

Breast cancer metastasis to the pituitary gland

Metástase de câncer de mama para a hipófise

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SUMMARY

Metastatic tumors to the pituitary gland are an unusual complication typically seen in elderly patients with diffuse malignant disease. Breast and lung are the commonest sites of the primary tumor. Prognosis of patients with breast cancer metastasis is poor and depends on the primary neoplastic extension. We report a 54 year-old woman with breast cancer metastasis to the pituitary stalk first diagnosed because of visual disturbance with no other symptoms. Pituitary gland stalk metastasis is a very uncommon find and this case report includes a literature review. *Arq Bras Endocrinol Metab.* 2014;58(8):869-72

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SUMÁRIO

Os tumores hipofisários malignos são raros e geralmente se constituem de metástases de neoplasias disseminadas. Câncer de mama e pulmão são os sítios primários mais frequentes e o prognóstico depende do grau de comprometimento da doença. Este é o relato do caso de uma mulher de 54 anos que apresentou uma lesão tumoral restrita à haste hipofisária, que se revelou como metástase do câncer de mama previamente conhecido. O acometimento da haste hipofisária é muito raro, motivo pelo qual descrevemos o caso com a revisão da literatura específica. *Arq Bras Endocrinol Metab.* 2014;58(8):869-72

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INTRODUCTION

Pituitary gland adenomas correspond to 5-20% of central nervous system tumors with an incidence of 94 cases per 100.000 in the adult population (1). Data from autopsies suggests a prevalence of approximately 12.6-20%, suggesting they are underdiagnosed (2,3). The majority of pituitary tumors are benign and primary carcinoma are equivalent to 0.1-0.2% of cases (4). Of all the pituitary tumor resections, approximately 1% corresponds to metastatic tumors (5,6). The pituitary is not a common site of metastasis. In the autopsy series, pituitary metastases were found in 1-3.6% of patients with malignant tumors (6,7).

In this report, we describe a rare case of a metastatic breast cancer to the pituitary, with an uncommon characteristic of stalk involvement.

CASE REPORT

A 54-year-old female was admitted in the oncology service of our hospital, presenting with blurred vision and diminished visual acuity in the last two weeks.

Her past personal history included invasive ductal breast carcinoma diagnosed 10 years before, treated with a left mastectomy, axillary dissection and adjuvant chemotherapy. In the previous year, lung and multiple bone metastases were diagnosed and she was treated with zoledronic acid, anastrozole and palliative radiotherapy.

The ophthalmic exam displayed a discreet papilledema in the left eye, which motivated a cranial MRI scan request. MRI revealed a mass with its epicenter in the pituitary stalk, with heterogeneous paramagnetic contrast enhancement, predominantly peripheral, delimiting the central areas of cystic degeneration measuring 1.6 x 1.0 x 1.1 cm, intimately related to the optic chiasm (Figure 1).

Laboratory investigation was compatible with hyperprolactinemia, hypocortisolism and incompatible with postmenopausal gonadotropins status of the patient (Table 1). The tumor in the pituitary stalk was resected due to loss of visual acuity by compression of the optic chiasm. After the surgery patient developed polyuria, polydipsia and hypernatremia

(serum sodium of 148 mg/dL). Synthetic vasopressin analogue (DDAVP – nasal solution 0.1 mg/mL) was given at a dose of 10 mcg 2x/day for only one day, with normalization of clinical and laboratory status.

Anatomopathological exam was consistent with infiltrative carcinoma and immunohistochemistry revealed the primary site in the breast. Markers as AE1/AE3, CK7, estrogen receptor, GCDFP-15, C-erbB-2 (score 3+/3+) and Ki67 in 5-10% of cells (Figure 2) were positive.

The patient improved clinically and restore ophthalmological disturbance without acuity examination after admission. Hospital discharge was accompanied by radiotherapy scheduling because the incomplete tumor resection due to technical difficulty and prednisone prescription. Outpatient follow-up has been maintained in the last 5 months and the patient is clinically

well, with levothyroxine replacement that was already prescribed due to pre-existing diagnosis of primary hypothyroidism.

Table 1. Pituitary function evaluation before surgery

	Patient	Normal value
ACTH (pg/mL)	8.7	5-46
Cortisol (µg/dL)	2.8	3.5-19.5
GH (ng/mL)	0.5	< 3.6
IGF-1 (ng/mL)	118	67-233
FSH (IU/L)	5.8	25.8-134.8
LH (IU/L)	1.4	13.5-96
TSH (mIU/L)	0.28	0.3-4.5
Free T4 (ng/dL)	1.1	0.9-1.7
Prolactin(ng/mL)*	83.3	3.4-24.1

* Absence of macroprolactin.

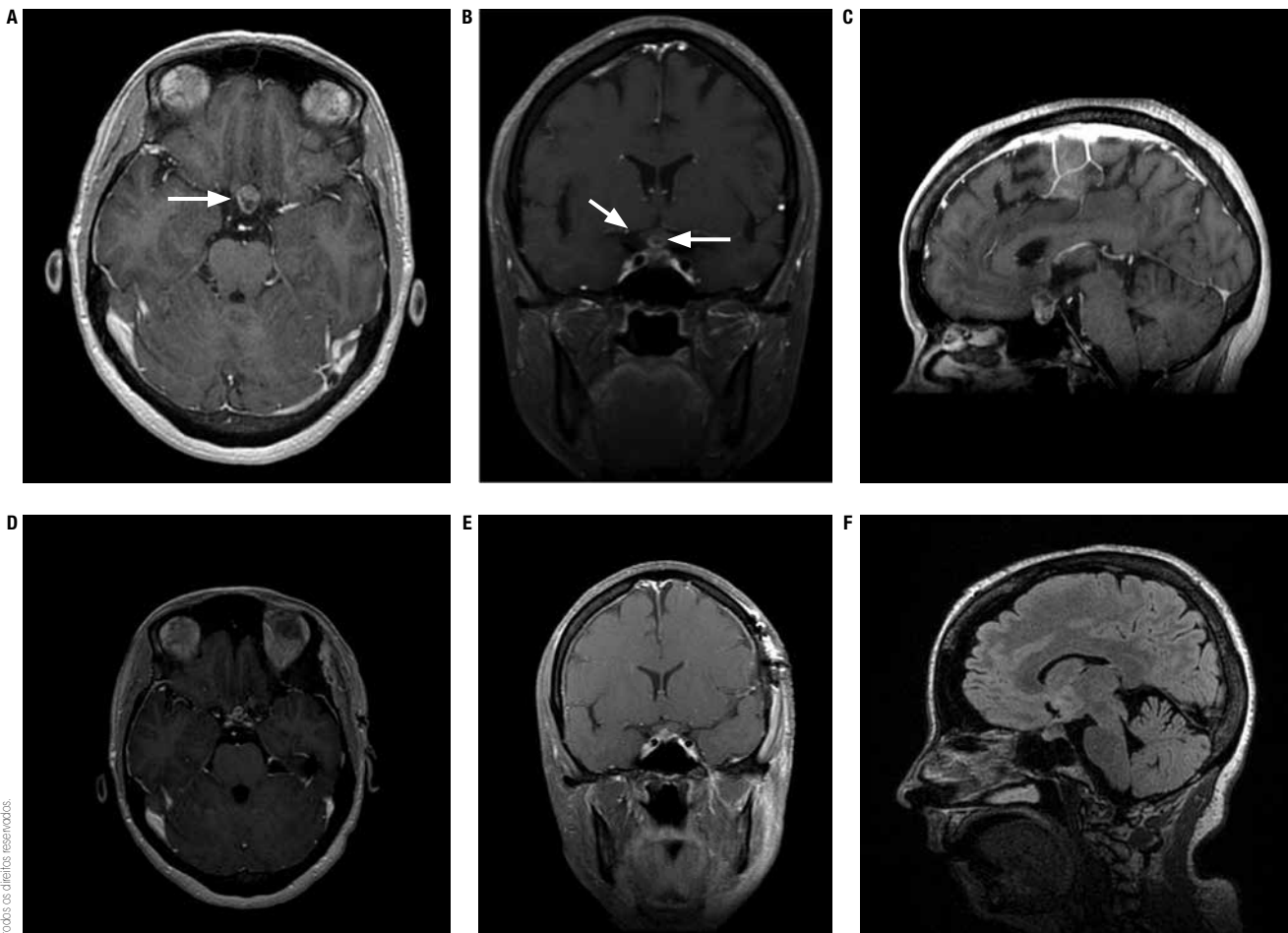


Figure 1. (A-C) Cranial MRI in the preoperative axial, coronal and sagittal, respectively cuts. Expansive lesion epicenter in the pituitary stalk, showing heterogeneous and predominantly peripheral uptake of the paramagnetic contrast medium, delimiting the central areas of cystic degeneration measuring 1.6 x 1.0 x 1.1 cm, intimately related to the optic chiasm. (D-F) Cranial MRI after 1 week of transphenoidal surgery in the axial, coronal and sagittal, respectively cuts.

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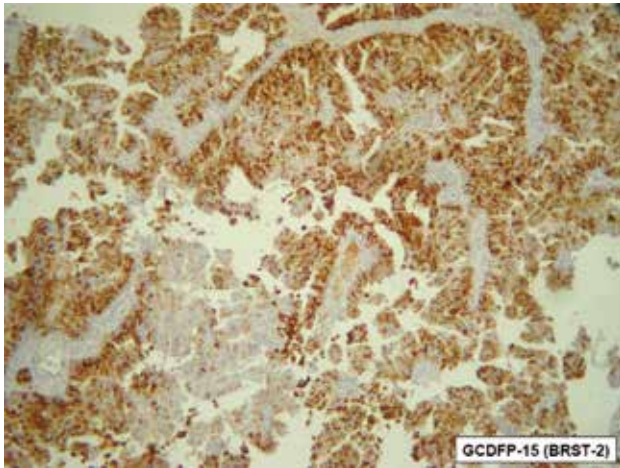


Figure 2. Positive immunohistochemistry to GCDFFP-15, a breast carcinoma marker.

DISCUSSION

Pituitary metastases are most prevalent in the sixth and seventh decades of life (8). Breast tumors (20-30%) and lung tumors (30-50%) (9) are the most common primary sites, but others are also described, such as the gastrointestinal tract, prostate, kidney, thyroid, pancreas, lymphomas, leukemias and plasmacytomas.

Generally, pituitary metastases are a part of widespread metastatic disease, associated with 5 or more sites of metastases, especially bone (6). Occasionally, breast cancer metastasizes to the pituitary, with reported rates ranging between 6 and 8% of cases (5), majority asymptomatic. Hypophysectomy of patients with breast cancer found 5.5% to 25% of metastases not previously diagnosed (7).

The present patient had multiple metastases from the breast carcinoma besides the pituitary stalk one. Immunohistochemical profile of pituitary stalk mass disclosed the presence of the estrogen receptor, which is consistent with the primary site in the breast. The presence of estrogen receptors becomes able to hormonal therapy (10). The positivity of c-erbB-2 and Ki67 are correlated with a worse prognosis. The c-erbB-2 proto-oncogene occurs in about 20% of all breast cancers and Ki67 is a nuclear non-histone protein that refers to a poorly differentiated tumor (10).

About metastasis location, the posterior lobe of the pituitary gland is most common site (69-79%) (11) due to its larger area of contact with the adjacent dura-mater and the lack of blood supply to the anterior lobe (5,7,9,12,13).

Mc Cormick and cols., reviewing the location of pituitary metastases in 201 cases, found the involvement of the posterior lobe alone or in combination with anterior lobe in 84.6%, and the involvement of the anterior lobe alone in 15.4% (13). However, especially in breast cancer, metastases occur preferentially to the anterior pituitary gland (6,11). Hematogenous dissemination is the most important mechanism of development of these metastases, but also occur by contiguity of adjacent bone metastasis or meningeal spread through the suprasellar cistern (9).

Pituitary metastases are symptomatic in only 2.5 to 18.2% of cases (5-7) because most occur in patients too debilitated by cancer with poor survival rates to become clinically evident. Still then, the systemic complications of malignancy, including nonspecific symptoms of weakness, vomiting and weight loss as well as the involvement of the CNS, may mask the dysfunction of the anterior pituitary. So the majority of cases have been discovered accidentally during autopsies (6). However, in some patients, symptoms related to pituitary metastasis may be the first manifestation of an occult malignancy (5).

The most noticeable symptom is diabetes insipidus (DI), reinforcing the predominance of metastases to the posterior lobe. DI occurred in 45.2% of cases among 190 patients with pituitary metastases (6) reaching 61% to 70% in other series (13,14). According to Houck and cols. 20% of patients diagnosed with DI may present pituitary metastases (15). However, the clinical presentation is variable (16), and may be associated with ophthalmoplegia, headache, visual field abnormalities and anterior pituitary dysfunction (5), and could also present with seizures, paralysis of III and IV cranial pairs and hyperprolactinemia.

Among the visual alterations, bilateral hemianopia is the most common (6). Given the invasiveness of tumors, visual loss may result from suprasellar extension and can result in painful ophthalmoplegia due to infiltration of the cavernous sinus (5).

Treatment is essentially palliative and depends on the extent of disease and symptoms. Radiotherapy and/or chemotherapy are recommended as initial treatment, especially in patients with disseminated metastases in combination with replacement of pituitary hormones for relief of symptoms (7,13,15). Surgical exploration and decompression alone or in combination with radiotherapy is essential if the pathological diagnosis would

guide the therapy plan or if suprasellar extension is causing pain or progressive visual deterioration.

There is no consensus on improved rates of survival with surgical resection, but there is improvement of symptoms by local decompression of the tumor although it does require the combination of different therapeutic modalities (17).

Prognosis is poor, not because of the location itself, but due to the aggressiveness of the primary tumor (18). Median survival rate was 6-7 months in clinical series (7,14,15). Among 72 patients in literature review, Ntyonga Pono and cols. (19) found only 10% of survivors one year forward diagnosis, with a maximum survival of 3 years. When the pituitary lesion is a single metastasis, survival can improve (7,14). Patients with more than 65 years of age at presentation, small cell lung cancer as the primary site and a short interval (less than 1 year) between the initial diagnosis of cancer and invasion of pituitary are related to worse prognosis (14). Pituitary stalk invasion presentation has a worse prognosis as 2-4 months of survival, approximately (5,20).

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