A case of young girl with high risk *RET* mutation successfully diagnosed as medullary thyroid carcinoma in very early stage.

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Introduction

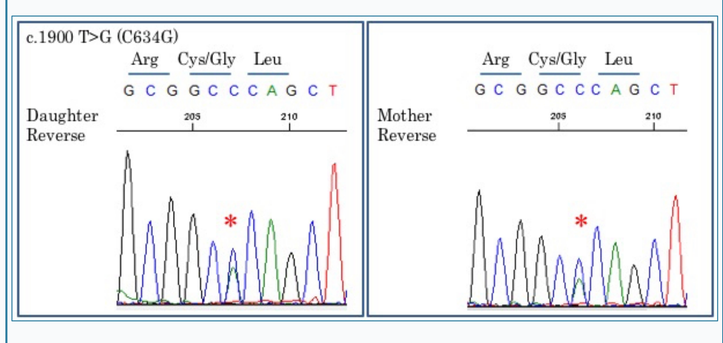
- Medullary thyroid carcinoma (MTC) in Multiple Endocrine Neoplasia type 2 (MEN2) shows near complete penetration.
- Presentation and prognosis of MTC highly depend on *RET* proto-oncogene mutation.

American Thyroid Association (ATA) guidelines recommend prophylactic surgery for the patients of MEN2 with high risk *RET* mutations.

Case Presentation

age	5 month-old		8 year-old	
event	The patient's mother was diagnosed as MEN2A. ↓ Gene analysis ↓ *RET* codon C634G mutation was detected (figure1)	Annual calcium infusion test to monitor calcitonin level and neck ultrasonography	Result of the test became positive (table1) but ultrasonography finding was negative	Total thyroidectomy and central neck lymph node dissection ↓ Stage I MTC (T1, N0, M0) was confirmed (figure2)

Figure1 Gene analysis of the patient and her mother



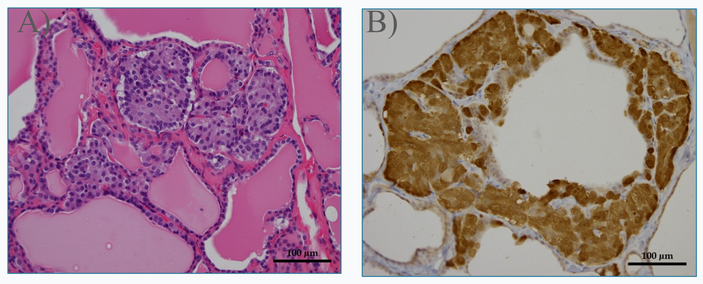
C634G: *RET* codon 634 mutations are classified as high risk group in ATA guideline for MTC and prophylactic thyroidectomy before 5 year-old is recommended.

Table1 Stimulated calcitonin level by calcium infusion test

age	serum calcitonin level			
	0'	2'	5'	reference value
8y	11.3	333	248	<6.40 pg/mL (ECLIA)

- Both basal and stimulated calcitonin levels elevated at 8 year-old.
- Elevation of basal calcitonin level was mild.

Figure2 Histopathological manifestations

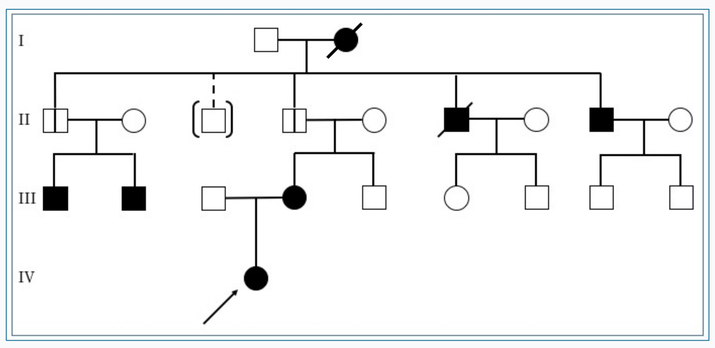


A) H-E stain ×200: Parafollicular cells are proliferating and partially destroying follicles.
B) Calcitonin immunostain ×200: Tumor cells are strongly reactive for calcitonin and invading into thyroid follicle.

Discussion

Phenotype of MTC varies even among family members with the same genetic defect.

Figure3 Familial history of MTC



Most family members in each generation of maternal lineage are affected with MTC. However there are asymptomatic members like the patient's grandfather and her uncle, who are estimated to have the same *RET* mutation.

Prophylactic thyroidectomy has some debatable problems.

- Higher risk of surgical complications at younger age
- Hormone replacement therapy for longer time
- Public health insurance coverage

Instead of prophylactic treatment…

- Detecting early stage MTC could be another major follow-up method.
- The timing of thyroidectomy should be decided for each individual case.

How ?

- Serum calcitonin level is a sensitive marker for detecting MTC.
- Deciding right time for thyroidectomy by serum calcitonin could relieve above mentioned problems.

Conclusions

We recommend that annual calcium infusion test should be performed for *RET* gene mutation carriers to detect MTC in early stage and perform thyroidectomy without delay.

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Reference

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Thyroid

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