

Case Report

Elevated CEA and Medullary Cell Carcinoma

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25 years old female was investigated for a nonspecific abdominal pain history and was found to have elevated CEA (carcinogenic embryonic antigen). The work up for gastrointestinal malignancy included upper and lower gastrointestinal endoscopy and a contrast enhanced CT abdomen. The endoscopy findings were inconclusive while the CT abdomen revealed a 1cm nodule in left adrenal gland, which was of doubtful clinical significance, and not likely cause of elevated CEA Figure 1.

On clinical examination she is a lady of average build and height. Her systemic examination including neck and abdominal examination were unremarkable.

Prompted by concerns of rising CEA whole body PET scan was requested, which showed a small thyroid nodule in right side of neck Figure 2, which was confirmed on subsequent ultrasound of thyroid. Her thyroid nodule biopsy showed medullary cell carcinoma. This was not surprising in setting of elevated CEA, and positive uptake on PET scan, hence, explaining the elevated CEA. Because of positive thyroid biopsy, RETS gene testing and serum calcitonin, level was requested. The genetic testing was negative for MEN 2 (Medullary endocrine neoplasia), but calcitonin level was significantly elevated (>20ng/ml). She has total thyroidectomy on 12/9/2012. Post operatively she had transient hypoparathyroidism and her serum calcitonin and CEA fall to zero level. She is on replacement therapy for post surgical hypothyroidism. Her follow up calcitonin CEA, level and urine metanephrine levels are within normal limits (Table1). CT abdomen, at 6 months follow up, showed a small increase in left adrenal nodule and it remained non functional.

Whole body PET scan Feb 2012

No abnormal uptake in abdomen to pelvis to indicate occult malignancy no abnormal activity in presumed small left adrenal adenoma. Focal uptake at inferior aspect of left thyroid lobe concerning for metabolically active thyroid lesion. Recommended us of thyroid,

CT abdomen 6/March /2012

A left hypodense adrenal mass 10x10 mm most likely represent incidentiloma few Para aortic lymph nodes largest measure 6mm on short axis

September 30 / November / 2013 follow up CT Abdomen

Left adrenal mass lesion 1.5 x 1.2cm slightly increased in size compared to previous CT study.

Medullary thyroid carcinoma and elevated CEA

MTC are neuroendocrine tumours of parafollicular or C cells of thyroid. The tumours occur usually in sporadic form but a quarter of cases are hereditary. The tumours may be part of multiple neuroendocrine neoplasias (MEN2). The most common presentation is solitary thyroid nodule (70-95% of patients) [1]. The diagnosis is made by fine needle aspiration biopsy of thyroid nodule. The sensitivity of fine needle aspiration is 50 to 80 %, although higher sensitivity can be obtained by addition of immunohistochemical staining with calcitonin [2]. The mutation in RET proto-oncogene are known to be cause of MEN2 and familial Medullary thyroid carcinoma.

Calcitonin is stored in secretory granules of C cells. The sensitivity and specificity of calcitonin being close to 100% for early detection of medullary carcinoma [3]. However calcitonin negative cases of MTC have been reported [4]. Anyway in some cases it is possible to observe false positive for high serum calcitonin levels in adult individuals. Conditions related to high calcitonin levels are renal insufficiency, hypergastrinemia (omeprazole), hypercalcemia, neuroendocrine tumours, inflammation and possible Hashimoto's thyroiditis [5]. Abnormal levels of calcitonin can be confirmed by pentagastrin stimulation test which only stimulates calcitonin secretion. In 2006 European guidelines recommended calcitonin screening [6]. 2010 summary of recommendations from European and American societies suggest that calcitonin screening should be considered before performing thyroidectomy for thyroid nodules [7].

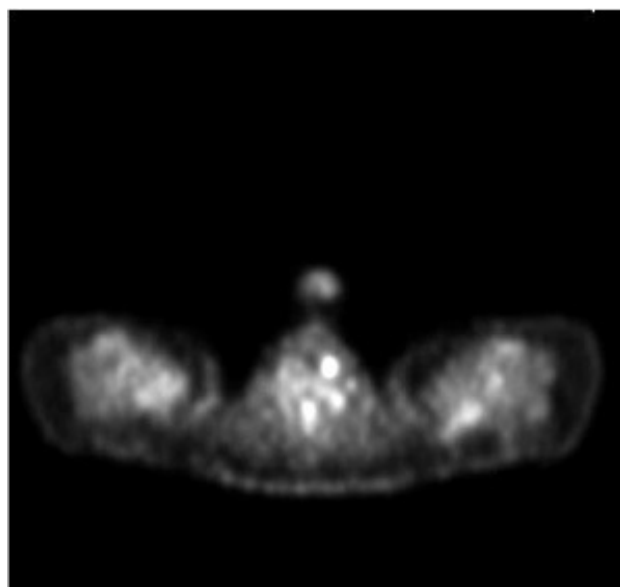


Table 1: comparison of results of CEA and calcitonin before and after surgery.

	Dec 2011	6 March 2012	11 June 2013
CEA	16.9ng/ml	25ng/ml	0.5g/ml
Calcitonin	>20ng/ml	<1ng/ml	1.2ng/ml
Urine nor adrenaline		157mmol/24hrs 27mcg/24hrs	100mmol/24hrs
Urine adrenaline		<27mmol/24hrs <5mcg/24hrs	<30mmol/24hrs
Urine Dopamine		1263nmml/24hrs 193mcg/24hrs	1300nmml/24hrs

CEA was first detected in 1965, when Gold and Freeman isolated it from colon cancer tissue [8]. CEA is another tumour marker used in follow up of MTC (Medullary thyroid carcinoma). CEA is a cytosolic enzyme tumour marker which is not specific biomarker for MTC, being generally expressed by many endocrine and non endocrine tumours. In MTC it is considered to have lower diagnostic accuracy than calcitonin. CEA is also a tumour marker of gastrointestinal malignancy. The patient with elevated CEA should be extensively investigated for gastrointestinal malignancy as was done in our case. In absence of gastrointestinal cause of elevated CEA, the possibility of tumour of neuroendocrine origin should be considered. A case series of 4 patients has been presented by Deepak Abraham et al., in his paper, "Medullary thyroid carcinoma presenting as initial elevation of CEA. Assessment of calcitonin and CEA doubling time post operatively provide sensitive measurement of prognosis and aggressiveness of metastatic MTC [9] Raised CEA level indicated the presence of large primary tumour, regional lymph node metastases and systemic metastases [10]. There is no available data in literature on percentage of patient of medullary thyroid carcinoma presenting as elevated CEA.

Medullary cell carcinoma is the third commonest thyroid tumour. Survival rates are worse than those of papillary or follicular thyroid cancer, but if the lesion is confined to thyroid, 10 years survival of 90% is not uncommon. The tumour arises from parafollicular cells (also called C cells) which produce calcitonin. Medullary cell carcinoma may arise sporadically or in association with other endocrinopathies (MEN-2). The initial work up of MTC includes ultrasound of neck and fine needle aspiration biopsy. Calcitonin is a very sensitive tumour marker. Though CEA is not a sensitive tumour marker for

MTC (Medullary cell carcinoma) in the absence of gastrointestinal causes of its elevation, the possibilities of neuroendocrine origin especially MTC should be considered. All patients with histology proven MTC should undergo RET proto-oncogene testing and work up for other tumours of MEN2 should be considered.

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