

Evaluation of Elevated Calcitonin in a Patient with Sporadic Medullary Thyroid Carcinoma



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Objective

To present a case of sporadic medullary thyroid cancer (MTC) with significantly elevated calcitonin levels but no evidence of metastasis.

Case Presentation

A 56 year old man with a past medical history of hypertension, dyslipidemia, and a pancreatic cyst presented to Endocrinology for type 2 diabetes mellitus after a pancreaticoduodenectomy was noted to have a palpable thyroid nodule on physical exam.

Thyroid ultrasound: 2x1.9x1.7cm right hypoechoic nodule (Figures 1 and 2) with increased blood flow

Cytology from FNA biopsy: medullary thyroid carcinoma - stained positive for calcitonin and negative for thyroglobulin

Calcitonin level of 1904 pg/mL, CEA 160.9 ng/mL

Plasma metanephrines and serum calcium were normal

Lateral neck ultrasound, CT neck/chest, MRI liver and bone scan negative for evidence of metastatic disease

Total thyroidectomy with central and right modified radical neck dissection was performed.

Surgical pathology:

- 2cm focus of medullary thyroid carcinoma on the right thyroid lobe with focal vascular invasion, two micro foci of papillary microcarcinomas on the right lobe
- One papillary microcarcinoma on the left lobe
- Fourteen lymph nodes were negative for malignancy (2 left paratracheal nodes and 10 from the right neck dissection)

Genetic testing ultimately revealed a variant of unknown significance of MSH6 with no RET mutation.

4 week post-operative calcitonin: undetectable, CEA 2.7 ng/mL

On continued follow up over the next 2 years, the patient's calcitonin levels remain undetectable with stable CEA levels (Figure 5).

Repeated post-operative thyroid ultrasounds show no evidence of recurrent disease in the thyroid bed or lymph nodes. The patient continues to follow regularly for active surveillance of medullary thyroid carcinoma.

Imaging



Figure 1: Transverse view of right thyroid nodule



Figure 2: Longitudinal view of right thyroid nodule

Pathology

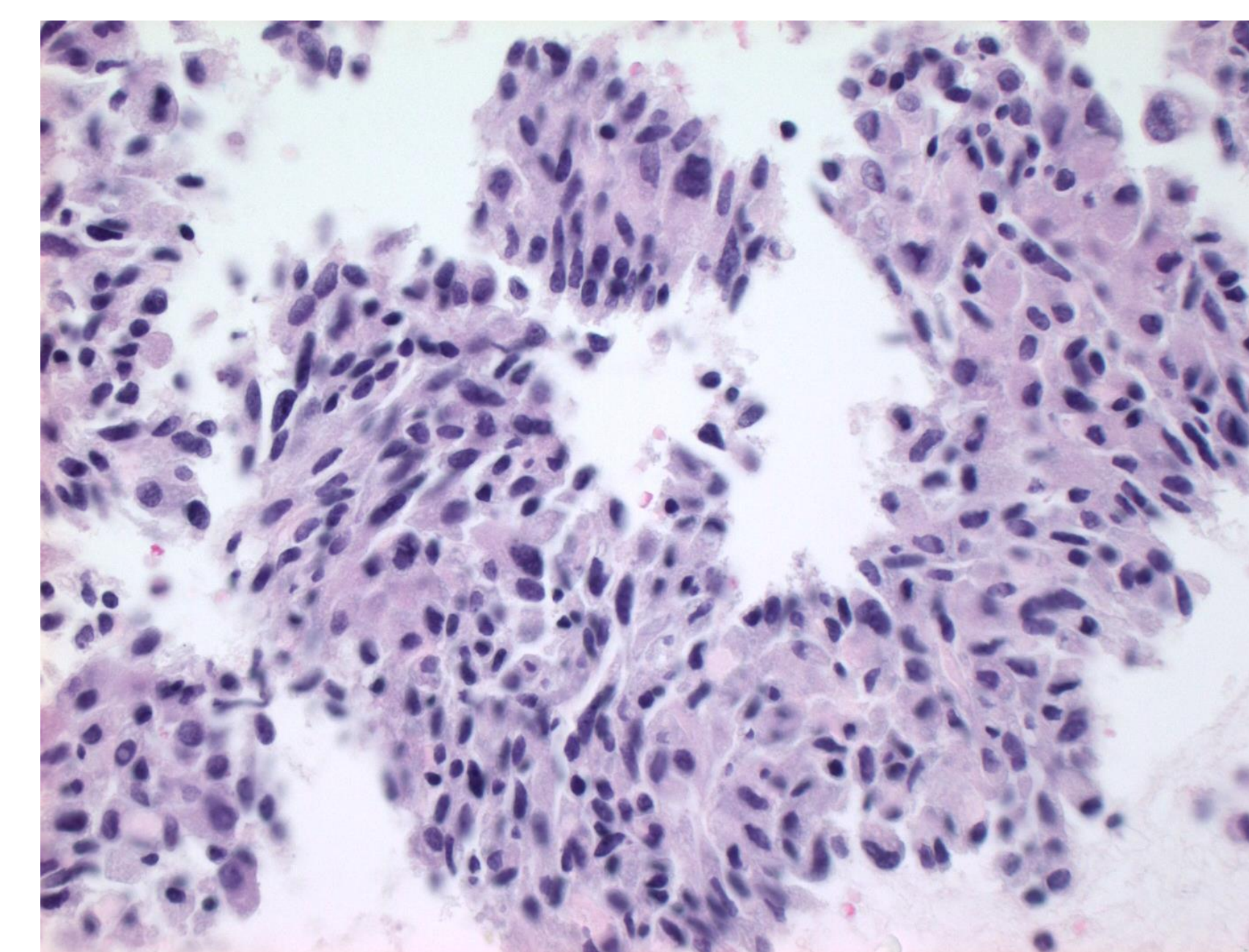


Figure 3: H&E stained slide of medullary thyroid carcinoma at 400x magnification

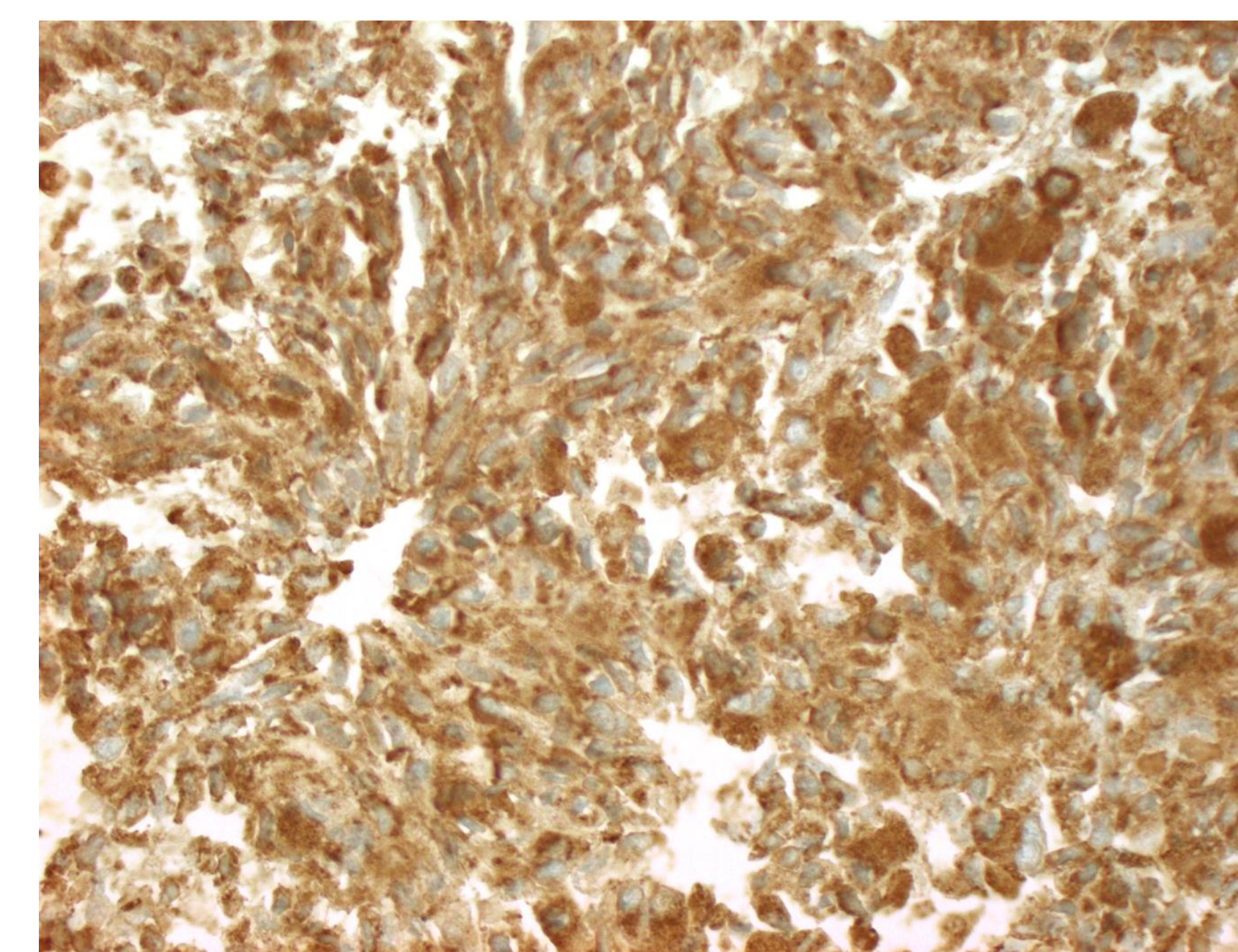


Figure 4: Confirmatory immunohistochemical stains at 400x magnification for calcitonin (positive)

Lab Data

	Jan 2018	March 2018	Nov 2018	April 2019	March 2020
Calcitonin (≤10 pg/mL)	1904	<2	<2		
CEA (0 - 5.0 ng/mL)	160.9	2.7	1.3	1.1	1.1

Figure 5: Preoperative and postoperative calcitonin and CEA

Background

Medullary thyroid carcinoma comprises nearly 2% of all thyroid cancers and originates from parafollicular C cells mostly found in the upper 2/3 of the thyroid gland.^{1,2}

Appropriate risk stratification based on anatomic characteristics as well as serum calcitonin and CEA guide management and can predict disease prognosis and mortality.¹⁻⁶ Data suggests that calcitonin levels are always elevated on diagnosis of MTC, and the degree of elevation is positively correlated to extent of disease.²⁻⁴

Aggressive surgical resection, including total thyroidectomy and prophylactic central neck dissection, for patients with node-negative disease has been standard of care. Lateral neck dissection is usually limited to patients with clinically positive lymph nodes or preoperative calcitonin greater than 20 pg/mL.^{3,5}

Our patient's calcitonin level of nearly 100 times the upper limit of normal was highly suggestive of aggressive disease including distant metastases thus validating further investigation.

The absence of distant disease on imaging was highly unusual but did correlate with excellent postoperative biochemical response. The patient also did not exhibit symptoms often associated with significant elevations in calcitonin (including flushing and diarrhea). This could suggest focal production of elevated calcitonin levels.

Conclusion

Early detection of medullary thyroid carcinoma and risk stratification using serum calcitonin can guide appropriate treatment and long-term monitoring. Elevated calcitonin can indicate aggressive disease but in combination with the absence of anatomic metastases and symptoms of calcitonin excess, could predict good response to initial surgical resection.

References:

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