMIP)- with small incisions and minimal dissection to successfully remove the suspicious gland [5-8].

This allowed for decreased operative times and improved cosmetic outcomes compared with traditional parathyroidectomy, while maintaining low recurrence rates with the use of ioPTH [9-11]. Given the minimal learning curve for OMIP for surgeons with traditional parathyroidectomy experience, and its equivalent success rate, minimally invasive parathyroidectomy caught on quickly and by 2002 the majority of surgeons were performing OMIP in selected patients [12,13]. Endoscopic adaptation of these

minimally invasive procedures allowed for even smaller incisions [14-16]. These endoscopic techniques can be performed by gasless video-assisted methods, such as the Minimally Invasive Video Assisted Parathyroidectomy (MIVAP) technique [17]. It has been shown that video-assisted and endoscopic Parathyroidectomy (PTX) for patients with primary hyperparathyroidism allow excellent results, with cure rates of 98% to 99%, which are as good as those obtained with conventional cervical exploration [18,19]. In contrast, reports on minimally invasive surgery for Secondary Hyperparathyroidism (sHPT) are limited [9,13]. Moreover, we think that MIVAP could be a valid approach for sHPT with ectopic glands.

Case Presentation

We present the case of a 53-year-old female patient with end-stage renal failure in dialysis. The values of parathormone were higher than 2000 pg/ml. The patient performed medical therapy with Cinacalcet and vitamin D for 2 years with little benefit. She was also awaiting kidney transplantation. Ultrasound of the neck showed multiglandular disease but failed to locate the lower right gland. A 99mTc-MIBI scintigraphy scan showed a well-defined area of abnormal tracer deposition in anterior mediastinum just below the manubriosternal junction, confirming the diagnosis of mediastinal ectopic hyperplastic parathyroid gland (Figure 1). High resolution CT scan of chest and neck was carried out: it confirmed that inferior right parathyroid gland was located beneath the lower pole of right thyroid in anterior mediastinum as well (Figure 2). After a multidisciplinary meeting including endocrinologists, endocrine-surgeons, nephrologists, radiologists and nuclear physicians, the patient was enrolled for Minimally-Invasive Video-Assisted Total Parathyroidectomy (MIVAP) by trans cervical approach.

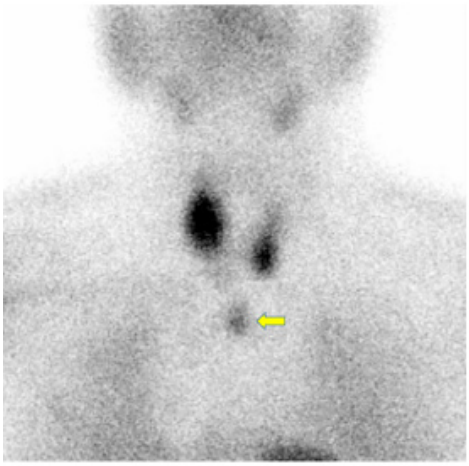

Figure 1: 99mTc-MIBI scintigraphy scan showing a well-defined area of abnormal tracer deposition in anterior mediastinum.

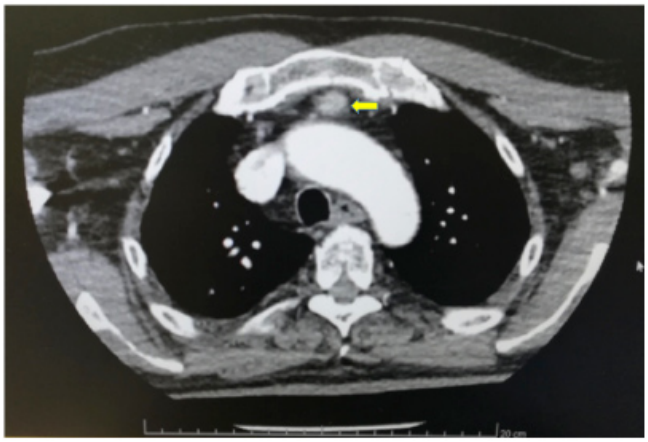

Figure 2: Chest CT scan showing mediastinal ectopic hyperplastic parathyroid gland.

She, subsequently, underwent total parathyroidectomy with trans cervical minimally-invasive video-assisted approach, during which right lower parathyroid tissue was identified and excised (Figures 3,4). The intraoperative PTH measurement showed a significative decrease of PTH levels. The histopathology report established parathyroid parenchyma composed of chief and oxyphil cells with intervening fibroadipose tissue. There was no evidence of malignancy. Postoperatively, serum calcium level every 12 hourly and PTH every 24 hourly was respectively repeated. Calcium with vitamin D supplements were administered. The patient was discharged in fourth postoperative day. At a 1-year follow-up the patient did not show any sign of recurrence.

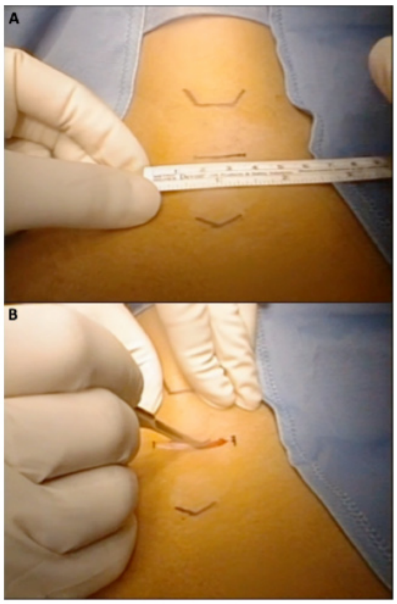

Figure 3: (A-B) Incision of skin.

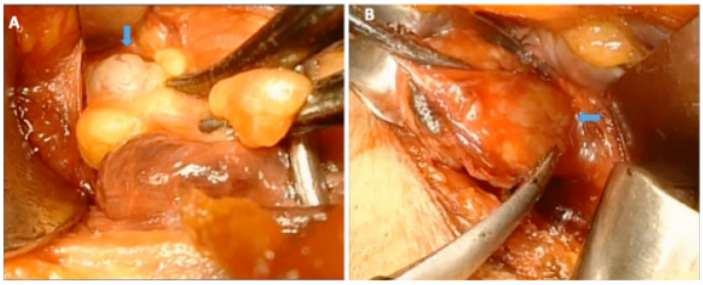

Figure 4: (A-B) Intraoperative dissection of mediastinal parathyroid gland.

Discussion

Parathyroidectomy is generally indicated in sHPT when medical therapy fails to control the disease. Despite adequate therapy with calcitriol, high levels of PTH, hypercalcemia, hyperphosphatemia, and serum calcium-phosphate production >70 represent accepted indications for surgery. Moreover, if patients experience clinical manifestations, including persistent or worsening skeletal symptoms (bone pain as an indicator of high-turnover bone disease), pruritus, and extraskeletal calcifications, they should be considered for surgery [20]. The most important challenge in the surgical treatment of renal hyperparathyroidism is the proper visualization of all parathyroid glands, including supernumerary ones. To reduce the pitfalls of surgical exploration, preoperative ultrasound has been considered effective, especially for detecting glands around and inside the thyroid lobes. Moreover, 99-TC-sestamibi scintigraphy may identify ectopic parathyroid glands [21]. The localization and subsequent treatment of an ectopic parathyroid gland can usually be challenging. There are various imaging modalities available for the diagnosis include ultrasonography, CT scan, Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT) and Technetium (Tc99m-Sestamibi) scintigraphy scan.

Among these, US is the most widely utilized modality due to its low cost and easy availability. High-resolution ultrasound can accurately localize adenomas relative to the thyroid gland. However, its ability to detect abnormalities depends on the experience and skill of the operator, and therefore, its sensitivity in localization of enlarged parathyroid glands varies greatly (44%-87%) [22]. Recently, scintigraphy scan is increasingly being utilized for the localization of ectopic parathyroid gland with reported sensitivity of up to 90% [23]. High-resolution ultrasound and parathyroid scintigraphy both have their own advantages. The former is good at localizing adenomas nearby the thyroid gland, whereas the latter is usually reserved for detecting adenomas in multi-nodular thyroid disease and at ectopic sites, whose incidence is up to 20% among all patients with suspicion of sHPT [24,25]. SPECT is combined with sestamibi scintigraphy to provide three-dimensional imaging. These hybrid imaging techniques with SPECT/CT combining scintigraphic datasets (SPECT) and anatomical (CT) has become increasingly valuable over the last few years [22].

Akram et al. in their case series found a study of 16 patients, in which SPECT/CT identified 39% more lesions compared with SPECT imaging alone. SPECT/CT permitted higher confidence in localization, especially for mediastinal adenomas [26]. The combination of MIBI with US raises the sensitivity to 78%-96% and with CT or MRI may raise the sensitivity and specificity to 100% [27,28]. These additional combinations are moderately cost effective and are indicated as a means for routine preoperative localization of ectopic parathyroid adenomas, especially in cases of 99mTc-MIBI scans failure [29]. Three different surgical procedures are described for patients with sHPT: subtotal PTX, total PTX with auto-transplantation, and total PTX without autotransplantation and without thymectomy [30-32]. Subtotal PTX and total PTX with autotransplantation, both performed with thymectomy, are considered the standard procedures in the treatment of sHPT and are associated with similar recurrence rates (up to 10%) [33]. We routinely prefer subtotal PTX because this procedure avoids the need for parathyroid cryopreservation and reduces the rate of postoperative hypoparathyroidism [34]. If all the glands show obvious macroscopic signs of pathology, we perform total parathyroidectomy. Mediastinal location represents the most frequent ectopic site in pHPT, ranging between 1.5% and 25% [35-37]. Mediastinal parathyroid glands can usually be removed through a conventional cervical incision, since they are located in most cases in the upper mediastinum, within or closed to the thymus; only 1% to 2% of patients require a direct thoracic approach [38].

The deep location in the anterior mediastinum is the main risk condition for unsuccessful cervical approach; Callender had previously reported effective parathyroidectomy by transcervical approach only in 25% of cases for glands located more than 6 cm below the head of the clavicle [39]. Thoracoscopy has been suggested as the technique of choice for ectopic glands located to the middle and lower mediastinal regions; some limitations have been reported in case of immediately retrosternal parathyroids in the upper part of the anterior mediastinum, with an increased risk of conversion [40,41]. However, thoracoscopic approach may be laborious; it requires single-lung ventilation, pleural incision, and cannot be safely performed in patients with compromised pulmonary function or chest adhesions. To the contrary, video-assisted transcervical approaches may be still less invasive, since the selective single-lung ventilation may be avoided; surgery may be performed with the patient in classic supine position with a comfortable incision, without violation of the pleural space; operative time are comparable to thoracoscopic procedures, while some difficulties have been reported to excise deep glands in the

posterior mediastinum.

The conventional approach for the management of sHPT due to multiglandular disease with ectopic mediastinal gland is neck exploration followed by excision of the tumor via median sternotomy or thoracotomy or Video-Assisted Thoracoscopy (VATS). However, ectopic glands have been renowned as the most frequent reason for a failed cervical exploration [42]. Consequently, precise preoperative localization is the key to successful surgical removal. The choice of the surgical technique greatly relies on the anatomical site of the ectopic glands. Before the introduction of VATS to thoracic surgery, mediastinal ectopic parathyroids were rejected by a lateral thoracotomy or a median sternotomy [43]. These surgical interventions are associated with a risk of injury to phrenic and recurrent laryngeal nerve, laceration of brachiocephalic vein, delayed wound healing, wound infection, mediastinitis and even death. The size of surgical incisions is often large and aesthetically unsound for the patient [44]. VATS offers significant advantages over both procedures and is being more frequently employed now [45].

It allows a better visualization of the tumor, a shorter operative time, shorter tube dwell time and shorter hospital stay with superior cosmetic result compared to sternotomy and thoracotomy scars as concluded by Amer et al. The side effects of VATS reported include hemorrhage, subcutaneous emphysema, pneumothorax, pulmonary edema, recurrent nerve palsy, recurrent pneumothorax, neuralgia, pleural effusion, and hemorrhage [46]. Between the minimally invasive options for parathyroidectomy, MIVAP offers several advantages in that it resembles traditional parathyroidectomy in technique thereby allowing the surgeon to perform a Bilateral Neck Exploration (BNE) [18,47] while maintaining a small (1.5-2.0 cm) cervicotomy and allowing for prompt identification of the recurrent laryngeal nerves and parathyroid glands with endoscopically enhanced magnification [48,49]. This permits broader indications for minimally invasive treatment of sHPT including those cases of multiglandular disease.

MIVAP with ioPTH, besides the classic advantages of minimally invasive techniques, adds a tool to confirm the radicality of excision [50,51]. Video-assisted and targeted approach, being able to avoid neck hyperextension and less tissue dissection, likely contributes to decreased pain levels with better cosmetic results in MIVAP patients [52]. The decrease in post-operative pain has also been demonstrated when comparing MIVAP to OMIP [49,53,54]. When comparing mean operative time between MIVAP and OMIP results reported in literature showed either equivalent (44 vs. 49 min) or longer (84 vs. 60 min) operative times in the MIVAP group [49,53]. It is important to note, however, that several studies have demonstrated that MIVAP operative times improve significantly with surgeon experience with mean MIVAP operative times in experienced hands as low as 28 minutes [18,55,56]. MIVAP may be faster and is probably easier to perform because it strictly reproduces the standard cervical exploration, with the obvious advantage of a smaller skin incision.

The excellent cure rates associated with MIVAP have been attributed to a combination of appropriate patient selection with pre-operative imaging, the use of ioPTH for evaluation of cure, and the ability to perform video-assisted BNE when the suspected adenoma cannot be identified or when there is concern for multiglandular disease [48,47,57]. In the absence of ioPTH or presence of questionable ioPTH results, MIVAP with video-assisted BNE has actually been demonstrated to be as effective in treating sHPT as MIVAP with ioPTH with similar operative times [58]. The ability to perform video-assisted BNE during MIVAP also contributes to the low conversion rate [18,52,47]. MIVAP allowed for localization and removal of the ectopic gland through the minimally invasive cervicotomy. By orienting the camera in a cranio-caudal direction it is possible to have an excellent view of the upper mediastinum. With this technique it is possible to carry out exploration of the upper mediastinum and the excision of ectopic glands in this area.

Conclusion

In sHPT, in the event of failure to locate all four glands with ultrasound and scintigraphy, the mediastinum should be cautiously investigated since it is the foremost location for ectopic gland after the neck. The video-assisted technique with image magnification can be very helpful in particular in cases of anatomical anomalies. MIVAP is a safe and effective minimally invasive procedure for an exhaustive BNE and resection of ectopic upper mediastinal glands. It should be considered as the first line approach for resection of these ectopic tumors. ioPTH allows to confirm the absence of concomitant ectopic localizations and to confirm the efficacy of the intervention in the intraoperative area. Comparative studies with conventional surgery are certainly required to confirm the early benefits and long-term results of this approach.

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