Medullary Thyroid Cancer

- Medullary thyroid cancer is actually a cancer of neuroendocrine tissue that is a part of normal fetal development. Eventually that tissue is then surrounded by thyroid tissue. Medullary is termed a “thyroid cancer” by virtue of its anatomic location only. It bears no resemblance to the “usual” thyroid cancers, papillary and follicular types.
    - Medullary type represents about 5% of all thyroid cancers.
- The cancer is located in what are called the “C-cells” or “parafollicular cells,” that normally secrete calcitonin, one of the hormones that regulates calcium in the body.
    - We can use calcitonin as a marker of disease progress and remission.
    - But sometimes these tumors make other hormones than just calcitonin, so we will check for those depending on the patient’s overall picture.
- **Medullary thyroid cancer can be random or hereditary. It can be associated with larger “clusters” of other hormone problems called Multiple Endocrine Neoplasias (MEN) types 2A (1 in 1.9 million) and 2B (1 in 38 million).**
    - **When it exists in a hereditary or MEN pattern, it is almost always associated with a mutation in a gene called RET, so DNA analysis is a very important part of diagnosis.**
- How is Medullary Thyroid Cancer diagnosed?
    - Usually patients present with a thyroid nodule that clearly shows medullary thyroid cancer after a biopsy.
    - Sometimes it is diagnosed after a patient presents with a cluster of symptoms that might look like MEN, and thyroid nodules are discovered as part of the diagnostic process.
- How do we manage medullary thyroid cancer?
    - First we need to get baseline levels of calcitonin and CEA, which are important markers of the disease and can guide us about how extensive the cancer is.
    - Second we need to have a DNA analysis for one of the RET mutations (there are over a hundred so far).
        - **If the RET gene mutation is POSITIVE, it is FUNDAMENTAL to the health and safety of your siblings and children that they be screened for certain cancers and offered appropriate genetic counseling.**
        - **We will happily assist with notifying your family with your permission and if you do not grant permission, <u>we are still LEGALLY AND ETHICALLY REQUIRED to notify anyone who could be affected by this mutation.</u> This will be facilitated through Methodist’s ethics and legal departments.**
    - If the RET gene is positive, we also must screen for other hormone problems that are included in the MEN 2A and 2B syndromes
        - Pheochromocytoma - a tumor of the adrenal gland that produces large amounts of adrenaline.

        - Hyperparathyroidism - excess production of parathyroid hormone that causes high levels of calcium and kidney stones.
    - Depending on how high the calcitonin level is, we may need extra imaging scans to check for spread of cancer to the neck, chest, liver or bones.
    - All patients with medullary thyroid cancer get to have a total thyroidectomy and usually manual inspections of lymph nodes in the neck.
        - The pathologist will tell us the staging of the disease based on the specimen removed during surgery.
    - About 3 months after surgery, we follow the calcitonin, CEA and any other markers that are important to the patient's overall clinical picture.
- **10 year survival rates** in general are pretty good.
    - Stage I = 100%
    - Stage II = 93%
    - Stage III = 71%
    - Stage IV = 21%
    - Patients whose calcitonin level goes to 0 after surgery have approximately a 97% survival over 10 years. This is called a biochemical cure.
- What happens if the follow up calcitonin is NOT zero?
    - First we consider new imaging to check the neck, liver, chest and bones, and even a liver biopsy.
    - If we think the remaining disease is confined to lymph nodes in the neck, it's usually worth a new surgery to remove them.
    - If it has gone elsewhere, there are a number of therapies that can be used, including antibody treatments, radiation or chemotherapy.
        - The response rates to chemo and radiation are somewhat low and frequently this is reserved for palliative care and to maintain stable levels of disease.
        - There are clinical trials available that are investigating the use of targeted molecular therapies.
    - We will continue to follow calcitonin every 3-6 months to try and understand how quickly the levels are doubling, and adjust the plans accordingly.

Additional Resources

- American Thyroid Ass'n https://www.thyroid.org/medullary-thyroid-cancer/
- Columbia University http://columbiasurgery.org/conditions-and-treatments/medullary-thyroid-cancer
- American Society of Endocrine Surgeons http://endocrinediseases.org/thyroid/cancer_medullary.shtml