

# Medullary Thyroid Carcinoma in Multiple Endocrine Neoplasia 2A A Therapeutic Challenge

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## Introduction

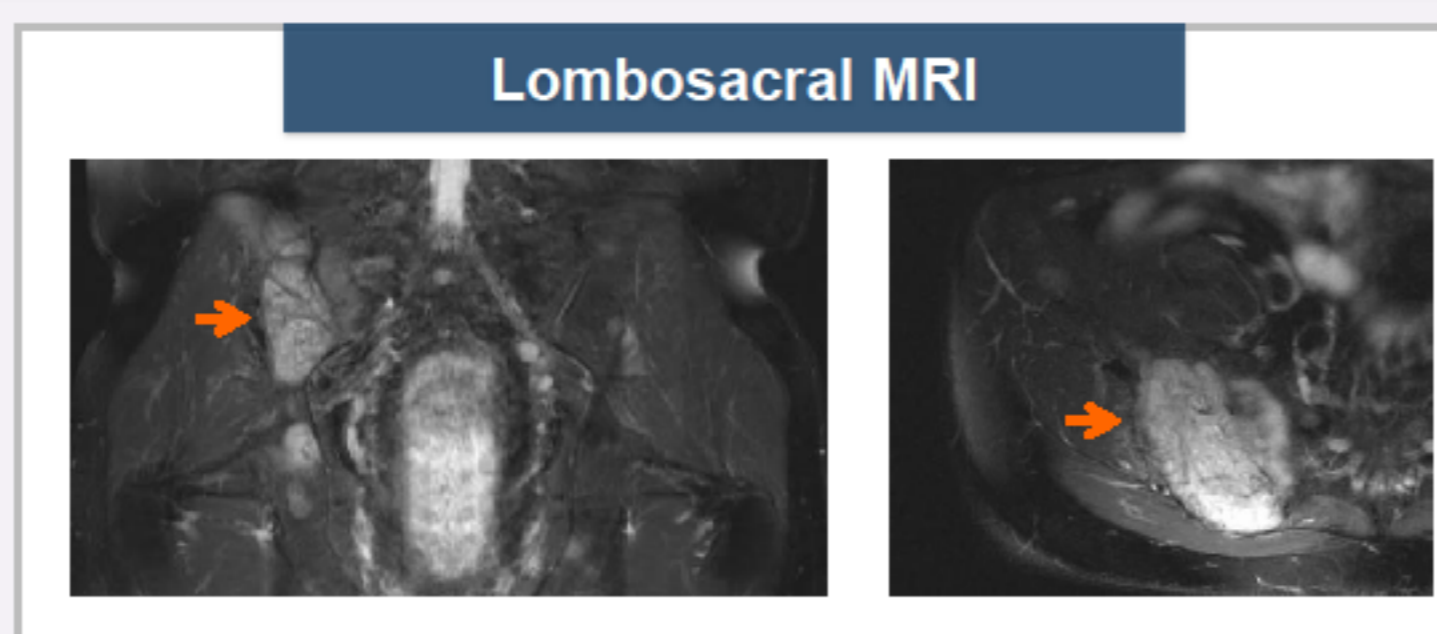
Medullary thyroid carcinoma (MTC) occurs in a hereditary pattern in 25% of cases and accounts for approximately 4% of thyroid cancers. Virtually all patients with multiple endocrine neoplasia 2A (MEN2A) develop MTC. MTC aggressiveness and natural history varies according to the *RET* mutation. Prophylactic thyroidectomy may cure and/or prevent metastatic disease in most cases, which is of paramount importance due to typical chemo and radioresistance.

## Case Report

A 27-years-old man with past history of colostomy at five months of age for Hirschsprung disease and total thyroidectomy at age of 14 years old for the genetic diagnosis of MEN2A (C620R *RET*). Patient's underwent genetic study when his mother was diagnosed with MTC and a germline mutation in *RET* gene (C620R) was identified. Patient's post-operative histological diagnosis revealed two MTC foci of 1 cm and 0.3 cm. Patient was lost to follow-up at the age of 16. In the last year he reported low back pain radiated to right thigh.

### Initial Evaluation

Low back pain

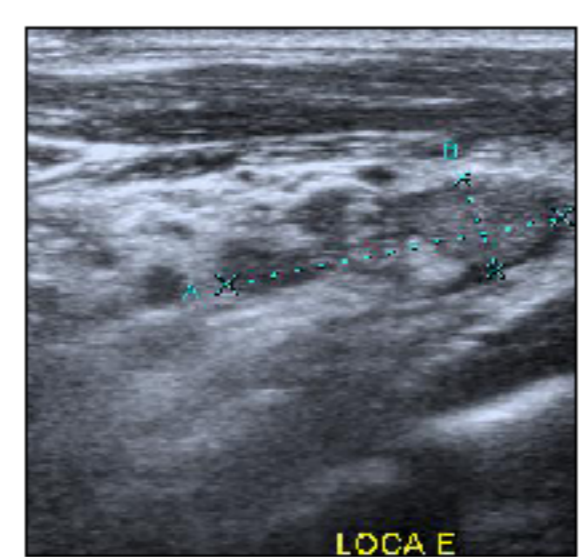


Iliac bone biopsy: lesion compatible with MTC

#### Examination of thyroid region

Detected two nodules in the left flank of the neck with 3 cm and 2 cm of diameter, hard consistency and absent mobility.

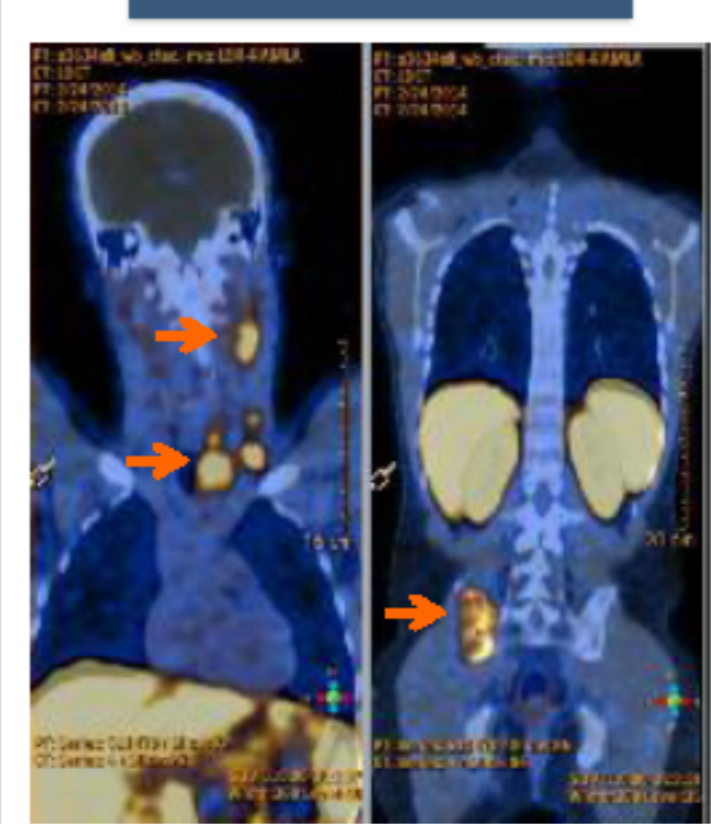
#### Thyroid



Left surgical site:  
Heterogeneous and irregular borders nodule (22x7mm) compatible with local recurrence

Left para-tracheal region:  
Two contiguous nodules with 37 mm and 28 mm (adenopathy?)

#### <sup>68</sup>Ga-DotaNoc PET



High uptake in the thyroid area, left para-pharyngeal region with high density of somatostatin receptors in the left cervical region and right iliac bone

	0 months	Reference
TSH	0.057	0.4-4 uIU/mL
FT4	1.2	0.8-1.9 ng/mL
Thyroglobulin	<0.2	1.6-60 ng/mL
Calcitonin	60 428	<10 pg/mL
CEA	1 947	<5.4 ng/mL
TPOAb	15	<40 UI/mL
TgAb	<20	<40 UI/mL
Total calcium	9.7	8.8-10.6 mg/dL
PTH	43	9-72 pg/mL
Plasmatic Metanephrines	90.2	< 90 pg/mL
Urinary Metanephrines	63.6	25-312 µg/24h

### Surgery

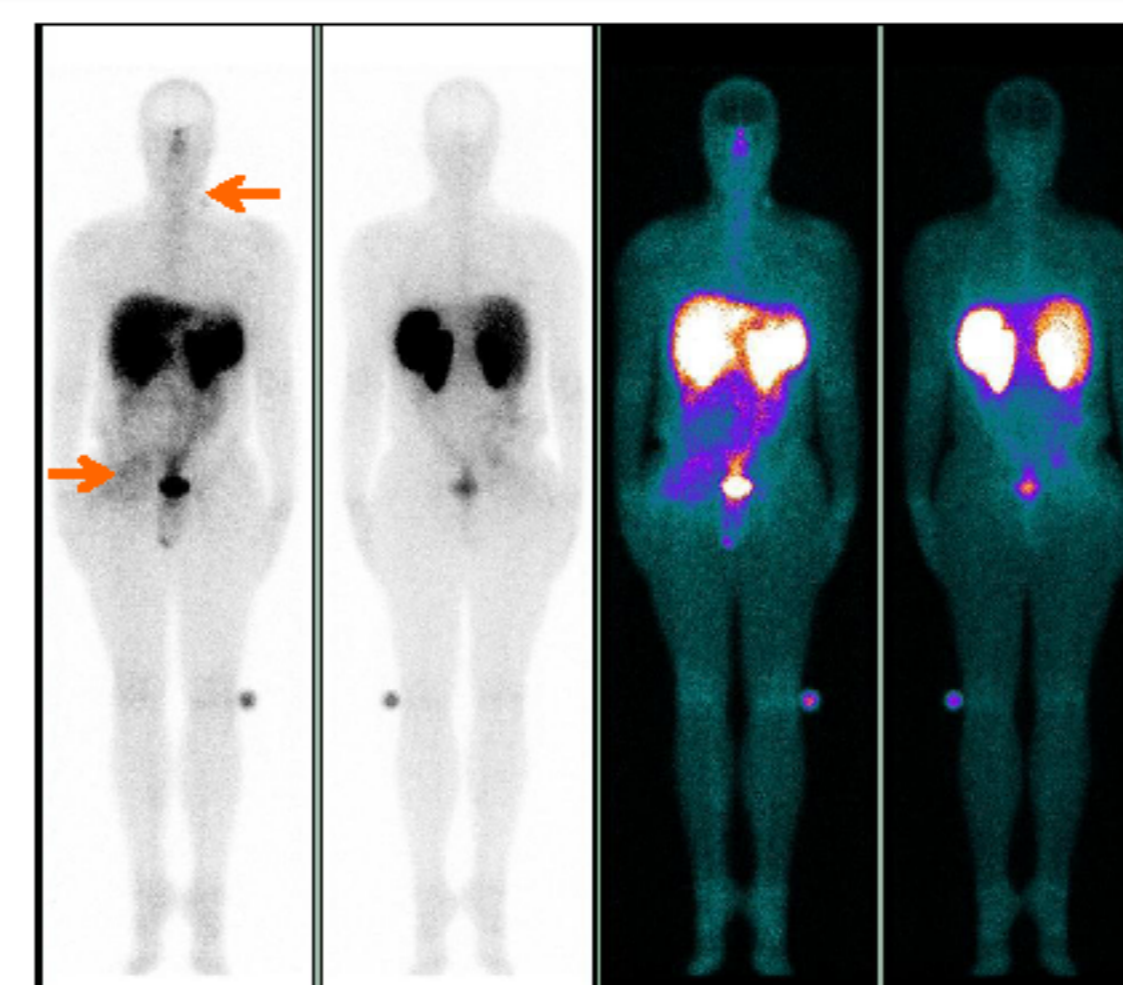
Bilateral cervical lymph node dissection  
Subtotal resection of iliac metastasis

Histology  
MTC metastasis

	0 months	+3 months	Reference
TSH	0.057	0.43	0.4-4 uIU/mL
FT4	1.2	1.4	0.8-1.9 ng/mL
Thyroglobulin	<0.2		1.6-60 ng/mL
Calcitonin	60 428	7 664	<10 pg/mL
CEA	1 947	222	<5.4 ng/mL
TPOAb	15	21	<40 UI/mL
TgAb	<20	<20	<40 UI/mL
Total calcium	9.7	8.9	8.8-10.6 mg/dL
PTH	43	32	9-72 pg/mL
Plasmatic Metanephrines	90.2		< 90 pg/mL
Urinary Metanephrines	63.6		25-312 µg/24h

### Therapeutic Approach

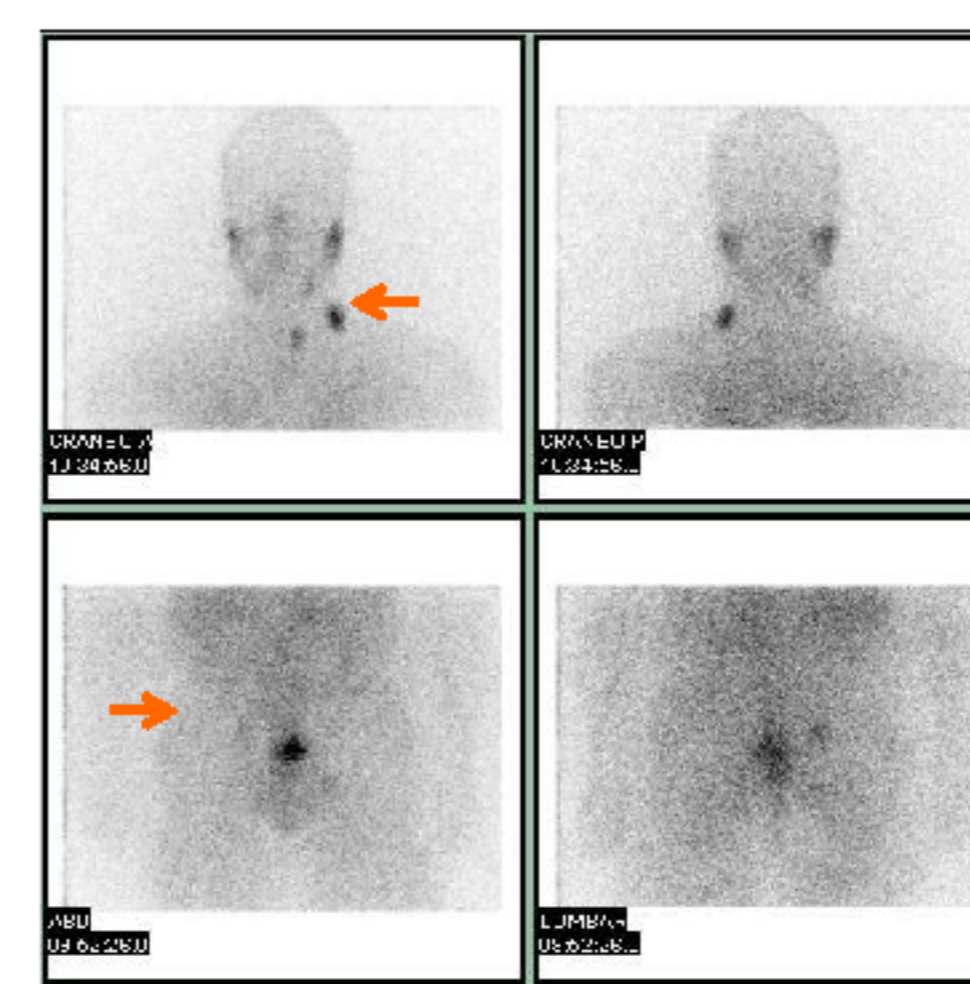
#### Post-therapeutic 200 mCi <sup>177</sup>Lu-DOTATATE Scintigraphy



Low uptake: withdrawal of <sup>177</sup>Lu-DOTATATE treatment

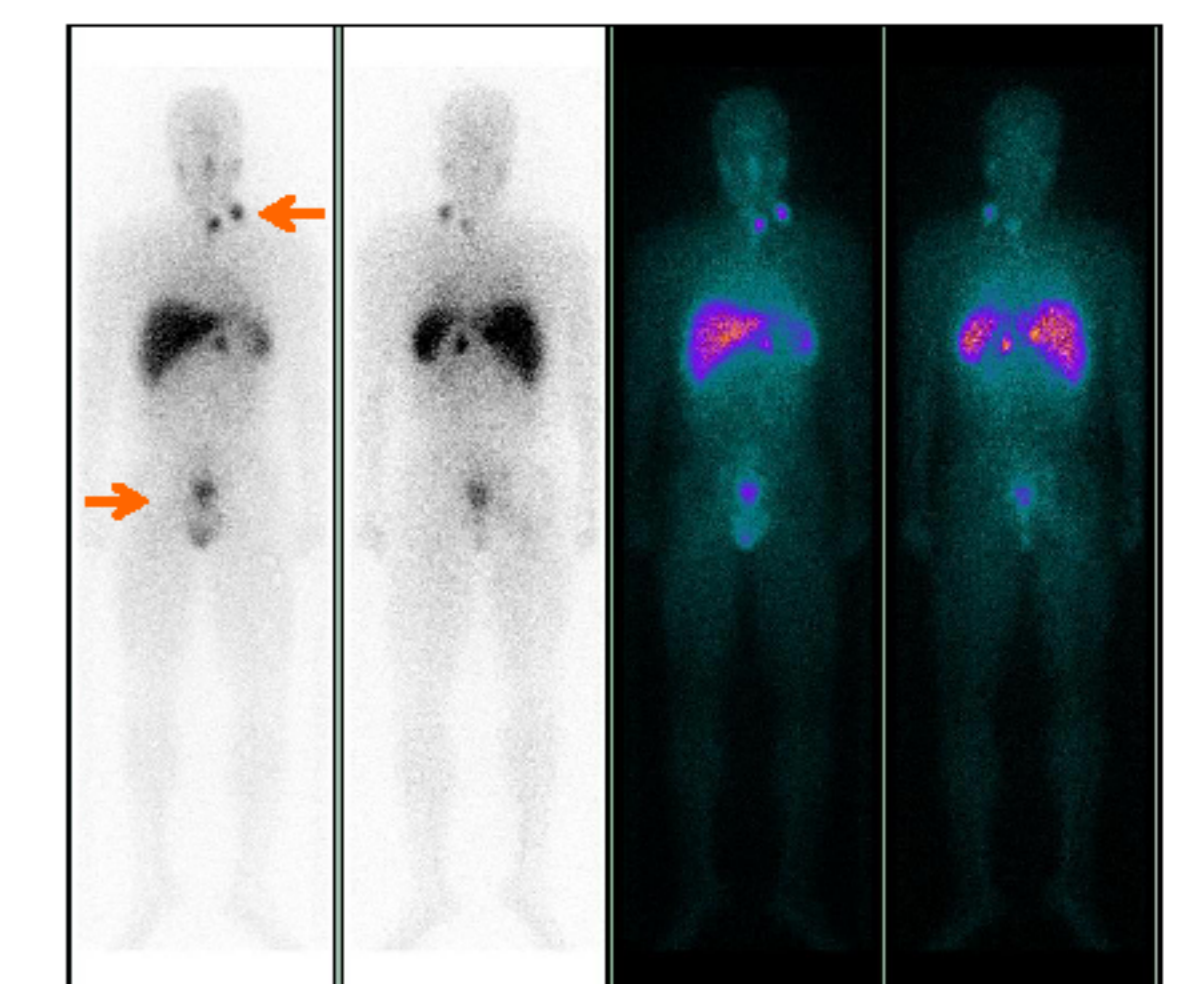
	0 months	+3 months	+9 months	Reference
TSH	0.057	0.43	1.4	0.4-4 uIU/mL
FT4	1.2	1.4	1.3	0.8-1.9 ng/mL
Thyroglobulin	<0.2			1.6-60 ng/mL
Calcitonin	60 428	7 664	> 2 000	<10 pg/mL
CEA	1 947	222	274	<5.4 ng/mL
TPOAb	15	21		<40 UI/mL
TgAb	<20	<20		<40 UI/mL
Total calcium	9.7	8.9	8.9	8.8-10.6 mg/dL
PTH	43	32	22	9-72 pg/mL
Plasmatic Metanephrines	90.2		32.3	< 90 pg/mL
Urinary Metanephrines	63.6		202.2	25-312 µg/24h
Chromogranin			423.3	<85 ng/mL

#### <sup>123</sup>I-MIBG Scintigraphy



Moderate/High uptake: treatment with <sup>123</sup>I-MIBG

#### 154 mCi <sup>123</sup>I-MIBG Scintigraphy



Moderate/High uptake: ongoing treatment

	0 months	+3 months	+9 months	+15 months	Reference
TSH	0.057	0.43	1.4	3.4	0.4-4 uIU/mL
FT4	1.2	1.4	1.3	1.4	0.8-1.9 ng/mL
Thyroglobulin	<0.2				1.6-60 ng/mL
Calcitonin	60 428	7 664	> 2 000	8 740	<10 pg/mL
CEA	1 947	222	274	359	<5.4 ng/mL
TPOAb	15	21			<40 UI/mL
TgAb	<20	<20			<40 UI/mL
Total calcium	9.7	8.9	8.9		8.8-10.6 mg/dL
PTH	43	32	22		9-72 pg/mL
Plasmatic Metanephrines	90.2		32.3	56.6	< 90 pg/mL
Urinary Metanephrines	63.6		202.2	176.2	25-312 µg/24h
Chromogranin			423.3	581.3	<85 ng/mL

## Conclusion

- CMT is the first manifestation of MEN2A. As shown in this case the age of prophylactic thyroidectomy is of decisive importance to the prognosis.
- Tumour somatostatin receptors heterogeneity may be responsible for different responses to radionuclides. The treatment of metastatic disease is challenging due to the poor response to systemic therapy and/or radiotherapy.

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