

CASE REPORT

Solitary Pituitary Metastasis of Advanced Breast Cancer Treated with Anti-Human Epidermal Growth Factor Receptor 2 Drug

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Metastasis to the pituitary gland from systemic cancer is a rare condition. The breast and lung are the most common sites of primary tumor metastasis. Most often, they occur in the setting of widespread metastatic disease, which most frequently occurs in elderly patients. However, an increase in the incidence of solitary pituitary metastasis of breast cancer as the first recurrence has been reported. Diabetes insipidus is the most frequent symptom at presentation, and visual field defects or cranial nerve deficits are common symptoms of pituitary metastasis. Unlikely these symptoms, deficiencies of anterior pituitary hormones may only become evident in critical situation because symptoms are of an insidious onset and sometimes nonspecific. We report here on a rare case of solitary pituitary metastasis from breast cancer presenting as hyponatremia without other symptoms.

Keywords: Breast neoplasms; Metastasis; Pituitary gland; Hyponatremia

INTRODUCTION

Recently, following the introduction of adjuvant therapy with the anti-human epidermal growth factor receptor 2 (HER2) therapy trastuzumab (Herceptin) in the treatment of breast cancer, an increase in the frequency of central nervous system (CNS) metastasis as the site of first recurrence has been reported [1]. However, it is difficult to diagnose pituitary metastases, as the symptoms are nonspecific and the radiological differences from primary tumors are trivial [2]. In this report, we describe a rare case of a solitary metastatic breast cancer to the pituitary, presenting as hyponatremia without other common symptoms.

CASE REPORT

A 59-year-old woman was brought to the emergency department because of nausea and dizziness. Three years prior, the patient was diagnosed as having breast cancer and underwent modified radical mastectomy and subsequent adjuvant chemotherapy. Because the

tumor expressed a novel HER2 mutation, the patient received trastuzumab chemotherapy, which was proven beneficial to patients. However, 18 months prior to presentation, solitary brain metastasis in the frontal cortex, without any other metastasis, was detected on brain magnetic resonance imaging (MRI) (Fig. 1). After tumor mass removal, systemic chemotherapy was initiated. Then, serial brain MRI was performed at 3-month intervals and showed no recurring mass in the operation site. However, the patient was brought to our emergency department with a chief complaint of dizziness, nausea, and poor oral intake. Laboratory examination results showed hyponatremia (Na level, 122 mmol/L; reference range, 135 to 150 mmol/L). To determine the cause of the hyponatremia, a hormonal workup was performed. The morning levels of cortisol (0.4 µg/dL; reference value > 10 µg/dL), adrenocorticotropic hormone (10.8 pg/mL), free T4 (6.09 pmol/L; reference range, 11.5 to 22.7 pmol/L), thyroid stimulating hormone (0.486 mIU/mL; reference range, 0.55 to 4.78 mIU/mL), insulin-like growth factor type 1 (28 ng/mL; reference range, 55 to 225 ng/mL), growth hormone (0.14 ng/mL; reference value > 1.0 ng/mL), follicle

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stimulating hormone (5.5 mIU/mL), luteinizing hormone (<0.07 mIU/mL), estradiol (<5.0 pg/mL), and prolactin (9.53 ng/mL; reference range, 4.79 to 23.3 ng/mL). All anterior pituitary hormones

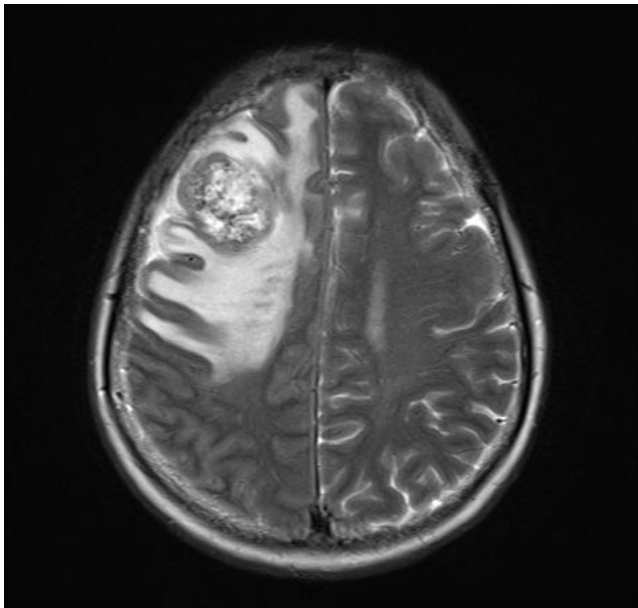


Fig. 1. Brain magnetic resonance imaging showing a $3.5 \times 3.5 \times 3.5$ -cm heterogeneous enhancing mass with cystic necrosis in the right frontal lobe. Severe vasogenic edema is seen around the tumor mass.

were lower than their normal limits. However, the patient had no visual symptoms and her urine amount was within the reference range. Brain MRI was performed and showed pituitary gland enlargement with heterogeneous enhancement that was indicative of pituitary metastasis (Fig. 2). We reviewed previous brain MRI findings and found that the pituitary gland had progressively, insidiously enlarged during the 10-month period. Dynamic sellar MRI was not performed in this patient. The thyroid function and gonadotropin levels had been normal until 8 months ago. Hormonal replacement with glucocorticoid and thyroxine was started, and both hyponatremia and associated symptoms were markedly improved. Gamma knife surgery for the pituitary metastasis was performed. A follow-up MRI revealed that the metastatic lesion had markedly decreased in size. The patient then received oral chemotherapy with a novel tyrosine kinase inhibitor and concurrent hormone replacement. At the last follow-up examination in the outpatient clinic, her general condition was found to be relatively good.

DISCUSSION

The pituitary gland is a rare site of metastasis of all neoplasms, accounting for only 1% of pituitary lesions [3]. Breast and lung can-

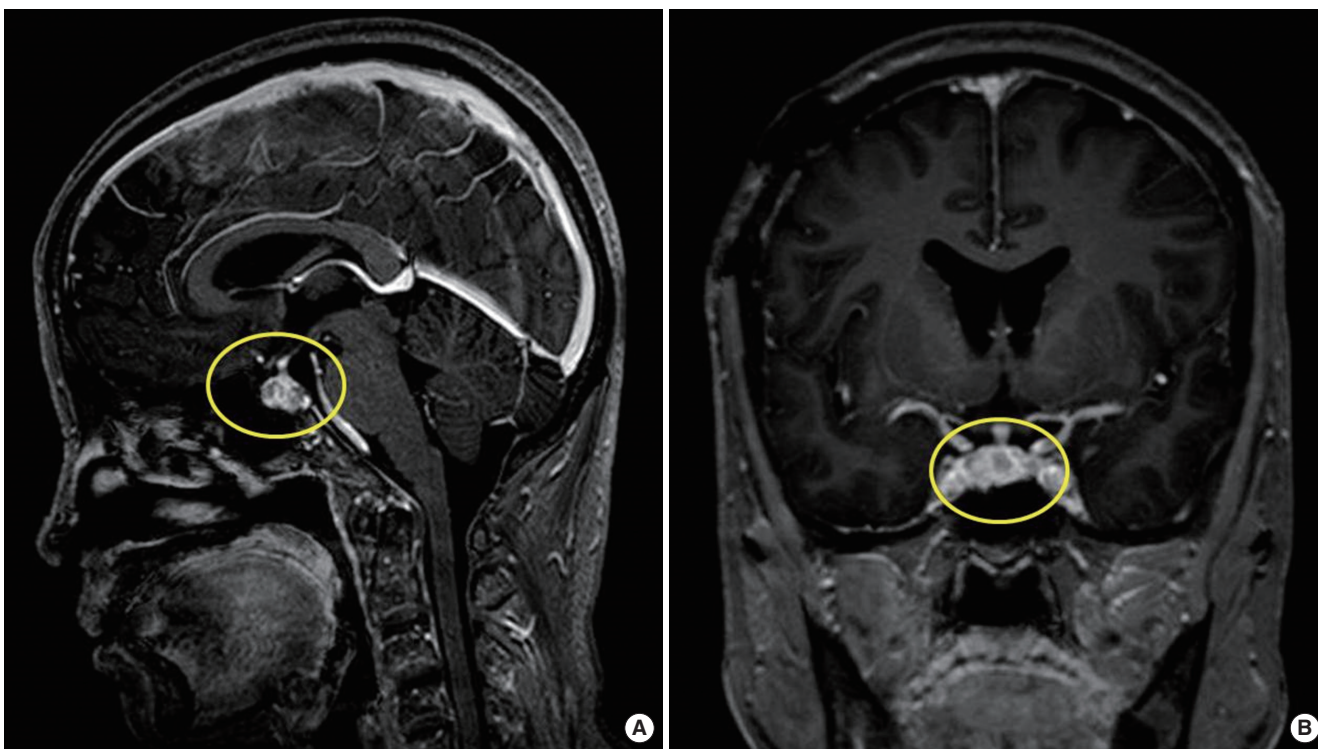


Fig. 2. Brain magnetic resonance imaging showing pituitary gland enlargement with heterogeneous enhancement that was indicative of pituitary metastasis (yellow circle). (A) Sagittal view and (B) coronal view.

cers are the most common primary neoplasms that metastasize to the pituitary gland. Most often, they occur in the setting of widespread metastatic disease, which most frequently occurs in elderly patients [4]. However, since the introduction of the novel targeted therapy with trastuzumab (anti-HER2 therapy) for the treatment of breast cancer, approximately one-third of patients with metastatic HER2-positive breast cancer will develop CNS metastases including pituitary metastasis [1]. However, solitary pituitary metastasis from breast cancer is extremely rare. There have been three other reports of isolated pituitary metastasis [5-7]. In Korea, only one report describes a solitary pituitary metastasis diagnosed after the end of adjuvant trastuzumab therapy [7]. It has been suggested that trastuzumab may not be active in the CNS, which could be a potential sanctuary site for disease progression [5]. In the case of solitary pituitary metastasis, differential diagnosis between pituitary metastasis and primary pituitary lesions such as adenoma, especially in the early stage of metastasis, is challenging [8]. Majority of pituitary metastasis are clinically silent and too small to cause radiological changes [4]. Even when symptomatic, radiological evaluation generally has not been useful in distinguishing from pituitary adenomas, unless other metastatic brain lesions coexist. But, rapid increase of a sellar mass with aggressive infiltration of adjacent tissues should raise suspicion of metastatic tumor [9,10]. And posterior lobe involvement is more common in the case of pituitary metastasis. Diabetes insipidus (DI) is the most frequent symptom at presentation, and visual field defects or cranial nerve deficits are common symptoms of pituitary metastasis [2]. By contrast, symptomatic anterior pituitary hormone deficiencies have been less frequently described at presentation. Among these symptoms, pituitary adenoma rarely presents with DI. In contrast to central DI, clinicians easily overlook a diagnosis of anterior hypopituitarism because of insidious onset and slow progression of hormone deficiency. In our patient, after metastasectomy for frontal lobe metastasis, conventional brain MRI was performed regularly. However, pituitary metastasis was detected only after the patient was brought to the emergency department because of symptoms of hyponatremia. Delayed diagnosis of pituitary metastasis

may lead to serious conditions such as pituitary apoplexy or adrenal crisis, especially in cancer patients with poor general conditions. With the development of novel therapeutic agents, the number of breast cancer survivors has increased worldwide. Therefore, the incidence of pituitary metastasis of breast cancer might have increased concurrently. Clinicians should consider the possibility of pituitary metastasis in these patients. In patients with symptoms indicative of hormone deficiency or those with suspicious conventional MRI results, pituitary hormone evaluation and dynamic sellar MRI should be considered. Early diagnosis and proper management for pituitary metastasis in cancer patients can lead to decreased morbidities associated with hormone deficiencies.

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