

A thymic carcinoid tumor causing Cushing syndrome in the setting of a multiple endocrine neoplasia syndrome type 1 (MEN 1)

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Introduction:

Multiple endocrine neoplasia syndrome type 1 (MEN1) associated thymic neuroendocrine tumors (Th-NETs), namely, thymic carcinoid tumors, are rare and have poor prognosis. Cushing syndrome (CS) caused by Th-NET in MEN1 syndrome is extremely rare. Herein, we report an extremely rare case of MEN 1 syndrome, papillary thyroid carcinoma and Th-NET, presented with CS.

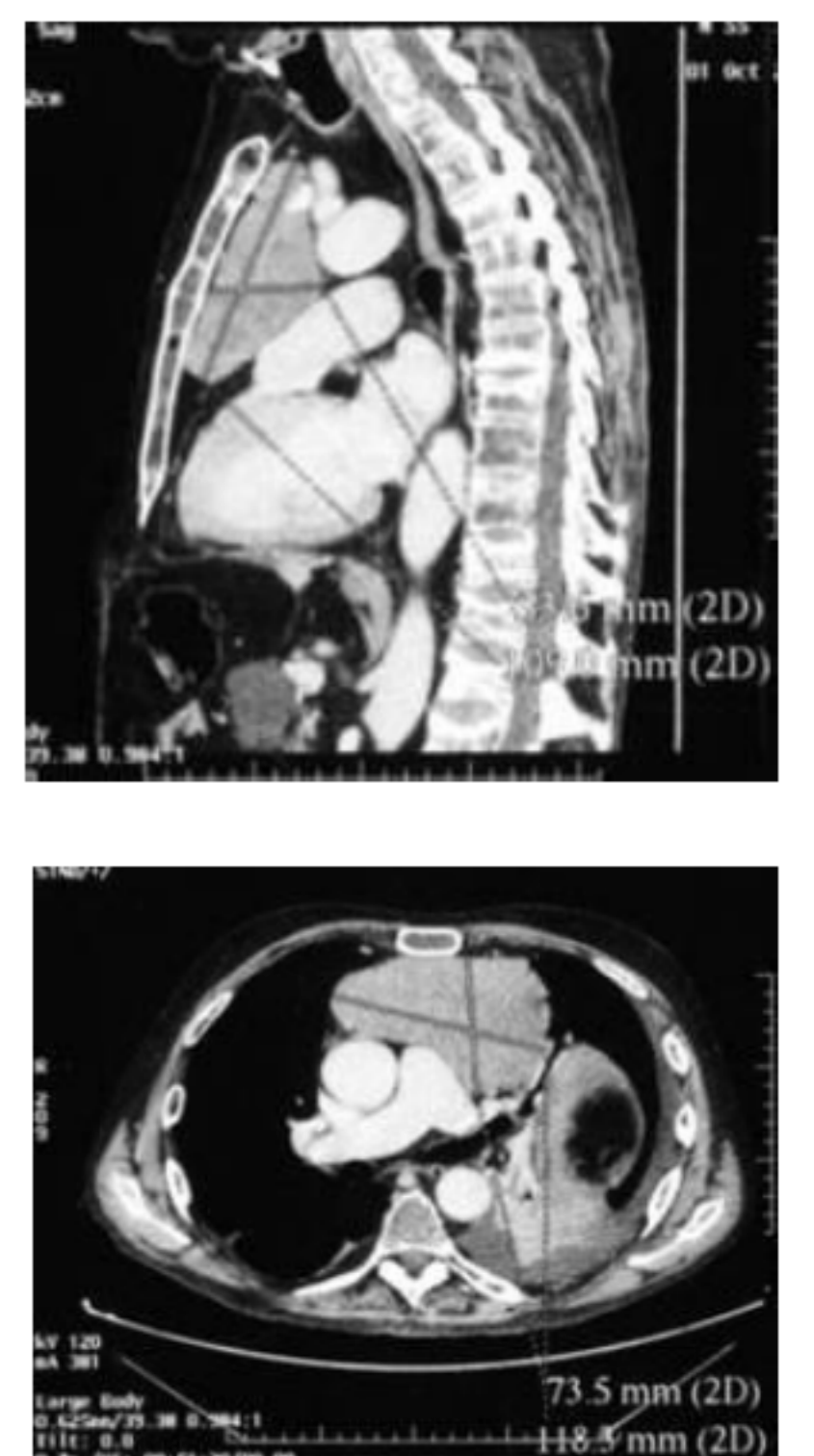
Objective: The aim of this clinical case report was to highlight the importance of screening MEN 1 patients for thymic carcinoid tumors that could present as ectopic Cushing syndrome.

Case report:

We report a case of a 55-year-old man with CS at presentation due to ectopic ACTH production in MEN1 syndrome. This patient had total gastric resection 30 years ago due to Zollinger-Ellison's syndrome and extirpation of two tumors of pancreas, when diagnosed with gastrinoma. The patient had a history of smoking for many years.

Three years prior to the manifestation of CS, the patient was diagnosed with primary hyperparathyroidism (PHPT) and thus treated with parathyroidectomy, near-total cervical thymectomy and total thyroidectomy. Histological analysis revealed hyperplasia of parathyroid glands, papillary thyroid carcinoma and regular thymic morphology. Based on gastrinoma and PHPT, the patient was diagnosed with MEN1 syndrome and the germline mutation of MEN1 gene was detected.

This time the patient presented with weakness, weight loss and hypokalemia (1.9 mmol/L). The results of endocrine tests for Cushing syndrome can be seen in Table 1. MDCT of the thorax revealed the large mediastinal mass (Picture 1. and 2.). Subsequently, the percutaneous biopsy of the tumor was done and the histopathological analysis revealed neuroendocrine carcinoma. The tumor was operated and the diagnosis of atypical thymic carcinoid with high proliferative activity index Ki67 (13.39%) was confirmed. Eight months after the operation control MDCT revealed recurrent mediastinal tumor which was reoperated. Three months after the reoperation the patient developed mediastinal lymphadenopathy following no clinical and laboratory signs of Cushing syndrome.



Picture 1. and 2. MDCT scanning of the thorax revealed the large upper frontal mediastinal mass

Table 1. Cortisol and ACTH levels and cortisol level in low dose (LDST) and high dose dexamethasone suppression test (HDST) at presentation with Cushing syndrome

Cortisol 08h (nmol/L)	Cortisol 20h (nmol/L)	Cortisol 24h (nmol/L)	ACTH (ng/L)	Cortisol in LDST (nmol/L)	Cortisol in HDST (nmol/L)
582,4	1413,0	679,4	647,2	448,6	308,2

Conclusions:

The presented case of MEN 1 is peculiar because the majority of Th-NETs in MEN1 are nonfunctional and ectopic secretion of ACTH seldom occurs. Although Th-NET did not show positive immunohistochemical staining for ACTH, level of ACTH in the blood significantly decreased after the operation. Therefore, it is not impossible that the carcinoid tumor may secrete ACTH precursors and CRH instead of ACTH. The present case highlights the importance of screening MEN1 patients for thymic carcinoid and reinforce the notion that subtotal transcervical thymectomy was not effective prophylactic tool in this case.

Topic: Neuroendocrine cancer

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