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Letter to the Editor

Breast carcinoma metastasizing to an adrenocortical adenoma: a case of tumour-to-tumour metastasis

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Summary
Tumor-to-tumor metastasis (TTM) refers to a malignant tumor metastasizing to a second, distict tumor. It is a rare phenomenon and the most common donor organs are the lung and breast. Here in, we report a case of TTM metastasis of breast carcinoma metastasizing to an adrenocortical adenoma (ACA) in a 40-year-old woman. To the best of our knowledge, this is the first case in which TTM of breast carcinoma metastasizes to an ACA.

Keywords: tumor-to-tumor, tumor metastasis, adrenal cortex neoplasms, adrenocortical adenoma

Introduction

Tumor-to-tumor metastasis (TTM) is a rare phenomenon in which a malignant tumor (donor) metastasizes to a second tumor (recipient). TTM must be distinguished from collision tumors, in which two different neoplasms coexist within the same organ[1].
We report a case of breast carcinoma metastasizing to an adrenocortical adenoma (ACA).

Case presentation

A 40-year-old woman with arterial hypertension and a history of grade II no special type (NST) breast carcinoma with lymph node metastasis diagnosed 4 years earlier, was evaluated. She had undergone neoadjuvant chemotherapy, mastectomy with axillary lymphadenectomy and radiotherapy. The tumor was staged as ypT2N2 (AJCC 8th edition) with partial response to chemotherapy. Genetic testing revealed a pathogenic variant in *CHEK2* gene. During follow-up, magnetic resonance imaging identified a 27x21mm right adrenal nodule with features suggestive of an adrenal adenoma; however, signal heterogeneity and contrast uptake did not allow exclusion of a collision tumour (Fig. 1a, 1b). The left adrenal gland was unremarkable.
Initial work-up showed normal 24-hour urinary free cortisol (UFC), metanephrine and normetanephrine levels, while DHEA-S was decreased. A right adrenal biopsy was performed but was nondiagnostic. Repeated

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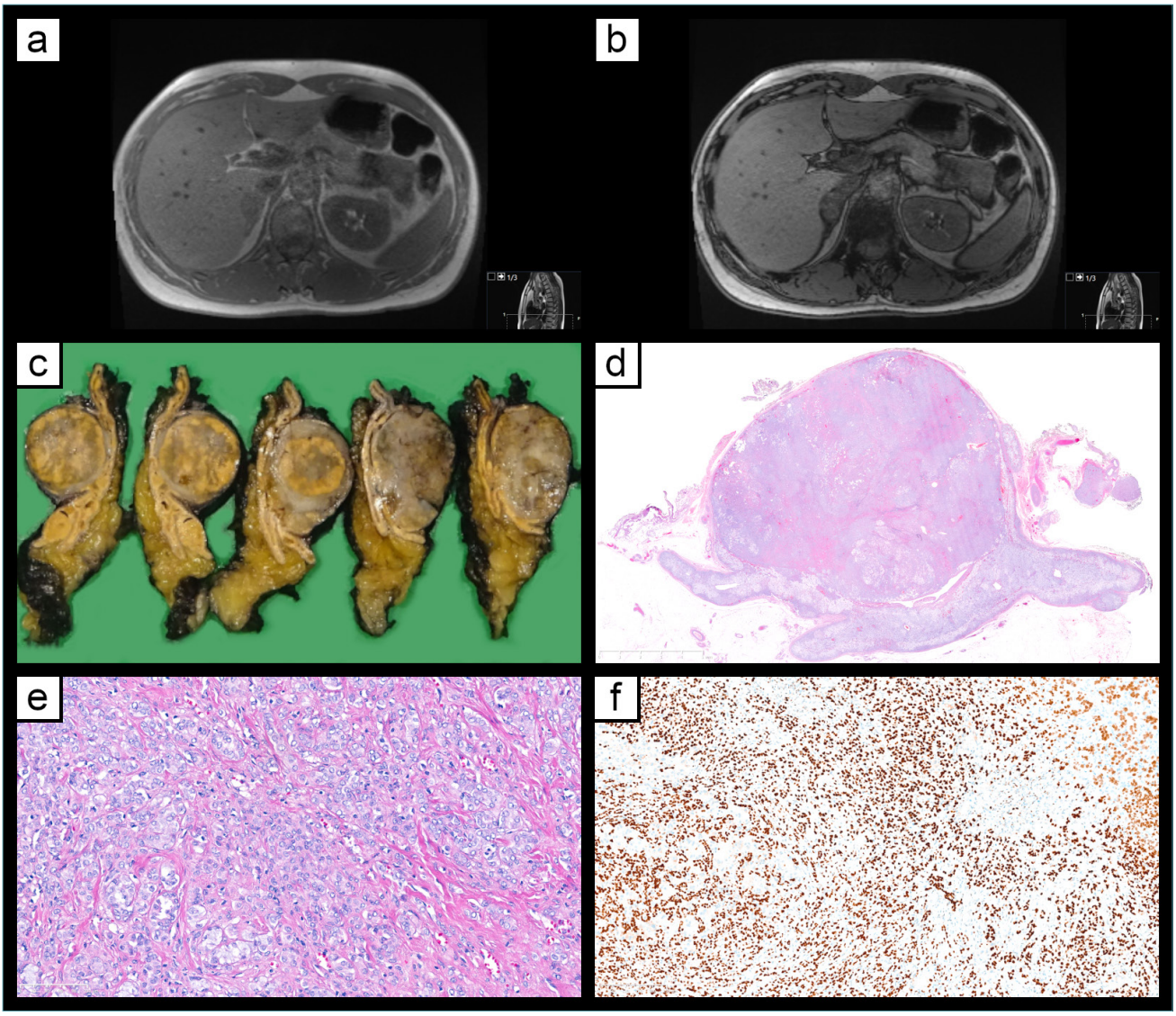

Figure 1. Magnetic resonance imaging images T1 GRE in phase (a) and out of phase (b), showing signal drop off on image b, feature that suggests the diagnosis of a 27x21mm adrenal adenoma, but with some heterogeneity, which raises concern for some malignant potential. (c) Macroscopic features of the specimen, on section, showing a nodular, compact, heterogeneous and yellow to white lesion. (d) Lower magnification of the right adrenal gland with an heterogeneous and nodular lesion. (e) On higher magnification, a second neoplasia was evident, composed of small nests of mild pleomorphic cells in a fibrous stroma. (f) Immunohistochemistry was performed for GATA3.

MRI and [18F]FDG-PET scans remained unchanged, and the lesion was interpreted as an adrenal adenoma. Clinically, there were no signs of hypercortisolism. Hormonal evaluation revealed persistently elevated serum cortisol after overnight 1 mg dexamethasone suppression tests, with normal 24-hour UFC and salivary cortisol levels. ACTH was suppressed. A 48-hour low-dose dexamethasone suppression test (2 mg/day) confirmed persistently elevated cortisol levels, supporting the diagnosis of mild autonomous cortisol secretion. She underwent right adrenalectomy without complications.

The specimen weighed 15 gm and measured 5x4.3x2 cm. An heterogeneous yellowish to whitish compact nodular lesion measuring 2.6x1.8x1.6 cm was identified on cut surface (Fig. 1c). Microscopy showed an ACA containing a second malignant epithelial neoplasm (Fig. 1d) composed of small nests with trabec-

ular and tubular architecture in a fibrous stroma. The cells were polygonal with eosinophilic cytoplasm and mild nuclear pleomorphism (Fig. 1e). Immunohistochemistry for CK19, GATA3 (Fig. 1f) and mammaglobin was diffusely positive in the metastatic cells. Estrogen and progesterone receptors were positive and HER2 was negative, consistent with the profile of the primary NST carcinoma.

The patient is alive with no evidence of disease recurrence to date.

Discussion

Herein we describe a case of breast NST carcinoma metastasizing to an ACA in a 40-year-old woman. According to Kunc et al., 685 cases of TTM have been reported to date. The breast and lung are the most frequent donor organs, while the meninges and kidney are the most common recipient organs. Among these, breast and lung metastases to meningiomas have the highest incidence of TTM (7.6% and 6.2% respectively). In their review, 57.5% of TTM cases occurred in females and 35.3% in males, while 7.15% lacked sex information[1].

In the literature, only three cases of TTM involving ACAs have been described. McMahon reported a case of bladder urothelial carcinoma metastasizing to an ACA in an 81-year-old woman[2]. Martin et al. described a 54-year-old woman with lung adenocarcinoma metastasizing to an ACA with Cushing's syndrome[3]. A third report described TTM of a lung squamous cell carcinoma metastasizing to an ACA in an 82-year-old woman[4]. Additionally, there is one report of breast ductal carcinoma metastasizing to a pheochromocytoma in a 35-year-old woman[5]. This is in line with the majority of donor tumors deriving from the breast and lung[1].

To the best of our knowledge, this is the first case describing TTM of breast carcinoma to ACA.

Currently, no specific guidelines exist for the management of TTM. Staging, evaluating the efficacy of therapies for both tumors as well as establishing objectives for treatment (curative versus palliative) are important steps in the managment of TTM[1].

Conclusions

In conclusion, TTM is a rare phenomenon with limited data regarding prognosis and management. This case highlights the need for clinical awareness and further research on this phenomenon.

Conflicts of interest statement

The authors have no conflicts of interest to disclose.

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Author contributions

Conception and design of the study: MLS and ER; acquisition and analysis of data: MLS and JM; drafting the manuscript: MLS, JM, VP, BV, JSN and ER; figures: MLS, VP and BV.

Ethical consideration

No ethical considerations.

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