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Case Reports

Medullary thyroid carcinoma metastatic to the pituitary gland: an unusual site of metastasis

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Abstract We present a case of metastatic medullary thyroid carcinoma involving the pituitary gland of a 23-year-old woman with multiple endocrine neoplasia type 2b who presented with diabetes insipidus and visual loss. The diagnostic features, including cytomorphology and immunohistochemistry, used to differentiate pituitary adenoma from metastatic medullary carcinoma are discussed. Pituitary metastases and tumor-to-tumor metastases in this region are also highlighted.

Keywords: Medullary thyroid carcinoma; Pituitary gland; Metastasis

1. Introduction

Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor arising from neural crest–derived parafollicular C cells within the thyroid. It represents only approximately 4% of all thyroid tumors [1]. Approximately 25% of MTCs are associated with a germ-line mutation in the RET proto-oncogene, leading to one of several autosomal dominant hereditary syndromes: multiple endocrine neoplasia (MEN) type 2a, MEN type 2b (MEN2b), or familial MTC [2-4].

Whether familial or sporadic, advanced disease with regional metastasis is present in more than half of patients at the time of diagnosis, with a 5-year survival rate ranging from 78% to 91% and continued mortality at 10 and 15 years [1,5,6]. Survival rates for MTCs vary between hereditary syndromes, with the best prognosis observed in patients with familial MTC and the most aggressive disease associated with MEN2b [7]. More specifically, the biologic aggressiveness of MTCs is associated with specific site mutations within the RET proto-oncogene [2,3].

We describe a case of MTC metastatic to the pituitary gland and the attendant diagnostic challenges. To our knowledge, this is the first report on this clinical scenario.

2. Case report

2.1. Clinical presentation

A 23-year-old white woman presented with polydipsia, polyurina, headaches, and lethargy. Her medical history was notable for MTC that was diagnosed when she was 8 years old, with lymph node metastases present at that time (Fig. 1A). A germ-line point mutation in RET consistent with MEN2b was discovered. The patient was an index case without family members with the mutation, a finding that is present in 50% of MEN2b cases [8]. Diffuse ganglioneuromatosis of the colon and of the appendix were also present, corroborating the MEN2b diagnosis (Fig. 1B). After thyroidectomy and neck dissection, no clinical evidence of metastatic disease was detected over the next 15 years despite persistently elevated calcitonin levels.

Based on the patient's clinical symptoms, a diagnosis of diabetes insipidus was made and visual impairment—specifically, bitemporal hemianopsia—was documented. Additional clinical findings included multiple subcutaneous nodules.

2.2. Imaging studies

On magnetic resonance imaging, a bilobed enhancing mass filled the sella turcica and exhibited suprasellar extension through the diaphragma sella (Fig. 2). Additional suspicious contrast-enhancing foci were identified in the cerebellum. A computed tomographic scan revealed multiple lung (Fig. 2) and bone lesions presumed to be metastatic

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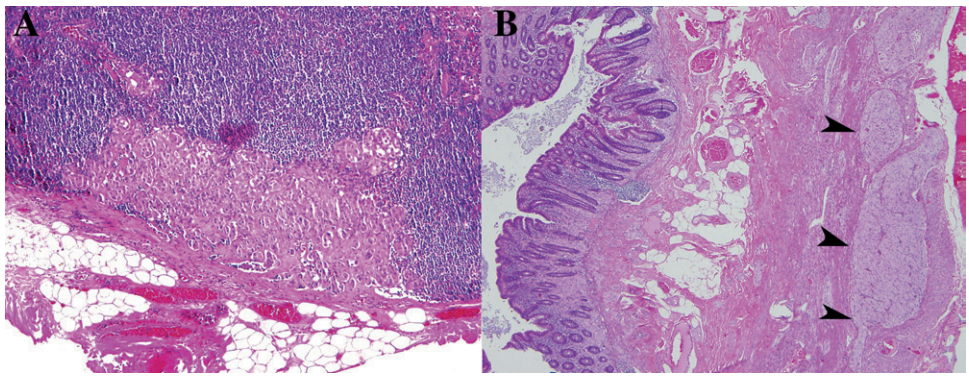

Fig. 1. Multiple endocrine neoplasia type 2b features seen in the case patient. Medullary thyroid carcinoma with lymph node metastases at the initial presentation 15 years earlier (A). Ganglioneuromatosis involving the appendix (arrows) (B).

MTC. Whereas metastases to the pituitary are relatively common in breast and lung adenocarcinomas, MTC metastatic to the pituitary gland has not been previously described; therefore, a primary pituitary mass lesion was also included in the clinical and neuroimaging differential diagnoses for the patient.

2.3. Surgical and pathologic evaluation

A transsphenoidal resection of the patient's pituitary mass was performed in the context of decreasing visual function and uncertain etiology of the pathologic process. Tissue obtained at the time of surgery was initially assessed by intraoperative smear preparations and frozen tissue sections. The cytologic features of the tumor included cell clusters and single large and spindle-shaped cells with convoluted grooved nuclei and coarse chromatin (Fig. 3A and B). Nuclei were eccentrically placed, creating "comet cells." Smaller homogenous round cells with condensed chromatin and no nucleoli were also noted scattered throughout the background (Fig. 3A, C, and D).

On frozen tissue sections, clusters of malignant cells infiltrated the background of normal adenohypophysis, which showed nests of mixed amphophilic and basophilic uniform small cells with round nuclei (Fig. 4A).

Formalin-fixed and paraffin-embedded hematoxylin-eosin sections demonstrated sheets and nests of large elongated cells with irregular nuclei with condensed patchy chromatin. Pseudorosettes and trabecular patterns were also observed with areas of tumor necrosis (Fig. 4B). No amyloid was identified. Diffuse positivity for carcinoembryonic antigen and patchy expression of calcitonin by immunohistochemical analysis confirmed the diagnosis of MTC (Fig. 4C and D). Dense fibrosis with invasion of the dura was also identified in additional specimens.

3. Discussion

To our knowledge, this is the first report of MTC metastatic to the pituitary gland. Several issues regarding the differential diagnosis of pituitary mass lesions in this clinical setting arise.

3.1. Multiple endocrine neoplasia type 2b

Multiple endocrine neoplasia type 2b is defined by the full penetrance of MTCs, which frequently arise in early childhood, with secondary tumors including pheochromocytoma (50% of patients), intestinal ganglioneuromatosis, and mucosal neuroma. Additional clinical findings include

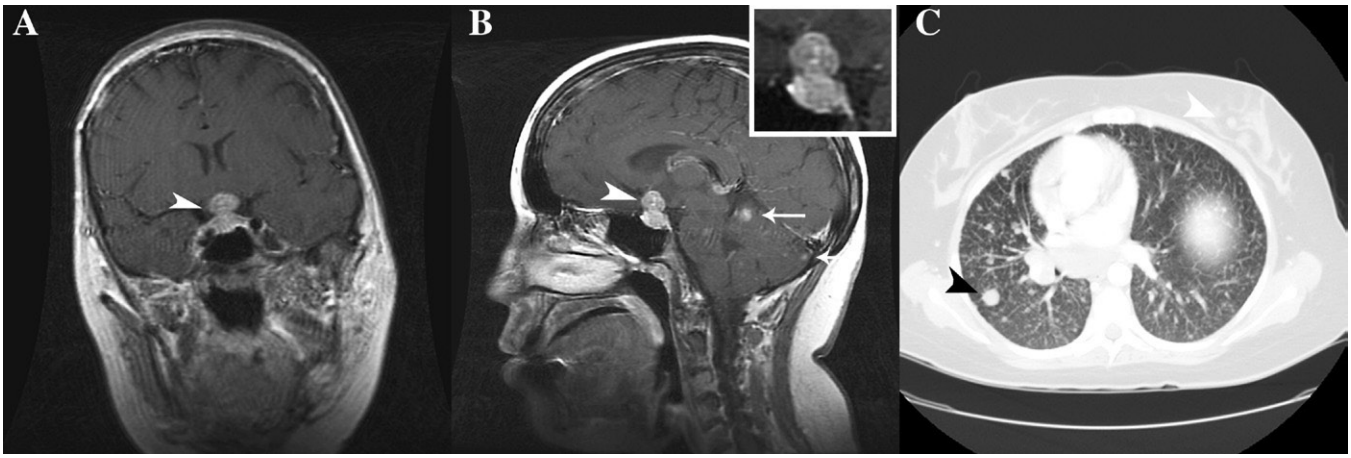

Fig. 2. Imaging studies. Panels (A) and (B) are T1-weighted postcontrast magnetic resonance imaging sequences showing a bilobed enhancing mass filling the sella turcica and suprasellar region (arrowheads and inset) and presumptive cerebellar metastases (arrows). Panel (C) is a computed tomographic scan image of probable lung metastasis (arrow).