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Case Report

A rare case of pituitary metastasis from breast cancer detected on fluorodeoxyglucose positron emission tomography/computed tomography that presented as insipid diabetes

ABSTRACT

Pituitary metastases are rare, are generally asymptomatic, and often remain undiagnosed. Breast cancer is the most common primary cancer metastasizing to hypophysis in women. However, it is difficult to clinically and radiologically differentiate pituitary metastases from pituitary adenomas. We report a case of pituitary metastases diagnosed on magnetic resonance imaging and positron emission tomography/computed tomography, which was the prime manifestation of a breast cancer in a 46-year-old female. This cancer was revealed by insipid diabetes.

Keywords: Breast cancer, insipid diabetes, pituitary metastases, positron emission tomography/computed tomography

INTRODUCTION

Pituitary metastases are rare and most often have an autopsy description. Occasionally, they may be the first manifestation of an occult primitive tumor, or the only secondary location of known neoplasia. Breast cancer is the most common etiology of pituitary metastases in women. Clinically and radiologically, the differential diagnosis between pituitary adenoma and metastases is not easy, essentially in the absence of known malignant neoplasia.

CASE REPORT

A 46-year-old female patient with cervical vertebral autograft in 1996 for cervical vertebral trauma was admitted with a 3-month history of a polyuropolydipsic syndrome (diuresis at 5l/24 h) and severe asthenia, without headache, visual or neurological disorders. Blood and urinary ionograms, serum creatinemia, and blood glucose were normal. Plasma osmolarity was at 292 mOsm/kg, while urinary osmolarity was at 138 mOsm/kg. The exploration of the thyrotropic, corticotropic, and gonadotropic axes revealed no significant anomaly, while the prolactin level was slightly elevated to 650 mUi/l (VN: 99–495). She was treated with 1-desamino-8-d-arginine vasopressin (DDAVP) at an oral dose of 0.1 mg twice daily. Cerebral magnetic resonance imaging (MRI) showed the presence of an intensely enhancing bilateral parietal tissue lesion (measuring 19.3 mm × 17.5 mm × 18.2 mm to the right and 7.7 mm × 8.2 mm × 9.3 mm to the left), of secondary appearance. It also showed a nodular enlargement of about

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8 mm taking the contrast, at the supradiaphragmatic portion of the pituitary stalk that may correspond to a pituitary adenoma or a secondary location [Figure 1]. The clinical examination revealed a 1-cm retro-mammary right breast nodule without signs of clinical malignancy. Mammography has objectified a suspect supra-areolar internal stellar opacity of the right breast. The ultrasound complement was in favor of a hypoechoic, infiltrating, multi-areolar lining process, measuring 16 mm × 14 mm at the upper inner quadrant of the right breast. The nodule biopsy showed a histological aspect of an infiltrating ductal carcinoma grade II of the modified Scarff-Bloom-Richardson grading system. Immunohistochemical profile showed a strong expression of estrogen receptors, a weak progesterone receptor expression, and overexpression of oncoprotein HER2 (score 3+). The abdominal ultrasound and the Computed Tomography (CT) of Thorax, Abdomen and Pelvis-(TAP) performed as part of the extension assessment revealed no abnormalities. An ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) was performed in our patient objectifying a bilateral parietal cerebral hypermetabolism (with a SUV_{max} of 22.9 and 21.6 at the right and left cerebral lesions, respectively), associated with an intense pathological hypermetabolism of the pituitary stem, with an SUV_{max} of 16.6, suggestive of secondary localization [Figures 2 and 3]. The FDG-PET also showed an intensely hypermetabolic mass of the right breast, a right axillary pathological ganglionic hypermetabolism, and a hypermetabolism of the inner end of the left clavicle [Figure 4]. The decision of the medical staff was to start with brain radiotherapy to control secondary lesions followed by systemic chemotherapy. The patient received stereotactic radiosurgery (SCR) from γ-knife for these brain lesions, followed by six cycles of docetaxel, trastuzumab, and pertuzumab chemotherapy every 3 weeks, followed by six cycles of trastuzumab and pertuzumab. Two months after the SCR, an MRI brain control showed the disappearance of the pituitary and the left insular lesions, with a clear regression of the right parietal lesion that presents only a discrete, incomplete peripheral enhancement. A bone scintigraphy revealed no abnormality, especially at the level of the left clavicle. A second brain MRI was performed 4 months after treatment of the brain lesions, objectifying the persistence of the right subcortical lesion in T1 hyposignal, hypersignal T2 without restriction of the diffusion presenting a very weak linear enhancement compared to the previous examination, evoking more an inactive lesion. Forty-two months after the diagnosis of insipid diabetes, the patient is still alive, but she required a moderate amount of DDAVP to control this disorder.

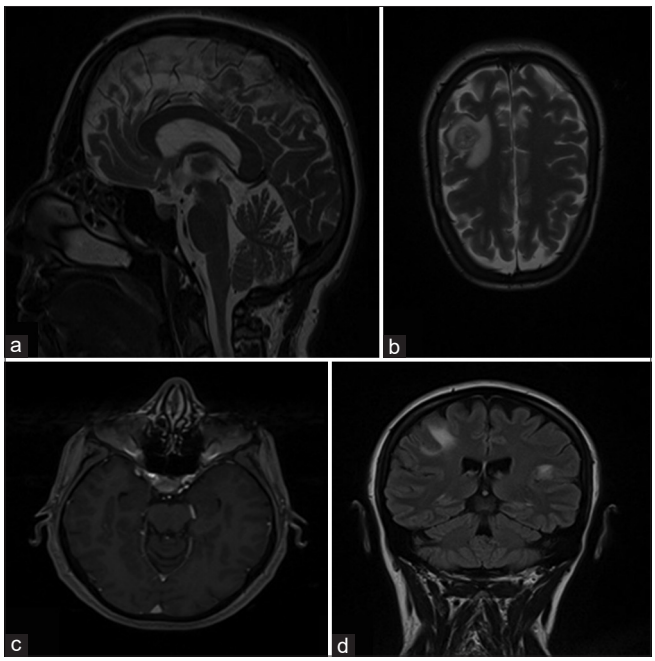

Figure 1: Cerebral magnetic resonance imaging: (a) sagittal view of T2-weighted image showing a pituitary mass, (c) axial view of T1 fat-saturated postgadolinium image showing enhancement of the pituitary mass, (b) axial view of T2-weighted image showing a right parietal subcortical mass surrounded by perilesional edema, (d) coronal flair image showing a bilateral parietal tissue lesion

DISCUSSION

The pituitary gland is rarely metastasized because <1% of surgically resected pituitary masses are diagnosed as clinical metastases.[1] Nevertheless, metastases in the hypothalamic–pituitary region are usually discovered incidentally in postmortem, most often in patients with advanced cancer, especially breast and lung cancers. In a series of 500 autopsies of cancer patients, pituitary metastases were found in 18 patients (3.6%). Six patients had breast cancer, of which only one had clinical symptoms.[2] The most common cancers with pituitary metastases are in order of frequency: breast cancer (39.7%), bronchopulmonary cancer (23.7%), and

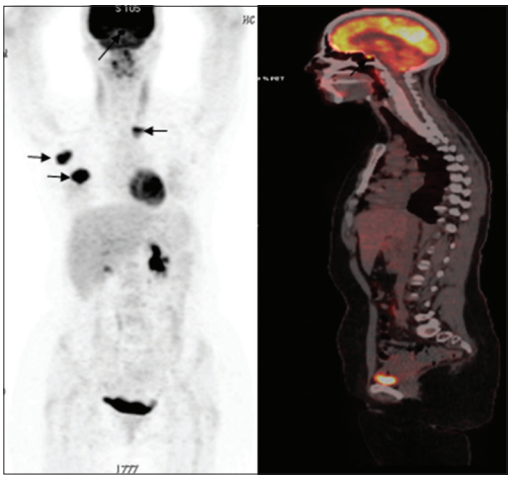

Figure 2: Positron emission tomography/computed tomography with ^{18}F-fluorodeoxyglucose, maximum intensity projection, and sagittal fusion image showing multiple hypermetabolic foci (indicated by arrows)

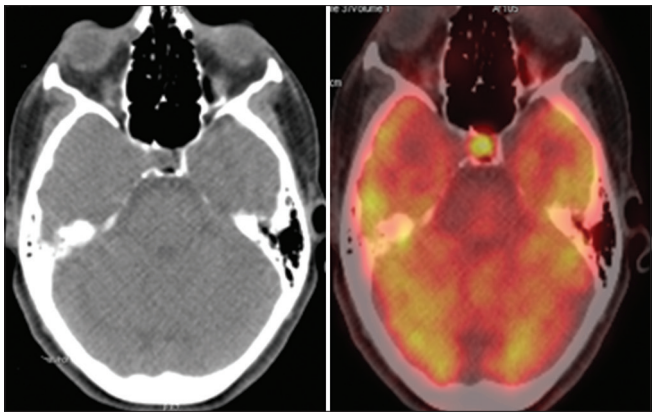

Figure 3: Positron emission tomography/computed tomography axial computed tomography image and axial fusion image showing hypermetabolic foci in the pituitary gland

digestive tract cancers (especially colon and stomach, 6.3%). In more than 3% of cases, the primary cancer is, however, not found.[3] These metastases are preferentially located in the posthypophysis. Pituitary metastases usually involve the posterior part alone or in combination with the anterior part in 85% of cases, whereas the anterior pituitary alone is involved in only 15% of cases.[4] This phenomenon might be explained by the fact that this part obtains its blood supply directly from the systemic circulation in contrast to the anterior part. In addition to this hematogenous pathway, metastatic dissemination of cancer to the pituitary gland can also be neuromeningeal or contiguous from metastatic bone lesions, as there is a close relationship between the pituitary lobe and the dura mater.[5-9] The presence of cerebral metastases in our observation would be in favor of the neuromeningeal diffusion hypothesis.

The most common clinical presentation of pituitary metastatic disease is insipid diabetes.[1,3] This would be explained by the predilection of metastases to posterior pituitary.

Diagnosis of pituitary metastasis is also difficult because the combination of malignant neoplasia and pituitary adenoma is possible.[3] In fact, the secondary aspect of pituitary involvement is difficult to establish without the help of a pituitary biopsy. Indeed, in a series of 500 autopsies of patients with cancer, pituitary metastases were found in 3.6% of cases, whereas pituitary adenomas were found in 1.8% of patients under autopsy.[7] Some elements may suggest the malignant origin. In fact, even if some pituitary metastases have a symptomatology similar to that of pituitary adenomas, insipid diabetes is reported in $<1\%$ of pituitary adenomas.[3,10] The sudden onset of insipid diabetes and the rapid onset of symptoms due to pituitary involvement suggest a malignant etiology.[3,10,11] Insipid diabetes is the most important criterion for differentiating a pituitary metastasis from a pituitary adenoma.[1,12]

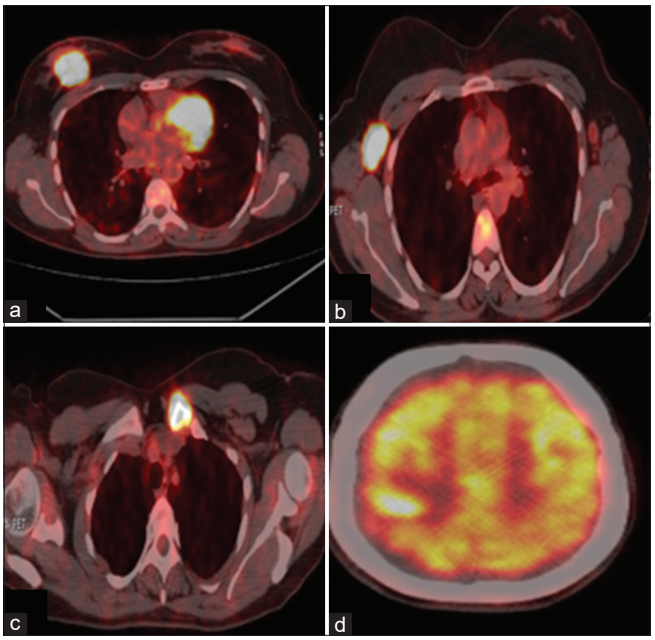

Figure 4: Positron emission tomography/computed tomography axial images showing: (a) hypermetabolic mass of the right breast, (b) hypermetabolic foci on a right axillary node, (c) hypermetabolic foci on the left clavicle, (d) right parietal cerebral hypermetabolic foci

MRI can help differentiate between pituitary metastases and adenoma. However, it is not always easy to make the difference. Pituitary metastases are usually isointense on T1-weighted images with a usually high intensity on T2-weighted images that enhance homogeneously after gadolinium.[1] This is in contrast to adenomas, which tend to be isointense on T1 and T2. Another evocative sign is the disappearance of the spontaneous hypersignal of the posthypophysis at T1 not injected.[1,12-15] Among the differential diagnosis of pituitary metastasis in the case of nodular thickening and enhancement of infindibulum are certain inflammatory pathologies: histiocytosis, sarcoidosis, Wegener's disease and tuberculosis, or tumoral, notably a germinome.

PET/CT scan is commonly used to stage different types of malignancies. ^{18}F FDG-PET may represent an ancillary tool for the detection and differentiation of pituitary lesions in certain circumstances. However, not all pituitary tumors are FDG avid. Moreover, it is difficult to differentiate pituitary metastases from pituitary tumors based on an FDG PET/CT-derived SUV_{max}. Reliable diagnosis might be generated by taking the patient's clinical history, the local infiltration in the sella area, and other imaging data into consideration.[16]

The treatment of pituitary metastases is mainly symptomatic and rarely curative. The substitution with desmopressin (DDAVP) has allowed the correction of polyuropolydipsic syndrome. When insipid diabetes or chiasmatic compression is suggestive of pituitary metastases, cerebral radiotherapy may be the

most appropriate therapeutic choice.[7-9,13,17,18] The resection of the lesions can be discussed if the diagnosis of malignancy is uncertain. In the presence of cancer with multiple metastases, including pituitary, single chemotherapy or chemotherapy associated with cerebral radiotherapy would be a treatment of choice. Our patient received stereotaxic cerebral radiotherapy followed by systemic neoadjuvant chemotherapy for metastatic disease.

Usually, insipid diabetes is irreversible after radiotherapy and chemotherapy, justifying definitive treatment with desmopressin. In a series of 19 patients with pituitary metastases, diabetes disappeared only in one patient after treatment with radiotherapy.[17] The prognosis of the disease depends on the type and degree of malignancy of the underlying tumor.[1,3,19] Indeed, the prognosis associated with the presence of pituitary metastases is bleak: the median survival was around 6 months in a study of 36 patients with symptomatic pituitary metastases.[10] The death would generally be due to advanced metastatic stage, other brain metastases, pulmonary embolism, a mass effect of metastases on the pituitary gland, meningeal carcinomatosis, and a locally advanced stage of the primary tumor.

CONCLUSION

Pituitary metastases are rare but should be suspected in patients with metastatic cancer who present with insipid diabetes, visual changes, or headache. Pituitary metastases of breast cancer is an uncommon problem. MRI of hypophysis must be performed irrespective of the presence of symptoms related to the suppression of chiasma opticum. However, pituitary adenomas might also coexist in metastatic breast cancer patients. The presence of insipid diabetes in particular should raise the concern for a pituitary metastasis. Treatment can include surgery, limited field radiotherapy or stereotactic, and γ-knife radiosurgery.

Ethics declarations

Ethics approval and consent to participate was not waived as this is a single case report.

Consent for publication

Patient's consent was obtained for publication of this case report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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