# Surgery Miami criteria for recurrent MEN-1 hyperparathyroidism in the forearm --Manuscript Draft--

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Mexico City, May 20th 2020

Dear editor:

It is an honor to me to present out article entitled "Miami criteria for recurrent MEN-1 hyperparathyroidism in the forearm". This is an article submitted for the section "Images in surgery". The material contained in it has not been published or submitted elsewhere.

The authors declare no having any conflicts of interest; and no financial support was needed for the realization of this paper.

I hope you find it suitable for be published in the journal "Surgery"

Best regards

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A 22 year-old-woman previously diagnosed with multiple endocrine neoplasia type 1 (MEN-1) presented to the endocrine surgery clinic for evaluation of recurrent hypercalcemia. She had history of pancreatic insulinoma treated with laparoscopic distal pancreatectomy on December 2015.

During follow up, biochemical diagnosis of primary hyperparathyroidism (PHPT) with initial serum calcium of 14.7 mg/dL and parathyroid hormone (PTH) of 524 pg/mL was established. <sup>99m</sup>Tc SPECT/CT, showed no ectopic parathyroid tissue. In January 2016, neck exploration was indicated. During surgical exploration, five parathyroid glands were identified, two in normal position in the left side and three in the right side (two in normal position and a supernumerary right inferior gland). Four parathyroid glands were resected leaving one complete macroscopically normal gland (PIV) *in situ*. Serum calcium levels remained above normal level and persistent hyperparathyroidism was diagnosed with PTH 454 pg/mL and serum calcium of 11.9 mg/dL. <sup>99m</sup>Tc SPECT/CT showed hypermetabolic tissue in right superior lobe. On March 2016 a neck exploration was performed. During this surgery, it was not possible to identify the right PIV gland, thus, an *en bloc* resection of the right thyroid lobe was performed. The specimen was inspected in the operating room and the PIV gland was identified firmly adhered and merged to the right thyroid lobe. Frozen section biopsy confirmed it was parathyroid tissue. The rest of parathyroid tissue was autotrasplanted to the left forearm implanting four pieces of 1 mm each in the brachioradialis muscle.

Normal calcium and PTH levels were reported immediately and in the following months after the operation (calcium 8.8 mg/dL, PTH 6.2 pg/mL). Thirty-six months after forearm auto transplantation, serum calcium and PTH levels progressively rose (11.9 mg/dL and 196 pg/mL in the right arm). Functional studies were done showing no hypermetabolism in the neck, and magnetic resonance imaging confirmed active parathyroid tissue in the left brachioradialis muscle (Figure 1A).

Left brachioradialis muscle exploration was indicated and performed on November 2019 under local anesthesia, with debulking of three pieces of parathyroid tissue that were marked in the previous operation with non-absorbable suture and metallic clips, until < 5 mm of parathyroid tissue was left in the brachioradialis muscle (Figure 1B). Simultaneous serial samples were taken from the transplanted and non-transplanted arm for quick Intraoperative PTH essay measurements (Access Intact PTH immunoassay system®) during resection. Exploration and resection were limited by the behavior of the PTH levels reported following the Miami guidelines and criteria (Baseline and 5, 10 and 15 minutes after resection). Intervention was deemed

complete when >50% decrease in PTH levels at 15 minutes after partial tissue resection in the left arm was reported (Figure 2).

At postoperative-day 1, patient presented without clinical signs of hypocalcemia and was discharged home. On follow up at 4 months, patient is clinically stable with mild residual hyperparathyroidism, calcium 10.4 mg/dL, PTH 64.8 pg/mL, phosphorus 3.5 mg/dL and albumin 3.54 g/dL. Histological examination of the resected specimens confirmed three implants, all compatible with adenomatous/hyperplasic tissue.

Primary hyperparathyroidism is a common clinical manifestation of MEN-1 patients. Standard surgical treatment consists of subtotal or total parathyroidectomy with forearm auto transplantation. Recurrence rates for these latter technique has been reported from 0 to 23%<sup>1,2</sup>. Whilst multiple reports of radio guided surgery for forearm reinterventions in patients with recurrent disease associated with secondary hyperparathyroidism have been described, <sup>3,4</sup> the Miami criteria for Quick Intraoperative PTH essay have been described as a useful tool to determine adequate resection and biochemical results in surgically treated patients with persistent or recurrent primary hyperparathyroidism <sup>5</sup>. This case report represents a novel application of the Miami criteria in a patient with recurrent primary hyperparathyroidism from grafted tissue in the forearm associated with MEN-1.

The authors declare no conflict of interest

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# REFERENCES

- 1. Melck AL, Carty SE, Seethala RR, Armstrong MJ, Stang MT, Ogilvie JB, et al. Recurrent hyperparathyroidism and forearm parathyromatosis after total parathyroidectomy. *Surgery*. 2010;148(4):867-875.
- Elaraj DM, Skarulis MC, Libutti SK, Norton JA, Bartlett DL, Pingpank JF, et al. Results of initial operation for hyperparathyroidism in patients with multiple endocrine neoplasia type 1. *Surgery*. 2003;134(6):858-864.
- Cutress RI, Manwaring-White C, Dixon K, Dhir A, Skene AI. Gamma probe radioguided parathyroid forearm surgery in recurrent hyperparathyroidism. *Ann R Coll Surg Engl.* 2009;91(7):10-12.
- Sippel RS, Bianco J, Chen H. Radioguided Parathyroidectomy for Recurrent Hyperparathyroidism Caused by Forearm Graft Hyperplasia. *J Bone Miner Res.* 2003;18(5):939-942.
- 5. Irvin GL, Carneiro DM. Rapid parathyroid hormone assay guided exploration. Oper Tech

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## Gen Surg. 1999;1(1):18-27.

### Footnotes

Figure 1.- A) Magnetic resonance showing parathyroid tissue in the left brachioradialis muscle. B) Intraoperative imaging of parathyroid tissue in the brachioradialis muscle

Figure 2.- Intraoperative parathyroid hormone monitoring, A) right arm, B) left arm (transplanted)

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This is a case report of a patient with recurrent primary hyperparathyroidism associated to multiple endocrine neoplasia type 1. The importance of this report is the usefulness of Miami Criteria in this group of patients, that has not been described before

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