Subthalamic Nucleus Tumor Causing Hyperphagia

—Case Report—

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Abstract

A 42-year-old woman with locally advanced breast cancer developed headache just after completing adjuvant chemotherapy. Magnetic resonance imaging revealed a mass located in the left subthalamic nucleus (STN) and involving the posterior part of the thalamus and the hypothalamus. The patient refused a radiologically guided biopsy and gamma knife treatment was not financially possible. Palliative whole brain radiotherapy with hormonal therapy was administered. The patient gained 19 kg body weight during 4 months follow up because of hyperphagia. This solitary tumor, either a breast cancer metastasis or a primary tumor, involving the STN is extremely unusual.

Key words: breast cancer, subthalamic nucleus tumors, metastasis, hyperphagia

Introduction

Breast cancer is one of the most common neoplasms and is among the leading causes of cancer deaths.¹³⁾ Central nervous system (CNS) metastasis of solid neoplasms including breast cancer can present as solitary or multiple lesions in various localities.¹⁷⁾ CNS metastases are estimated to occur in 20% to 40% of cancer patients, and two-thirds of cases become symptomatic during their lifetime.^{4,17)} Recently, the incidence has increased as a result of advances in imaging procedures and improvements in therapy, which leaves more cancer patients at risk as survival increases.^{4,17)} However, metastases involving the thalamic region are very rare compared to other localities in the CNS and may present with specific signs and symptoms.^{2,12)} Here, we present a locally advanced case of breast cancer associated with a solitary tumor located in the left subthalamic nucleus (STN) that involved the posterior part of the thalamus and hypothalamus manifesting as complaints of headache and hyperphagia just after completing adjuvant chemotherapy.

Case Report

A 42-year-old woman had undergone surgery for

locally advanced breast cancer after partial remission with four cycles of neoadjuvant EC chemotherapy (epirubicin 90 mg/m² day 1 and cyclophosphamide 600 mg/m² day 1, every 3 wks). Pathological examination showed that both the skin and 14/16 of the axillary lymph nodes were infiltrated. After the modified radical mastectomy operation, radiotherapy, and four more cycles of EC chemotherapy followed by two cycles of docetaxel (100 mg/m²/3 wks) were administered. Tamoxifen (20 mg/day) was also prescribed since the tumor was positive for estrogen and progesterone receptors. The patient complained of headache 6 months after the surgical intervention, just after the last cycle of the chemotherapy, and was admitted to our department.

Magnetic resonance imaging disclosed an enhanced 18 × 12 mm mass located in the left STN that involved the posterior part of the thalamus and the hypothalamus (Fig. 1). Peritumoral edema also affected the upper part of the midbrain and the dorsomedial nucleus of the left thalamus. Blood chemistry examination found no abnormalities in serum electrolytes, fasting and post-prandial glucose levels, kidney and liver function tests, serum growth hormone, prolactin, adrenocorticotrophic hormone, thyroid hormones (thyroid-stimulating hormone, free T₃ and T₄), estradiol, progesterone, follicle-stimulating hormone, luteinizing hormone, and plasma and urine osmolalities.

The patient refused radiologically guided biopsy,

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Fig. 1 Axial T₂-weighted (A, B), axial T₁-weighted (C), and axial (D), coronal (E), and sagittal (F) T₁-weighted magnetic resonance images following gadolinium-diethylenetriamine-penta-acetic acid administration demonstrating an enhanced mass located in the left subthalamic nucleus. The lesion and peritumoral edema also involve the upper part of the midbrain, the posterior part of the thalamus, and the hypothalamus.

and gamma knife treatment was not possible because of economic problems. Therefore, palliative whole brain radiotherapy of 30 Gy in 10 fractions with dexamethasone (4 mg per oral four times a day) was started. The dexamethasone dose was tapered to 12 mg/day at 2 weeks after the completion of radiotherapy and completely stopped by 5 weeks with 4 mg weekly reductions. Corticosteroid-induced diabetes mellitus did not emerge during this period. Tamoxifen administration was also stopped and an aromatase inhibitor with gonadotropin-

releasing hormone analog was started as a second line hormonal treatment. Hyperphagia was remarkable and the patient gained 19 kg body weight in 4 months. She is still being followed up with a stable thalamic lesion and overeating.

Discussion

Very few cases of metastatic tumors in the thalamic region have been reported. A 58-year-old woman presented with multiple metastatic thalamic lesions from carcinoma of the left parotid gland.²⁾ The diagnosis was established by stereotactic biopsy and treatment used external radiotherapy because of the localization. We could not plan a surgical excision for the same reasons in our case, although the lesion was solitary. Similarly, a case of thalamic metastasis from pancreatic cancer had a very poor outcome.¹²⁾ CNS metastasis from breast cancer generally presents very late in the course, in contrast to the early occurrence in our case.¹¹⁾

The hypothalamus is the regulator and coordinator of central autonomic activity. The current evidence suggests that hypothalamic obesity may or may not occur with hyperphagia due to disturbance of the autonomic nervous system. The caloric balance may be altered by ventromedial lesions causing hyperphagia, and lateral hypothalamic lesions may cause a syndrome of aphagia and weight loss in experimental animals.^{3,5)} Clinical manifestations such as progressive hyperphagia, obesity, memory impairment, and hypersomnolence could be caused by compression and necrosis of the ventromedial and posterior hypothalamic nuclei.^{1-8,10)} A patient with hyperphagia gained 16 kg in 60 days, due to a neoplastic lesion involving the midline via the hypothalamus and reaching the contralateral lenticular nucleus.⁶⁾ The hyperphagia and consequent obesity were associated with bilateral destruction of the ventromedial hypothalamic area. An endocrinologically normal woman with hydrocephalus related to a germinoma localized in the anterior hypothalamic, thalamic, and basal forebrain developed worsening anterograde amnesia and hyperphagia despite a functioning ventriculoatrial shunt.⁹⁾

Intraaxial germinomas restricted to the anterior hypothalamus or thalamus are rarely reported, so the clinical features of the present case may be unique. A woman with an intact median eminence and pituitary function presented with hyperphagia due to a low-grade astrocytoma in the third ventricle and medial anterior and mid hypothalamus, primarily on the right.¹⁰⁾ A 55-year-old man with hydrocephalus caused by a third ventricular tumor

had progressive hyperphagia and obesity.¹⁾ Necropsy found that a gangliocytoma had filled the third ventricle, resulting in compression and necrosis of the ventromedial and posterior hypothalamic nuclei. Another patient had lesions in the left intralaminar nucleus of the thalamus, right globus pallidus, and right dorsomedial nucleus of the hypothalamus and showed hyperphagic tendency, so hyperphagia might occur after destruction of the dorsomedial hypothalamic nucleus.¹⁶⁾

Our patient had hyperphagia due to a mass localized in the STN. The lesion and peritumoral edema also involved the upper part of the midbrain, posterior part of the thalamus, and the hypothalamus. The weight gain is likely to result as a specific limbic effect of STN stimulation, because the limbic STN and the adjacent lateral hypothalamus are intimately connected.^{9,14)} Our patient had no endocrinological deficit likely to cause hyperphagia during the clinical follow-up period.

Improvement is usually expected after radiotherapy, but a patient with a third ventricular tumor presented with amnesic disorder syndrome and vegetative abnormalities following irradiation treatment.⁷⁾ Given the onset of symptoms only after irradiation (the memory deficit in particular) and the non-invasive nature of the surgery, the probable etiology was post-irradiation syndrome. Our patient also received urgent whole brain radiotherapy with dexamethasone for both peritumoral and potential radiation-induced edema. The impact of this treatment on the development of hyperphagia is difficult to estimate relative to the possible radiation effect on the hypothalamus as an adjacent structure of the tumor.

Several factors interfere with the therapeutic strategy and prognosis, such as the histology of the primary tumor, patient's age and neurological status, localization and size of the metastatic lesions, and outcome of the extracranial disease.^{4,15)} Generally, surgical intervention or stereotactic surgery followed by whole brain radiotherapy is indicated in patients with controlled extracranial disease and good performance status who present with an isolated CNS metastasis.^{4,15)} We preferred whole brain radiotherapy in our patient for two reasons. Firstly, the early appearance of the thalamic lesion, while she was under hormonal treatment with tamoxifen and just after the end of adjuvant chemotherapy, so we expected new CNS and systemic metastases in the future. Secondly, we have few centers that can perform stereotactic treatments in Turkey and both the economic and insurance status of the patient did not allow this alternative.

Neoplasms in the thalamic region are rare and

may cause a wide spectrum of clinical symptoms with limited treatment alternatives, leading to a poor prognosis. The present case of solitary metastatic tumor involving the STN occurred in a patient with locally advanced breast cancer. Unfortunately, the lesion could not be identified by biopsy, but a concomitant primary CNS tumor or an early metastasis from breast cancer are both possibilities.

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