Pituitary metastasis in breast cancer: case report and literature review

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Abstract
Background: Breast cancer commonly metastasizes to the lung, vertebrae or liver but rarely to the pituitary gland. The majority of cases have been reported during autopsy; however, with the improvements in diagnostic methods, there has been an increasing number of cases reported in the clinical setting. The main symptoms of pituitary metastasis are reported to be headache, diabetes insipidus and visual field defects, which may cause confusion regarding the clinical diagnosis.
Case presentation: The present study describes a case of pituitary metastasis symptoms of diabetes insipidus and loss of vision in a patient with breast cancer. After the patient completed the evaluation, a neuroendoscopy-assisted endonasal transsphenoidal tumor resection was performed. The postoperative biopsy revealed metastatic breast cancer.
Conclusions: The present study analyzed this patient and 16 other cases of pituitary metastases collected from the PubMed database. Lung cancer, breast cancer and lymphoma could metastasize to the sellar region, while certain other tumors from the liver, parotid, colon, prostate, stomach, kidney, thyroid or skin were also observed. The clinical manifestation was often dominated by pituitary dysfunction, intracranial hypertension and visual field defects. Certain patients may suffer from oculomotor nerve paralysis, electrolyte imbalance, diabetes insipidus or a loss of vision. Imaging findings revealed that sellar metastases often invaded the suprasellar region. In a few cases, the lesion enclosed intracranial vessels, and invaded the cavernous sinus or Meckel's cave. These characteristics resulted in difficulties during surgery.
Background
The pituitary gland is not a commonly observed location for tumor metastasis, and these metastases account for 1.0-3.6% of all sellar tumors. (1) The primary metastatic lesion is most commonly found on the lung, breast, kidney or prostate. (2) When patients present with manifestations of metastasis, it typically indicated that the disease has entered its final stage. Despite advances in surgery, radiotherapy and chemotherapy, the overall median survival in the last 15 years is only 12.9 months. (3) To further enhance the current understanding of this disease, the present study describes 16 cases in the literature and lists the patient information, presentation and imaging characteristics.
Case Presentation
A 46-year-old female was admitted to the hospital with the chief complaint of polydipsia, polyuria and narrowing of the visual field in both eyes for over 4 months. Her urine volume was ~6,000 ml per day. The patient was diagnosed with right-side breast cancer 7 years ago. She underwent modified radical mastectomy with axillary lymph node dissection and postoperative radiotherapy and chemotherapy. The pathology revealed infiltrating ductal carcinoma. The patient was observed to have destruction in multiple bones (cervical, thoracic, lumbar, sacrum vertebra) after receiving an MRI scan 1 year ago. The most possible diagnosis was tumor metastasis, the patient refused to receive surgical therapy and therefore did not.

After she was admitted to hospital the neurological examination demonstrated a reduced level of vision (counting fingers), which was more serious on the left side than on the right side, and visual fields were lost on the temporal side of both eyes. No other neurological abnormalities were identified during the examination. The laboratory tests demonstrated that the pituitary hormones were unaffected; however, the level of the target organs' hormone release was diminished, with serum-free thyroxin levels of 9.99 pmol/l (normal range, 11.5–22.7) and cortisol levels of 0.73 ug/dl (normal range, 3.09–22.4). The blood α-fetoprotein level was slightly elevated. MRI revealed a homogeneously enhanced lesion in the sellar and suprasellar regions (the largest diameter was 25 mm) compressing the optic chiasm and third ventricle (Fig. 1). A 1 mm metastasis was also observed at the left temporal pole. The ophthalmological examination revealed a complete temporal side visual field impairment on the right and an atypical visual field impairment on the left. Thus, a diagnosis of pituitary tumors was considered. In addition, pituitary metastasis of breast cancer was highly suspected.

The patient underwent neuroendoscopy-assisted endonasal transsphenoidal tumor resection. The lesion was identified in the pituitary gland, exhibiting a yellow-red color under an endoscope with sufficient blood supply, and normal pituitary tissue could not be identified. Due to its hard consistency, it was difficult to remove the tumor, even with CUSA (Cavitron ultrasonic aspiration). These characteristics were inconsistent with pituitary tumors, and further frozen samples suggested a diagnosis of a suspicious malignant tumor. The tumor and capsule were completely resected after the
suprasellar area was clearly exposed.

Tissue biopsy confirmed that metastatic breast cancer, and the immunohistochemistry analysis (Fig. 2) was positive for Her2(3+), Ki67(+,25%), P53(+), E-cad(+), ER(+) and GATA-3(+). Following surgery, the patient was treated with hydrocortisone and desmopressin to control the urine volume, as well as levothroid and prednisone to maintain adenohypophysis function. At the time the patient was discharged, her diabetes insipidus had alleviated, and her visual field impairment improved. As such, she was advised to continue taking levothroid and desmopressin.

Discussion

The intracranial zone is a common site of metastasis, but metastases to the sellar and suprasellar regions are not commonly observed. An autopsy case of pituitary metastasis was reported by Benjamin for the first time in 1857. (4) Currently, the majority of cases have been identified during autopsy, while only a few cases were diagnosed via patient symptoms. The preoperative diagnosis of pituitary metastasis remains a challenge in the clinical setting. A case series and review study revealed that the main clinical symptom noted was signs of cranial hypertension. (2) In this case, the patient's symptoms were no different from those of other sellar region diseases, but the ophthalmological examination and MRI scan revealed some intriguing results. Generally, pituitary adenoma primarily causes temporal visual field defects by oppressing the optic nerve. The atypical visual field defect may be caused by the tumor invaded the optic nerve fibrous bundle. In addition to the metastasis in the sellar region, an intracranial metastasis located in the left temporal lobe was also identified, and this tumor obtained its blood supply from the left middle cerebral artery (M1-M2).

The most unique characteristic of the lesion was observed intraoperatively. It took a long time to remove the tumor tissue due to its solid consistency. Even with the use of CUSA (Cavitron ultrasonic aspiration), tumor removal remained the largest obstacle during surgery. Subsequently, a literature review was performed by searching the PubMed database. The initial search string used was "Pituitary OR Sella OR Sellar AND Metastatic." A total of 16 patients with pituitary metastasis were reported in the previous 10 years. (5–20) The collected information and primary lesion data are presented in Table I. The average age of all patients was 61.5 years, and the
number of females was twice as high as that of males (11:5). The most common primary tumor was lung carcinoma (n = 4); breast carcinoma and lymphoma were both reported twice. In addition, hepatocellular carcinoma, parotid carcinoma, colon carcinoma, prostate carcinoma, gastric carcinoma, melanoma, renal carcinoma and thyroid carcinoma were reported a single time each. In addition, there were six cases of other tissue metastases identified, including lung metastasis (n = 1), cerebral hemisphere metastasis (n = 2) and bone metastasis (n = 3).

Table II presents a symptomology graph to describe the patient presentation. The incidence of hormone secretion disorders caused by pituitary dysfunction (81.3%) was the highest, followed by intracranial hypertension (56.3%) and visual field defects (43.8%). Oculomotor nerve paralysis and reduced vision were both observed in one-third of the patients. Electrolyte imbalance, diabetes insipidus and retrobulbar pain were also reported in less than a quarter of the cases. In the majority of cases, the patient presented with pituitary dysfunction caused by anterior pituitary lobe compression and complained of listlessness, feebleness, poor appetite and weight loss. Headache, vomiting and optic disk atrophy were the main signs of intracranial hypertension, which occurred in half of these cases. These symptoms could be persistent or intermittent, with variable degrees, which was the main contributing factor for patients visiting the emergency room. Bitemporal visual field defects were a common manifestation of pituitary lesions, but in metastatic cases, the shape of the visual field defect could be atypical. There were two patients with unilateral visual field defects, while nasal visual field hemianopia was only observed in one case. Not all instances of electrolyte imbalance were caused by diabetes insipidus, but on the contrary, electrolyte imbalance did occur as a result of diabetes insipidus.

The majority of patients received MRI scans, and the image descriptions are presented in Table III. Case 12 did not include the results of the MRI scan, as the files were created in 1980, and the data were not recorded. Pituitary mass extension into the suprasellar region was revealed in eight patients (53.3%). A quarter of the cases had one or more encased intracranial arteries. A few lesions extended into the cavernous sinuses, unilaterally or bilaterally, and extended inferiorly into Meckel's cave. Two cases of pituitary apoplexy were reported, which was the main cause of severe headaches.
Conclusion
In summary, we report this case of pituitary metastasis of breast cancer and an analysis of pituitary metastases cases to illuminate the chief symptoms and specialized radiographic characteristics.

Nevertheless, pituitary metastasis can be easily confused with other benign tumors, and it should be strongly suspected if the patient has any primary tumor.

Declarations

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None.

Authors’ contributions
All authors participated in the patient’s care. GH, LC and XZ performed the operation of the patient. JY and SX performed the preoperative and postoperative treatment of the patient. SX constructed the conception and design of this report. All authors have read and approved the final manuscript.

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Availability of data and materials
We declared that all data and materials described in the manuscript will be freely available.

Ethics approval and consent to participate
Not applicable.

Consent for publication
The patient accepted to publish this case report.

Competing interests
The authors declare that they have no competing interests.

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Tables
Due to technical limitations, all tables are only available for download from the Supplementary Files section.

Figures

Figure 1

MRI imaging revealed a homogeneously enhanced lesion in the sellar and suprasellar regions (the largest diameter was 25 mm) compressing the optic chiasm and third ventricle.
(A) Hematoxylin and eosin staining confirmed metastatic breast cancer.

Immunohistochemistry analyses were positive for (B) ER, (C) E-cad and (D) GATA-

**Figure 3**

*Timeline*

- Diagnosis of breast cancer 7 years ago
- Polydipsia and polyuria and narrowing of the visual field 4 months ago
- Neuroendoscopy-assisted endonasal transphenoidal tumor resection.
- Diagnosis as multiple bone metastasis 1 year ago
- Admitted to our hospital and underwent all of the examinations
- Biopsy demonstrated that the final diagnosis was pituitary metastasis of breast cancer

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.xlsx
- Table2.xlsx
- Table3.xlsx