Medullary Thyroid Carcinoma

- Tumor of thyroid parafollicular C-cells
- Sporadic or Familial
- Calcitonin – tumor marker

Multiple Endocrine Neoplasia type 2

- MEN 2A
  - MTC (100%)
  - Pheos (45%)
  - Hyperpara (25%)
  - Hirschprungs (2.3%)
- MEN 2B
  - MTC (100%)
  - Pheos (45%)
  - “Marfanoid” (100%)
  - Megacolon (100%)
  - Neuromas (100%)

FMTC-MTC Only
Hirschprung’s Disease

- Bowel obstruction in infancy
- Approximately 2% of MEN 2A patients affected

Cutaneous Lichen Amyloidosis-MEN 2A

MEN 2B
Nerve Enlargement in MEN 2B

- MTC Database at Washington University
  - IRB-approved prospective database
  - Sporadic and Familial MTC
  - Primary and re-operative data

RET Proto-Oncogene

Preventative Thyroidectomy in Children with MEN 2A

- TT performed in 50 consecutive patients under 20 with MEN 2A
- All patients evaluated clinically and biochemically 5 years following TT
- Basal and stimulated calcitonin undetectable in 44/50
- Mild elevation of stimulated calcitonin level in 4 patients

Samuel Wells, MD
Preventative Thyroidectomy in Children with MEN 2A

- Factors correlated with cure:
  - Age below 8 years
  - Normal preop stimulated calcitonin
  - Absence of MTC in the resected gland

Skinner, Moley et al NEJM 2005

Controversies in MEN 2 Preventative Thyroidectomy

- Age at thyroidectomy
- Parathyroids-to transplant or not to transplant?
- Central node dissection- When to perform?

76 yo woman whose daughter and grandson found to have MTC/MEN 2A
- Palpable thyroid mass
26 y.o. F with Headache, Palpitations, Hypertension

Palpable MTC
- Check plasma metanephrines before OR
- CT, neck USG, laryngoscopy
- Calcitonin testing
- Preserve parathyroid function!
- Genetic counseling and Testing after surgery

Medullary Thyroid Carcinoma
Management of Palpable Medullary thyroid Carcinoma and Extent of Node Dissection

Node dissection in palpable MTC
- Surgery is the only curative therapeutic option
- Post-operative elevated calcitonin in over 50% of patients
- Guidelines for extent of node dissection not well established
RLN Invasion by tumor

Lymph Node Metastases

MTC Surgical Management

- Initial operation
  - Total Thyroidectomy
  - Central Lymph Node (Level VI) Dissection
  - Ipsilateral Lateral Dissection (II – V)
  - Consider contralateral neck dissection
  - Preserve parathyroid function

- Re-operation
  - Compartment-oriented anatomy
  - Microdissection
ATA MTC guidelines (in preparation)

Management of the patient with elevated calcitonin

If there is palpable or imageable disease on trachea or great vessels resect!

Re-operative Procedure

- Microdissection
  - Central (Level VI)
  - Bilateral Lateral (Levels II through IV)
  - Bilateral Level V if disease evident preoperatively
Re-operation for MTC
• Postoperative calcitonin normalization

<table>
<thead>
<tr>
<th>Series</th>
<th>N</th>
<th>Percent with normal CT postop</th>
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<tr>
<td>Norton 1980</td>
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<td>Tisell 1986</td>
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<td>Frank-Raue 1992</td>
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<td>Moley 1993</td>
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<td>Moley 1997</td>
<td>45</td>
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<td>Gimm 1998</td>
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Operative Complications

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<th>RLN injury</th>
<th>Hyoparathyroidism</th>
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<td>% of Total</td>
<td>Number of pts</td>
<td>% of Total</td>
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<td>2</td>
<td>3</td>
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<td>5.43</td>
<td>2.17</td>
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Reoperations for Medullary thyroid carcinoma
8-10 Year follow-up

Re-operations with Curative Intent
- 93 patients, 105 operations
- 4 patients died of Disease (4%)
- 56 patients – eligible for 8-10 yr follow-up
- 14 (26%) calcitonin <10 pg/ml

Re-operations for Palliation
- 55 patients, 59 operations
- 11 (20%) calcitonin <100 pg/ml

Reoperation for MTC- Conclusions
• Long-term eradication of disease is possible in MTC
  - 22% of patients with CT < 10 pg/mL
  - More than 1/3 with CT < 100 pg/mL
  - 78% without radiologic recurrence at 8-10 years
  - Disease-free survival 71.4% at 10 years
• Compartment-oriented microdissection performed in expert hands with minimal morbidity
Sporadic microscopic Medullary Thyroid Carcinoma (SmMTC)

Distant metastases from MTC

Locally Advanced, Recurrent MTC
Development of a *Drosophila* model for MEN 2
(Cagan, Goodfellow)

*Drosophila* Ret2B

Genetic screen for enhancers and suppressors of the *Drosophila* Ret eye phenotype

Response to Zactima

Calcitonin

Baseline 1st dose 2 months

6/12/06 1.9 cm 9/11/06 1.0 cm