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Pituitary Gland Metastasis of Breast Cancer: A Case Report

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ABSTRACT

Pituitary gland is an uncommon site of metastasis for malignancies. However, breast cancer is the most common primary metastasizing to hypophysis in women. It may cause hormonal problems in different patterns due to mass affect and invasion to pituitary gland. We present a 53-year-old woman with HER-2 positive breast cancer presenting with intermittent symptoms of diabetes insipidus and rapidly developing pituitary mass treated with transsphenoidal surgery and thereafter the recurrent lesion with cyberknife stereotactic radiotherapy and systemic chemotherapy.

Keywords: Breast cancer, Pituitary gland, Metastasis

ÖZET

Hipofize Metastaz Yapan Meme Kanseri: Olgu Sunumu

Malign hastalıklarda nadiren hipofiz metastazı görülmektedir. Ancak, kadınlarda hipofize en sık metastaz yapan primer malignite meme kanseridir. Metastatik tümörün kitle etkisine veya hipofiz bezine invazyonuna bağlı olarak değişik kombinasyonlarda endokrin problemler görülebilir. Elliüç yaşında HER-2 pozitif meme kanseri olan bir kadın hastada intermitan diabetes insipitus semptomlarına neden olan ve hızlı gelişen metastatik hipofiz kitlesi ortaya çıkmıştır. Kitle transsfenoidal cerrahi ve arkasından rekürrens olduğunda cyber-knife stereotaktik cerrahi ve sistemik kemoterapi ile tedavi edilmiştir.

Anahtar Kelimeler: Meme kanseri, Hipofiz, Metastaz

INTRODUCTION

The pituitary gland is an uncommon site for metastasis of malignant tumors. It is detected less than 1% of patients undergoing pituitary surgery and 5% in autopsy series of patients with known malignancy.[1] Breast and lung cancer are the most common primary neoplasms metastasizing to the hypophysis in women and men respectively.[2-4] Although breast cancer is the most common primary tumor, diagnosis of pituitary insufficiency and metastasis can be difficult in the follow up. Cancer patients may have signs and symptoms similar with pan-hypopituitarism and it can easily be attributed to the chemotherapy recieved or the primary disease especially in metastatic stage. Clinicians must bear pituitary insufficiency in mind due to metastasis to hypophysis in breast cancer patients.

CASE REPORT

A 53-year-old female admitted with a 3 month history of polyuria, polydipsia and fatique. She had a diagnosis of breast cancer in 2003. She had modified radical mastectomy with lobular carcinoma and infiltrative ductal carcinoma (mixed type) histopathology (T2N2M0). Immunohistochemical staining for estrogen and progesterone receptors were both negative. However, overexpression of HER2 was detected by immunohistochemistry. Adjuvant chemotherapy with 6 cycles of epirubicin and cyclophosphamide and locoregional radiotherapy were both administered. Three years later, patient developed liver and bone metastasis. Because of metastatic disease she received 9 cycles of combination regimen of weekly paclitaxel, trastuzumab and carboplatin followed by eight weeks of paclitaxel and trastuzumab combination after stopping carboplatin because of the allergic reaction. During the follow up NCI grade 3-4 neuropathy occurred with paclitaxel, and she was switched to receive a combination regimen of capecitabine with trastuzumab. While she was on this chemotherapy she complained newly occurring polyuria, polydipsia and fatique approximately four years after the diagnosis of breast cancer. She had a mild, intermittent headache but did not have any other cranial symptoms. Later on she developed constipation, cold intolerence, somnolence, confusion and bradycardia. Her laboratory results were consistent with central diabetes insipidus, hypocortisolism and secondary hypothyroidism. Her follicle stimulating and luteinising hormone and estrogen levels were decreased. However patient was post-menopousal after adjuvant chemotherapy she received. Routine laboratory tests showed mild elevation of liver function tests, anemia and mild thrombocytopenia. The patient was diagnosed as pan-hypopituitarism. The patient's cranial and hypophyseal MRI revealed sellar mass consistent with hypophyseal macroadenoma with a diameter of 2.5 cm (Figure 1A and 1B). She was put on desmopressin acetate, prednisolone followed by levothyroxine sodium replacement therapy. Her symptoms resolved. In the fourth year of diagnosis trastuzumab and capecitabine was discontinued because of the decreased ejection fraction of left ventricle on echocardiography and since she couldn't tolerate capecitabine because of NCI grade 3-4 hand-foot syndrome. The patient was switched to a metronomic treatment of oral cyclophospamide and methotrexate regimen.

The patient underwent trans-sphenoidal surgery. Breast cancer metastasis to the pituitary gland was established histologically. Immunohistochemical staining was strongly positive for pan-cytokeratin and GCDFP-15, positive for cerbB-2 and negative for estrogen and progesteron receptors as the primary pathology. Two months later following surgery, postoperative MRI revealed recurrent lesion compressing optic chiasm and extending towards bilateral cavernous sinuses. A cyberknife stereotactic radiotherapy was performed. During ten months of follow up no recurrent sellar mass was observed. In this period the patient received capecitabine and lapatinib combination treatment. Then progression in bone and liver metastasis was noted and while we were planning to switch her chemotherapy to gemcitabine she was again admitted to our hospital because of nausea, fatique and jaundice. Replacement therapy for pan-hypopituitarism was re-started immediately. Laboratory tests showed elevation in liver function tests and hyperbilirubinemia. An abdominal ultrasonography revealed diffuse metastatic lesions in the liver. Approximately in one week liver failure developed and the patient died.

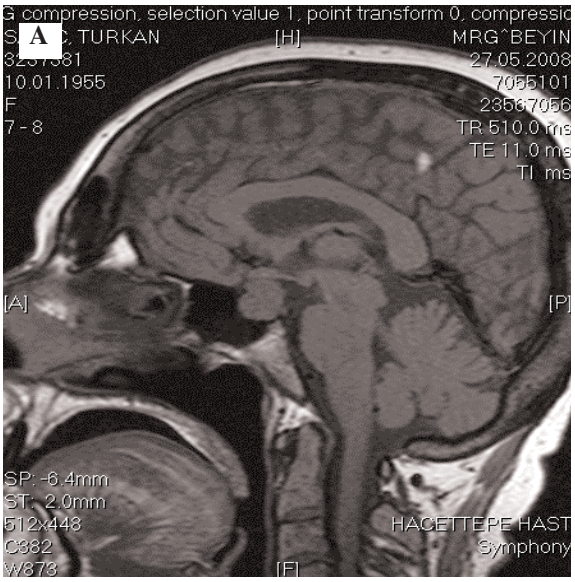

Figure 1A. Sagittal MRI showing pituitary mass

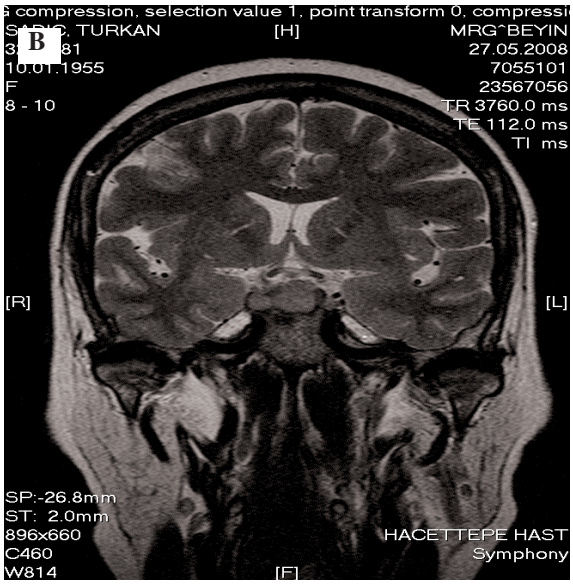

Figure 1B. Coronal section of MRI showing pituitary mass

DISCUSSION

Hypophyseal metastasis of cancers is an uncommon occasion. Also less than 1% of hypohyseal masses surgically resected are diagnosed as metastatic tumours.[1] The metastasis to the pituitary more commonly involves posterior lobe alone or in combination with anterior pituitary in 85% of cases, while anterior pituitary alone is involved only in 15%.[4] Breast and lung cancer are the most common primary neoplasm metastasizing to the pituitary in women and men respectively.[2-4] Breast cancer being the most common cancer metastasizing to the pituitary can be explained with the prolactin rich environment of the pituitary enhancing the proliferation of tumor cells of breast.[2-5]

The most common symptom of pituitary metastasis seems to be diabetes insipidus.[1,6-10] Visual impairment resulting from optic chiasm compression seems to be second most common presentation.[1,12-15] Complete or partial pituitary insufficiency is the third most common presentation of pituitary metastases.[1,5-18] It is usually associated with a mass effect of a large tumour.

Diagnosis of pituitary metastasis might be missed in absence of overt clinical symptoms of hormonal insufficiency and vision problems caused by a large metastatic hypophyseal mass compressing chiasma opticum. Patients may have signs and symptoms of nausea, vomitting, fatique, weight loss could be seen in pan-hypopituitarism and also be easily attributed to the side effects of chemotherapy received or the primary malignancy.[1] Thus panhypopituitarism and pituitary metastasis can be underdiagnosed. However when diabetes insipidus developed polyuria and polydipsia becomes generally a frank symptom makes patient admitting to doctor. Diagnosis of pituitary metastasis is also difficult. Because up to 16 % of patients with overt malignancy may also have pituitary adenoma.[5,19] However, diabetes insipidus is reported less than 1% of pituitary adenomas.[5,8] Sudden onset of diabetes insipidus, the rapidity of symptom development and a rapidly growing sellar tumor suggest pituitary metastasis.[5,8,11] Diabetes insipidus is the most important criterion for differentiation of pituitary metastasis from adenomas.[1,10] Thus the clinician must be suspicious of pituitary metastasis in a patient with known cancer and clinical presentation listed above. However, metastasis is usually suspected during surgery and diagnosed histologically after surgery.[1,19] A residual or recurrent sellar mass might be treated with modern radiotherapy techniques as cyberknife stereotactic radiosurgery as in our case regarding the difficulty of a second surgery.

Prognosis of pituitary metastasis is poor.[1,4,9] Median survival in clinical series is 6 to 7 months.[5-7] But the prognosis and survival primarily depend on characteristics of the tumor.[1,5,19,20] However there is no survival data specific to the pituitary metastasis of breast cancer.

In conclusion; pituitary metastasis of breast cancer is an uncommon problem. MRI of hypophysis must be performed whether symptoms related to suppression of chiasma opticum present or not. However pituitary adenomas might also co-exist in metastatic breast cancer patients. Clinical presentation might occur mostly with diabetes insipidus but also insufficiency of other hormones of pituitary gland. An uninterrupted replacement treatment of pituitary hormones is crucial.

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