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Diplopia as a Presenting Symptom in a Gastric Gastrointestinal Stromal Tumor

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Gastrointestinal stromal tumors are the most common mesenchymal neoplasm of the gastrointestinal tract. Distant metastasis of gastrotintestinal stromal tumors occurs in ~50% of the cases and is usually found in the liver and peritoneum. We present a patient with diplopia which was due to a metastatic gastrointestinal stromal tumor of the clivus. Transsphenoidal resection of the tumor was performed and post-operative treatment with oral imatinib mesylate was done. One month after the surgery, treatment was started with imatinib and the patient's diplopia improved within 15 days. Follow-up computed tomography was taken 2 months after the initiation of oral imatinib, and the size of the main gastric mass has decreased. To our knowledge, this is an extremely rare case of gastrointestinal stromal tumor with metastasis to the clivus with diplopia as the presenting symptom. We report our clinical findings along with a review of the relevant literature.

Key words: gastrointestinal stromal tumor – imatinib mesylate – C-KIT – diplopia – clivus

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors of the GI tract with an incidence of 10–20 cases per million (1–3). GISTs are KIT (tyrosine kinase receptor—CD117)-expressing and KIT-signaling-driven mesenchymal tumors with an activating mutation in either KIT or PDGFRA (Platelet-Derived Growth Factor Receptor Alpha) (4–8). They represent about 5% of all sarcomas and are the most common mesenchymal neoplasm (80%) of the GI tract, even though they account for <3% of all GI cancers (9). They commonly occur in the stomach (50–60%) and the small intestine (20–30%), whereas sites such as the large intestine (10%), esophagus (5%) and other abdominal organs including mesentery and omentum (5%) can also be points of origin (5,10,11). Metastatic disease is present at diagnosis in about 50% and the most common metastatic sites are the liver and the peritoneum (5,12,13).

The gold standard therapy for local disease is surgery, and the treatment for metastatic disease is the tyrosine kinase inhibitor, imatinib mesylate (14–16). Here, we report a case of a patient presenting with diplopia due to a metastatic clivus GIST which was surgically removed and then treated with imatinib.

CASE REPORT

The patient was a 70-year-old male who complained of right side diplopia for 2 months. He visited our neurological outpatient clinic and had a computed tomography (CT), magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) done (Fig. 1). Initial radiographic finding suggested meningioma in the sella and the Rt cavernous sinus, with differential diagnosis being invasive pituitary macroadenoma or metastasis. As his diplopia was progressing rapidly, leading to decreased quality of life, it was decided that there was little time for systemic evaluation. So he was referred to our neurosurgery department, and emergency tumor resection via transsphenoidal approach was planned in order to relieve his visual disturbance.

The patient was admitted and transsphenoidal tumor resection was performed by collaboration between the

Figure 1. Initial brain computed tomography (CT) showing a clivus mass.

Figure 2. (A) Positron emission tomography CT showing primary stomach mass with multiple metastasis to the liver and lung. (B) Initial abdominal CT showing primary stomach mass and multiple liver metastasis.

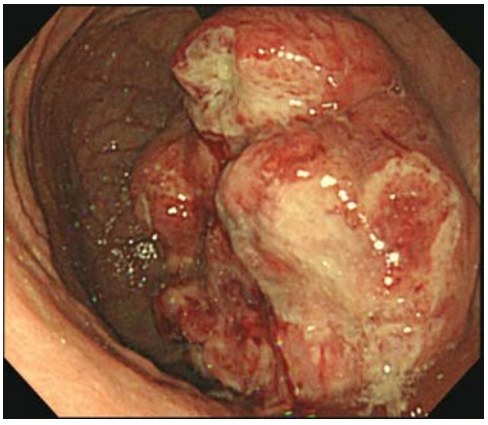

Figure 3. Gastrofibroscopy showing main stomach mass.

neurosurgery and otolaryngology departments. The tumor was subtotally removed and the sella floor and pituitary were intact from tumor invasion. Initial frozen biopsy results were consistent with meningioma or schwannoma. In order to rule out metastatic cancer, positron emission tomography (PET) CT was performed and results showed a primary stomach mass with multiple metastasis to the bone, liver and lung (Fig. 2). A gastrofibroscopy was done to confirm the main stomach mass (Fig. 3), and biopsy was performed. The stomach biopsy results were spindle cell tumor, compatible with GIST (Fig. 4), so immunehistochemistry staining of the clivus sample was done. The results were positive for CD34 and C-KIT with moderate cellularity, confirming C-KIT positive malignant GIST (Fig. 5). By the Miettinen classification, the main gastric mass measured 10 cm in the longest diameter, and the mitotic index was 20–22/50 hpf, with high risk of disease progression. It was decided to treat the patient with imatinib mesylate without any further surgery. Immediate post-op MRI showed main mass removal with remnant tumor in the Rt cavernous sinus. The patient was discharged without any complications.

Follow-ups are being done by the oncology and neurosurgery outpatient clinics. The patient has been taking imatinib mesylate for 2 months. The diplopia have improved within 15 days and a follow-up brain (Fig. 6) and abdominal CT have respectively shown complete regression of the Rt cavernous sinus mass and reduction of the main stomach mass. The patient is currently ongoing imatinib mesylate therapy without significant adverse effects.

DISCUSSION

GISTs represent about 5% of all sarcomas and are the most common (80%) mesenchymal tumors of the gatrointestinal tract, occurring predominantly in the stomach and small intestine (50–60 and 20–30%, respectively) with an annual incidence of 10–20 per million (4,5,17,18). Median age of onset is about 60, with no gender predilection (1,5,17). Although rare familial cases have been reported, the majority is sporadic in nature and the precipitating risk factors are unknown (19–23).

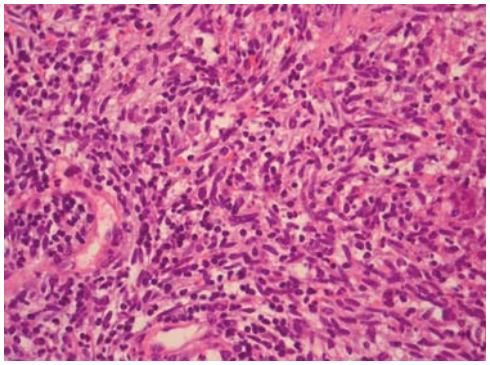

Figure 4. H&E stain (×400) showing spindle cells compatible with gastrointestinal stromal tumor.

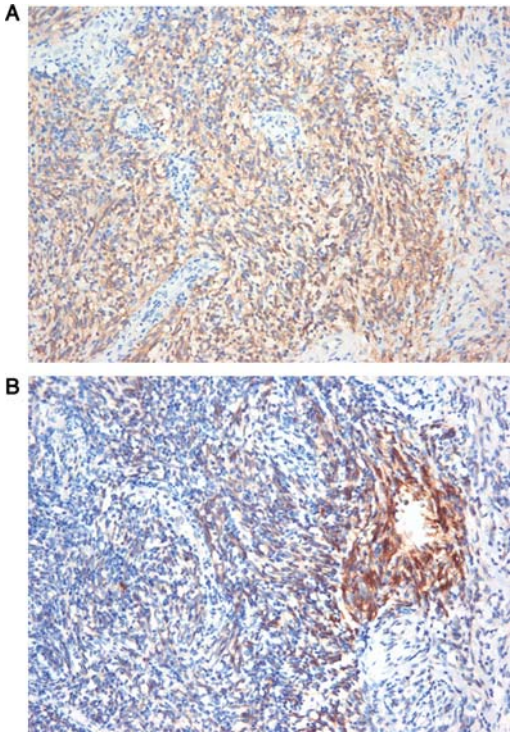

Figure 5. (A) CD34 positive stain. (B) C-KIT positive stain.

Although GISTs have an uncertain clinical behavior ranging from benign to malignant, they always have a malignant potential, even if they seem to be benign (15,24). The metastatic GIST is generally responsive to imatinib mesylate (16,25). Research of the relevant literature by internet leads us to believe that this is only the second case of clivus metastasis reported, with the first being a metastatic clivus GIST originating from the rectum. But the first case was KIT negative and the patient did not respond to imatinib and soon expired (26). Questions regarding the decision to go ahead with surgery and the effectiveness of imatinib can be asked. As the patient's diplopia was progressing rapidly, it was decided to go ahead with surgery as systemic evaluation would have taken too much time. Even if we had known that the clivus tumor was a metastatic GIST, we probably would have progressed with surgery as imatinib takes time to take effect. However, surgery did not immediately relieve the patient's diplopia and the symptoms persisted up to 1 month after the operation. Generally, metastatic tumors to the clivus show poor prognosis, and the sixth nerve palsy rarely improves, even after surgery (27–29). It is worth noting that the diplopia of our patient improved only 15 days after the start of imatinib therapy and follow-up study after 2 months of treatment shows no evidence of disease in the clivus and marked improvement of the main gastric GIST. To the best of our knowledge, our case is the first case of KIT-positive gastric GIST metastatic to the clivus with remarkable improvement with imatinib.

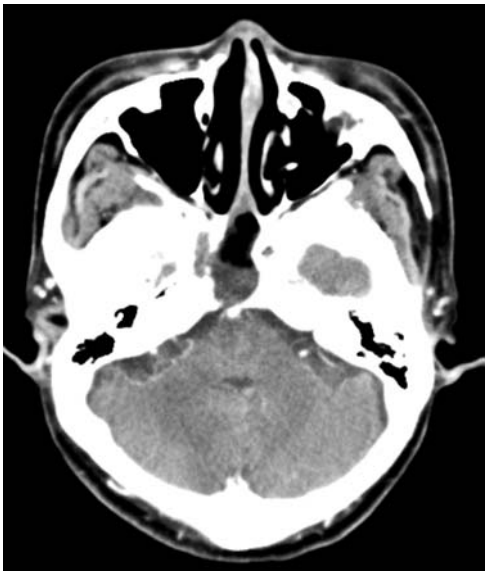

Figure 6. Follow-up brain CT at post-op 3 months showing no sign of tumor recurrence.

CONCLUSION

We report here a case of a GIST metastatic to the clivus, initially presenting with diplopia, which was first transsphenoidally resected and then systemically treated with oral imatinib. The diplopia of our patient improved only 15 days after the start of imatinib therapy. After 2 months of treatment, there is no evidence of disease in the clivus and marked improvement of the main gastric GIST. We think this is the first KIT-positive gastric GIST metastatic to the clivus responsive to imatinib.

Conflict of interest

None declared.

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