Metastatic gastric cancer in the pituitary (MGCP) is rare. Few are known on the clinical and radiological characteristics of MGCP. To date, the coexistence of metastatic pituitary tumors and intracranial aneurysms has not been reported in literatures.

We present a case of MGCP with internal carotid aneurysm in a 57-year-old woman, who presented with oculomotor paralysis, postorbital pain, and hypopituitarism as onset symptoms. The patient had a history of the surgical removal of gastric cancer. Magnetic resonance imaging and single-photon emission computed tomography revealed a recurrent sellar mass with intracranial and multiple bone metastases. The patient underwent subtotal removal of the tumor, followed by conformal radiotherapy and chemotherapy. Ten months after surgery, the patient died due to deterioration of her overall condition.

We also reviewed and analyzed the clinical data, imaging features, and treatment methods of additional 4 cases with MGCP, which were reported in literatures. This study provides important clinical information for the diagnosis and treatment of MGCP.

Abbreviations: CTA = computed tomography angiography, DSA = digital subtraction angiography, ICA = internal carotid aneurysm, MGCP = metastatic gastric cancer in the pituitary, MP = metastasis in the pituitary, MRI = magnetic resonance imaging, SPECT = single-photon emission computed tomography.

INTRODUCTION

Metastasis in the pituitary (MP) is a rare cancer-associated complication, accounting for <<1% of all sellar or parasellar tumors and ~5.1% of all metastatic brain tumors. Although MPs can be seen in young people, they usually affect elderly people with gender predominance. Diabetes insipidus and hypopituitarism are the most common symptoms of tumors metastatic to the pituitary. The pituitary gland may be the only metastatic site of a tumor, and MP may cause the first clinical presentation of tumors with multiple metastases. Breast cancer and lung cancer are the most common primary tumors metastatic to the pituitary gland in women and men, respectively. MP from gastric cancer is rarely reported in literatures. Gastric cancer commonly metastasizes via the lymph node, peritoneum, blood, or bone marrow, and common metastatic sites are the liver, peritoneum, lung, and bone. Intracranial aneurysm is found in only 0.3% of brain tumor patients, and a coexisting aneurysm can trigger or exacerbate the disease course of tumors. None of the patients had a history of gastric cancer. In this study, we present the first reported case of MGCP with a left ICA in the siphon segment in a 57-year-old woman, presenting with oculomotor paralysis, postorbital pain, and hypopituitarism. In addition, we reviewed 4 other known cases with MGCP and summarize the clinical manifestations and imaging characteristics of MGCP. Our study provides important clinical information for diagnosis and management of MGCP.

CASE REPORT

In September 2014, a 57-year-old woman visited our hospital presenting with diplopia, paroxysmal headache, and postorbital pain without obvious causes. The patient had right severe ptosis 1 week later. Four years earlier, the patient underwent subtotal gastrectomy for gastric antrum carcinoma followed by 1 cycle of FOLFOX (Oxaliplatin + leucovorin + 5-FU) and 4 cycles of XELOX (Xeloda + oxaliplatin) chemotherapy. She had no family history of gastric cancer.

On physical examination, the patient had right oculomotor paralysis with right eyelid drooping and was unable to perform the inward, upward, and downward movement of the right eyeball. She had diplopia without nystagmus. The right pupil was dilated with blunt pupillary reflex. Visual field and visual acuity of both eyes were normal. Computer tomography (CT) scan of the orbit, chest, and abdomen were unremarkable. Brain CT revealed a destroyed occipital base and dorsum sellae surrounded by soft-tissue density shadows. Brain magnetic
resonance imaging (MRI) revealed a round mass of 25 mm in diameter in the enlarged sellae (Figure 1A and B). T1-weighted images (T1-WI) revealed a round mass with isointense and hyperintense signals, whereas T2-weighted images (T2-WI) revealed a mass with a hyperintense signal with heterogeneous enhancement after Gadolinium-DTPA injection. The sellae was elevated with a left displacement of the pituitary stalk and a left shift of the bilateral optic chiasma and cavernous sinus. The patient was diagnosed with a giant pituitary adenoma. Laboratory findings revealed reduced levels of free triiodothyronine (FT3), free thyroxine (FT4), and cortisol (Table 1). CT angiography (CTA) of the intracranial artery revealed an ICA of 3.0/C2 3.0/C2 3.4 mm at the inner edge of the siphon segment and the aplastic left posterior cerebral artery. Digital subtraction angiography (DSA) revealed that the blood supply to the pituitary was from the meningeal pituitary branch of the right intracranial artery and the aneurysm (Figure 1C and D).

The patient underwent transnasal transsphenoidal surgery to remove the tumor. The tumor was red and solid with rich blood supply, and infiltrated into the clivus with close adhesion to the bone. The upper left of the tumor surrounded the artery aneurysm. The tumor was subtotally resected in pieces. The aneurysm remained unprocessed due to its small size and wide neck. Postoperative pathological examination revealed that the tumor was adenocarcinoma resembling primary gastric carcinoma (Figure 2A and F). Optic tissues and pituitary tissues were distributed among the adenocarcinoma tissue. The tumor was immunopositive for gastric cancer markers such as CK7, CK20, CDX-2 and villin, and neuroendocrine tumor markers such as CgA and Syn (Figure 2). The Ki67 index was 60%. The patient

**TABLE 1.** Laboratory Findings

| Hormone   | Preoperative | Postoperative | Postradiotherapy | Normal Level | Unit |
|-----------|--------------|---------------|-----------------|--------------|------|
| FT3       | 3.20         | 1.85          | 2.56            | 3.50–6.50    | pmol/L |
| FT4       | 9.75         | 9.09          | 5.89            | 12.00–22.00  | pmol/L |
| STSH      | 0.61         | 0.37          | 0.34            | 0.51–4.94    | mIU/L |
| Cortisol  | 33.22        | 250.88        | 25.27           | 118.60–618.00 | nmol/L |
| CEA       | 3.99         | 5.68          | 2.91            | 0.00–5.00    | µg/L  |
| CA199     | NE           | 50.89         | 21.94           | 0.00–35.00   | µg/L  |
| CA724     | NE           | 7.35          | 49.74           | 0.00–6.90    | U/mL  |

CA199 = carbohydrate antigen 199, CA724 = carbohydrate antigen 724, CEA = carcinoembryonic antigen, FT3 = free triiodothyronine, FT4 = free thyroxine, NE = not examined, STSH = sensitive thyroid-stimulating hormone.
was diagnosed with MGCP. After surgery, postorbital pain and headache disappeared, and no relief was seen in other symptoms and signs. The patient was treated with intravenous injection of hydrocortisone (100 mg, q.d.) and oral administration of levothyroxine sodium tablets (50 μg, b.i.d.). Laboratory findings revealed that FT3, FT4, and sensitive thyroid-stimulating hormone (STSH) serum levels further decreased, whereas carcinoembryonic antigen (CEA), CA199, and CA724 serum levels were elevated.

One month after the surgery, the patient complained of bone pain, headache, dizziness, fatigue, and nausea with vomiting. MRI revealed a giant round sellar mass of 28 mm in diameter with an unclear boundary. The tumor was isointense or hyperintense on T1-WI, and isointense or hypointense on T2-WI with heterogeneous enhancement. SPECT revealed that multiple bone metastases occurred in the skull, skull base, 3rd thoracic vertebra, and the right sacroiliac joint (Figure 3). Recurrence of the sellar mass and multiple bone metastases was considered. One month later, MRI indicated that the sellar mass increased and infiltrated into the bilateral optical nerves. The patient received intensity-modulated conformal radiotherapy with DT5040cGy in 28 fractions in the brain.

![FIGURE 2. Hematoxylin and eosin (H&E) staining (A and F, 100×) and immunohistochemical staining (B, C, D, E, G, H, I, J, K, and L, 100×) of the primary gastric carcinoma (A–E) and MP (F–L). Primary gastric cancer was ulcerative gastric adenocarcinoma with poor to moderate differentiation, histological grade II, and pT4aN0M0 stage. The tumor was immunopositive for CK7 (B), CK20 (C), CDX-2 (D), and villin (E). MGCP revealed poorly differentiated atypia adenocarcinoma cells (F), was immunopositive for CK7 (G), CK20 (H), CDX-2 (I), and villin (J), and was also immunopositive for CgA (K) and Syn (L). H&E = hematoxylin and eosin; MGCP = metastatic gastric cancer in the pituitary; MP = metastasis in the pituitary.](image)

![FIGURE 3. SPECT and MRI revealed that the pituitary mass recurred with multiple bone metastasis and intracranial metastasis after surgery. (A) SPECT performed 1 month after surgery reveals the tumor metastasis in the skull, skull base, 3rd thoracic vertebra, and the right sacroiliac joint. MRI performed 3 months after surgery reveals the pituitary mass (B) and left frontoparietal mass (C) that recurred. MRI = magnetic resonance imaging, SPECT = single-photon emission computed tomography.](image)
lesion area. After radiotherapy, the patient developed bilateral ptosis, diplopia, and occasional vomiting. FT3, FT4, STSH, and cortisol levels sharply decreased, suggesting the pituitary crisis precursor. The patient was immediately treated with intravenous injection of hydrocortisone (100 mg, b.i.d.) and oral administration of levothyroxine sodium tablets (50 µg, q.d.). One week after radiotherapy, symptoms improved and the left ptosis was relieved. The patient received oral administration of prednisone (5 mg at 8:00 am and 2.5 mg at 3:00 am) and levothyroxine sodium tablets (50 µg, q.d.) daily. One month after the radiotherapy, MRI revealed that the size of the sellar mass did not change. A soft-tissue mass of 38 × 42 mm in size was found in the left frontoparietal area with a slightly hypointense signal on TIWI and T2WI, which was enhanced after contrast injection (Figure 3). SPECT revealed that bone metastasis was aggravated. The patient received intravenous injection of zoleodonate (5 mg) twice in 2 weeks, followed by 2 cycles of chemotherapy with oxaliplatin (200 mg on the 1st day), and gimeracil and oteracil potassium capsules (60 mg, b.i.d., from the 1st day to the 14th day). One month after chemotherapy, MRI revealed that the size of the tumor mass in the sellae and left frontoparietal area became larger, and the brain midline slightly shifted to the left. FT4, STSH, cortisol, CEA, and CA199 levels returned to normal, whereas the FT3 level (3.23 pmol/L) was slightly lower than normal. The CA724 level increased to 49.74 U/mL. The patient had stable symptoms and was discharged from the hospital. At the latest follow-up (in August, 2015), the patient died due to deterioration of her overall condition.

This study was approved by the Second Affiliated Hospital of Dalian Medical University, China. The patient provided informed consent.

DISCUSSION

Carcinomas originate from almost every tissue and can metastasize to the pituitary. Metastatic tumor cells can reach the sellae via hematogenous spreading, extension from juxtapitellar tissues and the skull base, and dissemination through lymphatic microvessels. The most common tumors metastatic to the pituitary are breast cancer and lung cancer, followed by lymphatic microvessels. The most common tumors metastatic to the sellae and the skull base, and dissemination through lymphatic microvessels.13 The most common tumors metastatic to the pituitary are breast cancer and lung cancer, followed by lymphatic microvessels.13 The most common tumors metastatic to the sellae and the skull base, and dissemination through lymphatic microvessels.

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| Authors                  | Gender/Age (Year) | MP Origin/Pathological Stage | MP Phenotype | Other Metastasis | Interval (Month) | Clinical Presentation                                                                 | Treatment                                                                 | Survival Time (Month)/Status |
|-------------------------|-------------------|------------------------------|--------------|------------------|------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------|-----------------------------|
| van Seters et al, 1985  | F/66              | Gastric-esophageal          | MP coexisted with recurrent pituitary adenoma | Several regional lymph nodes | 0                | Sudden blindness, headache, nausea, somnolence, ophthalmological, elevated PRL level | Surgery                                                                    | 0.4/dead                    |
| Izumi et al, 1999       | M/68              | Upper and central stomach   | MP coexisted with meningeal carcinomatosis | Parenchyma of the bilateral adrenal glands | 0                | Cerebral salt wasting syndrome (CSWS), disturbed consciousness, dizziness, subclinical hypothyroidism | None                                                                      | 1/dead                      |
| Pozzessere et al, 2007  | M/60              | Definite site is unknown/pT2bN3M0 | MP occurred after liver metastasis | Liver | 5                | Headache, post-ocular pain, diplopia, panhypopituitarism, elevated PRL level | Surgery, radiotherapy, pituitary hormone replacement therapy | 3/dead                      |
| Lea˜es et al, 2011      | M/50              | Antrum of stomach           | MP as the 1st presentation of the gastric cancer | None | 0                | Headache, diplopia, ptosis, sexual dysfunction, low levels of gonadotropins and total testosterone, elevated levels of PRL, CA199 | Surgery | Following-up/alive |
| The present case        | F/57              | Antrum of stomach/pT4aN0M0  | MP as the 1st presentation of the metastatic gastric cancer | Multiple bone metastases and intracranial metastasis | 48               | Diplopia, post-orbital pain and headache, hypopituitarism, ptosis, elevated levels of CEA, CA199, and CA724 | Surgery, radiotherapy, chemotherapy, hormone substitution therapy | 10/dead                     |

Interval (month), the time from the diagnosis of primary gastric cancer to the detection of the metastatic gastric cancer in the pituitary. CA199 = carbohydrate antigen 199, CA724 = carbohydrate antigen 724, CEA = carcinoembryonic antigen, F = female, M = male, MP = metastasis in the pituitary, PRL = prolactin.
insipidus, rapid development of anterior pituitary hormone deficiencies, high level of cancer biomarkers, positive findings in SPECT/PET examinations, and atypical appearance of the tumor. Definitely, pathological diagnosis is conclusive.

In summary, we describe a rare case, in which a patient had a sellar mass close to the left internal carotid artery aneurysm. MP should be considered in patients with a history of gastric cancer and had rapidly aggravated diplopia, postorbital pain, headache, and hypopituitarism. CEA, CA199, and CA724 serum levels may be useful markers for monitoring disease progression. Combined treatments including surgical treatment, radiotherapy, chemotherapy, and hormone replacement therapy may be important for improving the survival of patients with MP.

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