APMB - Atti della Accademia Peloritana dei Pericolanti
Classe di Scienze Medico Biologiche
Vol. 109(1) 2021

ISSN 1828-6550

DOI: 10.6092 / 1828-6550 / APMB.109.1.2021.CCS3

Clinical Case Seminar

CCS 3 (1-6)

Radioguided Parathyroidectomy for Recurrent Hyperparathyroidism: an effective multi-institutional approach at the University of Messina Hospital

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Abstract

Secondary hyperparathyroidism (SHPT) is a common complication of chronic kidney disease (CKD). The progressive decline in renal function, in fact, leads to the alteration of the metabolism of calcium (Ca), phosphorus (P) and vitamin D. Difference of other forms of hyperparathyroidism, renal SHPT has many pathogenetic peculiarities, which have been only in part clarified. Furthermore, in the long course of CKD, SHPT sometimes transforms into a hypercalcemic condition resembling the autonomous form of hyperparathyroidism (tertiary hyperparathyroidism; THP). The clinical consequences of SHPT in CKD patients are manifold, encompassing not only bone and mineral disorders, but also other metabolic and organic changes which frequently burden these patients. Although the medical therapeutic tools have substantially increased in number and improved in their efficacy in recent decades, we have as yet no demonstration of a clear benefit regarding the major clinical outcomes. Furthermore, some of these patients still require a surgical approach. Herein we discussed the clinical management and surgical treatment for a case of a recurrent secondary hyperparathyroidism.

KeyWords: Endocrine surgery; parathyroid disease; hyperparathyroidism; CKD

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Clinical Case

The classic pathogenesis of secondary hyperparathyroidism began with the trade-off hypothesis based on parathyroid hormone (PTH) hypersecretion from renal failure, resulting from a physiological response to correct metabolic disorder of calcium, phosphorus, and vitamin D. The initial treatment involves dietary phosphate restriction and phosphate binders. Deficiency of 1,25(OH)2D is managed by applying calcitriol or its analogs (alfacalcidol or paricalcitol). The other options are calcimimetics, and in some patients, a combination of vitamin D compounds and calcimimetic has to be used to achieve the therapeutic goals. If pharmacological treatment

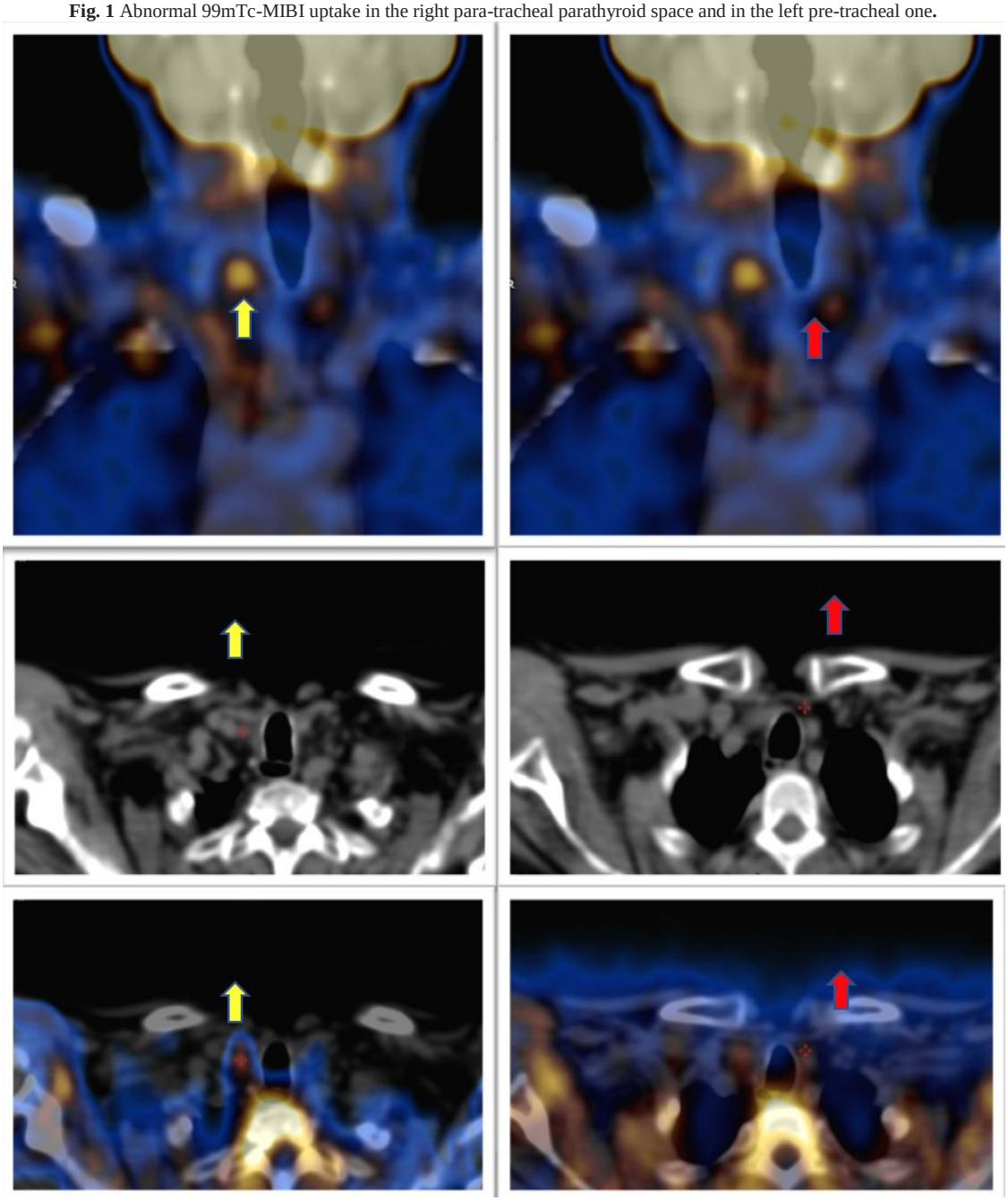
fails, parathyroidectomy should be considered (1). Hence, surgical parathyroidectomy should be considered, especially if concomitant disorders exist, such as persistent hypercalcemia or hyperphosphatemia, tissue or vascular calcification including calciphylaxis, and/or worsening osteodystrophy. Parathyroidectomy is associated with 15%-57% greater survival in patients on dialysis, and it also improves hypercalcemia, hyperphosphatemia, tissue calcification, bone mineral density, and health-related quality of life. The hungry bone syndrome occurs in approximately 25% of patients on dialysis, and profound hypocalcemia requires high doses of oral and intravenous calcium along with calcitriol supplementation. However, unsuccessful surgery with persistent hyperparathyroidism due to inadequate preoperative or intraoperative localization may be observed in about 10% of patients.

An 80-year-old woman was referred to our Division of Endocrine e Minimally Invasive Surgery at the Policlinic University of Messina with the diagnosis of recurrent secondary hyperparathyroidism. Nothing to report in her family history. In personal medical history, previous surgeries for multinodular goiter and intestinal obstruction. The patient has been treated by the nephrologist for chronic renal failure. During the periodic clinical checks she underwent, elevated intact PTH values were highlighted with normal calcium values (blood urea 74 mg/dl; creatinine 1.5 mg/dl; calcium 10.30 mg/dl; ionised calcium 1.2 mmol/L; PTH 196.20 pg/ml). In June 2020, the Patient, after having performed parathyroid scintigraphy documenting hyperaccumulation of the tracer in correspondence of the lower parathyroid glands, underwent surgery. However, the intraoperative findings did not show pathological parathyroid glands. Thus, all possible sites of glandular ectopy were explored: thyrothymic ligaments, retro esophageal space and carotid sheat, bilaterally. Following the possible surgical strategies and the scintigraphic evidence (compatible with the pathology of the lower parathyroid glands), the stumps of the lower thyroid arteries were identified, and a second ligation was performed at their origin (trunk thyroid-cervical). The Patient's post-operative course was regular. However, following the surgical procedure, neither PTH nor calcemia values were decreased.

In agreement with the Division of Nuclear Medicine colleagues, the decision was made to program a second intervention, this time radio-guided to easily and effectively identify the pathological parathyroid glands. The Patient was thus hospitalized again in January 2021. The Patient underwent parathyroid scintigraphy using 99mTc-methoxi-isobutyl-isonitrile (99mTc-MIBI; 370 MBq). Planar images of the neck-thorax region (anterior view; magnification: 1.4; matrix: 256*256; time frame: 600 sec.) were obtained 10 (early images) and 120 (late images) minutes after tracer administration. Single photon emission computed tomography/computed tomography (SPECT/CT) imaging was also obtained after early and late planar imaging.

Planar imaging showed two focal areas of abnormal 99mTc-MIBI uptake located in the lower part of the neck. Abnormal tracer uptake was noted at early imaging and confirmed at late one (Figure 1).

Fig. 1 Abnormal 99mTc-MIBI uptake in the right para-tracheal parathyroid space and in the left pre-tracheal one**.**



SPECT-CT images confirmed parathyroid lesions showing abnormal 99mTc-MIBI uptake in a slight right para-tracheal parathyroid and in a tiny left pre-tracheal one (2).

During the second surgical procedure, all the possible anatomical sites of the parathyroid glands were re-explored. Thanks to the radio-guided approach, we were able to identify the parathyroid glands located in the strap muscles. This localization is certainly unusual and not to be referred to as ectopia; rather, we considered that during the previous thyroidectomy the parathyroid glands

were not spared and the surgeon provided for fragmentation and grafting in a pocket created in the strap- muscles, without positioning of clips that would have made them easier to identify.

Discussion

Scintigraphy of the parathyroid glands has a very high sensitivity (greater than 90%) in the identification of parathyroid adenoma. In comparison, it has an "only" sensitivity of 80% in secondary hyperparathyroidism (this is because the hyperplastic glands have a volumetric increase often not particularly significant). The scintigraphic examination is beneficial in the localization of ectopic parathyroid (3), especially the one with mediastinal localization challenging to identify with morphological imaging methods.The refinement of preoperative instrumental diagnostics through ultrasonography and scintigraphy with 99mTC-MIBI has significantly contributed to realizing a targeted, faster, less invasive surgical procedure with greater guarantees of success. However, still today, in 5.8% of cases, according to literature data, the lesion remains unrecognized at the first surgical approach(4). This datum is to be related to the extreme variability of location and number of the parathyroid glands that originate embryologically from the third and fourth pockets, but which, during migration, can go deep into the anterior mediastinum and in the posterior mediastinum making their retrieval extremely difficult. Preoperative imaging and localization are crucial to a successful surgery. US is the most commonly used imaging modality due to its advantages of low cost and simple manipulation, but it is limited in the detection of ectopic parathyroid glands and is dependent on the examiner's experience. Zhang et al have demonstrated that the ability of early 99mTc- MIBI SPECT/CT to detect parathyroid lesions in SHPT patients is superior to that of US, dual-phase99mTc-MIBI scintigraphy and delayed 99mTc-MIBI SPECT/CT (5).

But when we think we have found and technically well removed the pathological parathyroid (s), are we sure we have solved the case and have obtained the cure? In single adenoma hyperparathyroidism, healing is achieved in 100% of cases. At the same time, in the presence of multiple lesions, the surgical procedure is often inadequate, so much so that in 3.2% of cases, the PTH values remain high.

It is clear how important it is to know if the lesion removed was the only one or, in the case of hyperplasia if the extension of the parathyroidectomy was adequate.

Radio-guided surgery has, compared to traditional surgery, the advantage of tracking more anatomical structures quickly and with greater precision challenging to identify; this prompts the surgeon to practice increasingly limited and present incisions a lower aesthetic impact (6).

Radio-guided parathyroidectomy has the advantage that it can be used, in the case of single adenomas,

even under local anesthesia, but above all to be very useful in re-interventions and/or ectopias, with the only negative exception of the deep mediastinal localization, due to the interference of myocardial uptake. The only limitations on the use of this technique can be logistical-organizational.

Urkan et al also demonstrated that radio-guided occult lesion localization ROLL and guided parathyroidectomy is a feasible technique for parathyroid surgery, especially for parathyroid adenomas. It is a minimally invasive procedure that does not require exploration of the healthy tissue which reduces the complication rates. It reduces also surgeon-based failure and complications by standardizing the surgery. For these qualities, ROLL-guided parathyroidectomy is superior to the classical approach (7).

Based on our esperience the use of radio-guided surgery of the parathyroid glands reduces the time of surgery and hospitalization, gives more guarantees of success in terms of radicality, decreases costs significantly, and favors minimally invasive techniques.

Conflicts of interest

The authors declare no conflict of interest.

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Communicated and received February 18, 2021, Revised and Accepted May8, 2021 published on line May 13, 2021