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Case report

Orbital metastasis from a gastrointestinal stromal tumor: A case report

Yan Yu[1], Xiaoqian Ji[1], Wei Li, Changfan Wu*

Department of Ophthalmology, Yijishan Hospital of Wannan Medical College, Wuhu, 241000, China

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ABSTRACT

Background: Gastrointestinal stromal tumor (GIST) is the most common primary mesenchymal tumor. The most common metastasis sites are the liver and the surface of the peritoneum. In this study, we present a case of orbital GIST metastasis.

Case presentation: A 43-year-old woman who had a history of small intestinal stromal tumor 4 years ago suffered GIST metastasis to the left orbit. MRI confirmed the presence of a lacrimal gland lesion with isointense on T1 and hyperintense on T2 weighted images. Histopathology analysis of the tumor showed predominantly spindle or oval cells with nuclear pleomorphism and increased mitoses. The tumor also stained positive for c-KIT (CD117) upon immunochemistry, confirming the diagnosis.

Conclusions: GISTs typically occur as sporadic solitary tumors, and their common metastasis sites are the liver and the surface of the peritoneum. Orbital involvement is extremely rare. The orbital GIST metastatic tumor has special imaging properties, as evidenced by histopathology, immunochemistry, and magnetic resonance imaging (MRI).

1. Introduction

Gastrointestinal stromal tumor (GIST) is the most common primary mesenchymal tumor. The most common metastasis sites are the liver and the surface of the peritoneum[1]; orbital metastasis of GIST is very rare.[2–4] In this study, we report the third case of an orbital GIST metastasis, as confirmed with histopathology and immunohistochemistry, as well as the patient's clinical manifestation and MRI characteristics.

2. Case report

In July 2013, a 43-year-old woman was referred to the hospital. She presented with left eye proptosis and vision loss of about one month. She had undergone surgical resection of a small intestinal stromal tumor in 2009 and partial resection of liver metastatic tumors in 2011. Histopathology showed GIST with cells that were spindle or oval in shape and had apparent nuclear pleomorphism and mitotic count (0–5/100HPF) in the hepatic caudate lobe and right posterior lobe of the liver. Immunohistochemistry demonstrated that AE1/AE3, EMA and Des were negative. CD117, DOG-1 and S-100 proteins were positive. CD34 and Ki-67 were mildly positive.

In the ophthalmic examination, the visual acuity was 20/20 in her right eye and 20/40 in her left eye. The intraocular pressure was right eye,16.0 mmHg, left eye, 25.0 mmHg. External examination revealed a left proptosis of 6 mm. Ocular movement was limited in all directions. The left orbital tension was slightly higher. A fundus examination revealed the optic nerve head and retinal edema in the left eye (Fig. 3). The right eye and the systemic examination were normal.

On 24 July 2013, the orbit was scanned with magnetic resonance imaging (MRI). MRI confirmed the presence of a lacrimal gland lesion which was isointense to eye muscles on T1-weighted images and hyperintense on T2 weighted images (Fig. 2B and Fig. 2C). Coronal T1-weighted strengthened scanning images after gadolinium injection showed enhancement (Fig. 2A). The ultrasound pattern also showed a well circumscribed homogenous hypoechoic mass in the superior aspect of the left orbit without retinal detachment. Orbital metastasis increased the intra-orbital tension, resulting in optic disc and retinal edema. Optical coherence tomography (OCT) showed optic disc and retinal neuroepithelium edema (Fig. 3).

The patient underwent lateral orbitotomy and lumpectomy after one week. The mass was exposed and revealed a moist, soft, gelatinous, and fleshy-pink tissue at the top of the left outside of the orbit. In the case operation, the orbital metastatic tumor was a large amount of gelatinous reddish tissue, and the texture of the tumor was fragile due to the lack of fibrous stroma. Postoperative left exophthalmos and eye movement returned to normal. Upon ophthalmic examination post-

* Corresponding author. Department of Ophthalmology, Yijishan Hospital of Wannan Medical College, 92 West Zheshan Rd, Wuhu, 241001, PR China.
E-mail addresses: 564868073@qq.com (Y. Yu), 42100053@qq.com (X. Ji), siisii98@gmail.com (W. Li), wucangfan@sina.com (C. Wu).
[1] These authors have made equal contributions.

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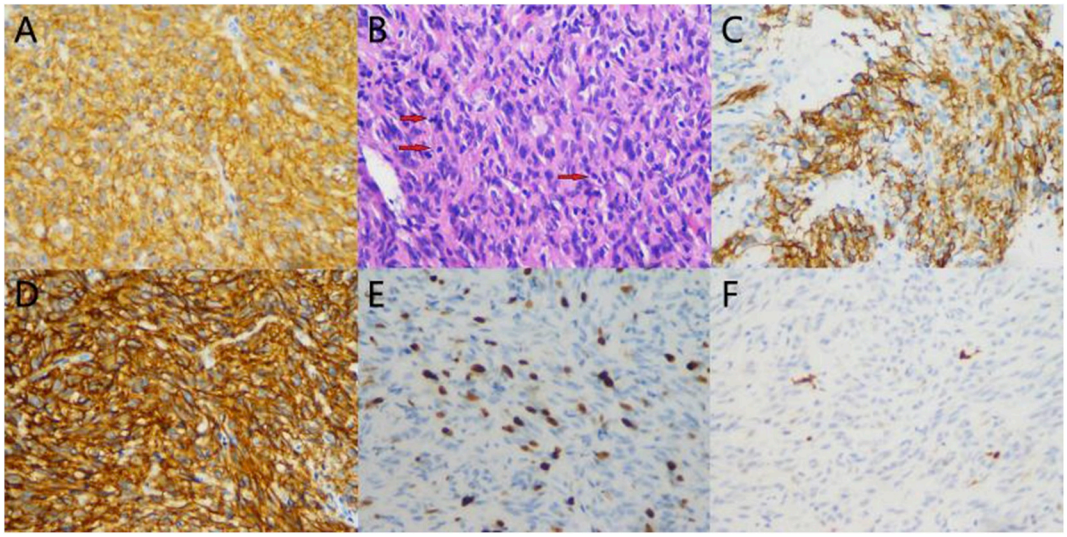

Fig. 1. At high power (400 ×), immunohistochemical staining was positive for CD117 (400 ×) in the orbital metastasis (Fig.1A). At a high power (400 ×), hematoxylin and eosin staining of the tumor revealed a cellular neoplasm composed of sheets of epithelioid and spindled cells, with round or oval nuclei. The nuclei of the tumor cells were unusual upon digital microscopy. Here, abnormal mitoses are indicated with arrows in the photograph (Fig.1B). At high power (400 ×), immunohistochemical staining was partly positive for CD34 in the orbital metastasis (Fig. 1C). At high power (400 ×), immunohistochemical staining was positive for DOG-1, KI-67 and S-100 in the orbital metastasis (Fig. 1D, E and F).

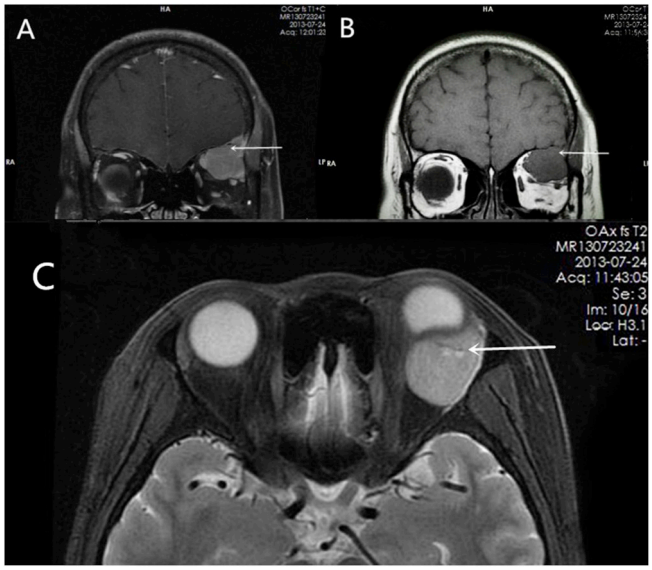

Fig. 2. MRI confirmed the presence of a lacrimal gland lesion with isointense to eye muscles on T1 and hyperintense on T2 weighted images (Fig. 2B and .C). Coronal T1-weighted strengthened scanning images after gadolinium injection showed enhancement (Fig. 2A).

operation, the visual acuity was 20/20 in her right eye and 20/25 in her left eye. The fundus examination after the operation revealed that the optic nerve head and retinal edema had disappeared in the left eye. A histopathological examination (HPE) of the specimen was reported as a metastatic GIST. Hematoxylin and eosin staining of the tumor revealed a cellular neoplasm composed of sheets of epithelioid and spindled cells, with round or oval nuclei. The nuclei of the tumor cells were unusual upon digital microscopy imaging. Here, abnormal mitoses are indicated with arrows in the photograph (Fig. 1B). Immunohistochemical staining showed that c-KIT (CD117) (Fig. 1A), bcl-2 and DOG-1 were positive (Fig. 1D), and weakly positive for SMA, S100,Ki-67 and CD34 (Fig. 1F, E and 1C). However, CD99, Calretinin, ALK-1 and PR were negative. These results paralleled the expression of the liver tumors. The postoperative diagnosis was a left orbital metastasis of GIST. After leaving the hospital, the patient had no orbital oncology recurrence six months at follow-up. Apart from the liver, whole body bone emission computed tomography (ECT) in July 2014 reveled concentrated radionuclide in the right shoulder blade. The patient has been taking Glivec since 2004.

3. Discussion

GIST is the most common primary mesenchymal tumor and is derived from the directional differentiation of mesenchymal cells in the gastrointestinal tract from the esophagus to the rectum.[1] GIST represents 0.1–3% of gastrointestinal malignancies. Of these malignancies, 60–70% occur in the stomach, and 20–30% occur in the small intestine. It can occur at any age, but occurs primarily in people 50 years old or older. The incidence between men and women is similar. Research suggests that the main driver of GIST pathogenesis, occurrence and development is KIT (CD117) and/or PDGFRA mutations.[5] Intraperitoneal direct dissemination and metastasis to the liver from hematogenous are the most common methods, while lymph node metastasis is rare. The recurrence interval of GIST after operation is 19–25 months.[6] Because of its high rate of recurrence and metastasis after operation, a combination of surgery and molecular-targeted drugs have become the primary treatment of recurrent and metastatic GIST.[7]

Orbital metastasis of the primary tumor occurs more in breast, lung, liver and prostate cancers. However, orbital metastasis derived from GIST is rare. Few studies have reported orbital GIST metastasis. Akiyama et al. reported the case characteristics of magnetic resonance imaging and computed tomography scanning of GIST metastasis involving the optic nerve and superior orbit with no biopsy diagnosis from orbital tissue. Computed tomography (CT) of the left orbit revealed a space-occupying, high-density mass extending from the left optic canal to the left cavernous sinus. MRI confirmed that the tumor involved the orbital apex and the greater wing of the sphenoid bone.[2] Li LF et al. demonstrated a case with GIST metastasis to the skull and orbit. CT scanning showed that the left orbital roof and part of the left temporal bone were eroded by the tumor. Immunohistochemistry was positive for CD117 and CD34. The patient received external beam irradiation and continued on Nilotinib after surgical excision of the orbital mass.[3] David Woo et al. described case features including computed tomography imaging, histopathology and immunohistochemistry

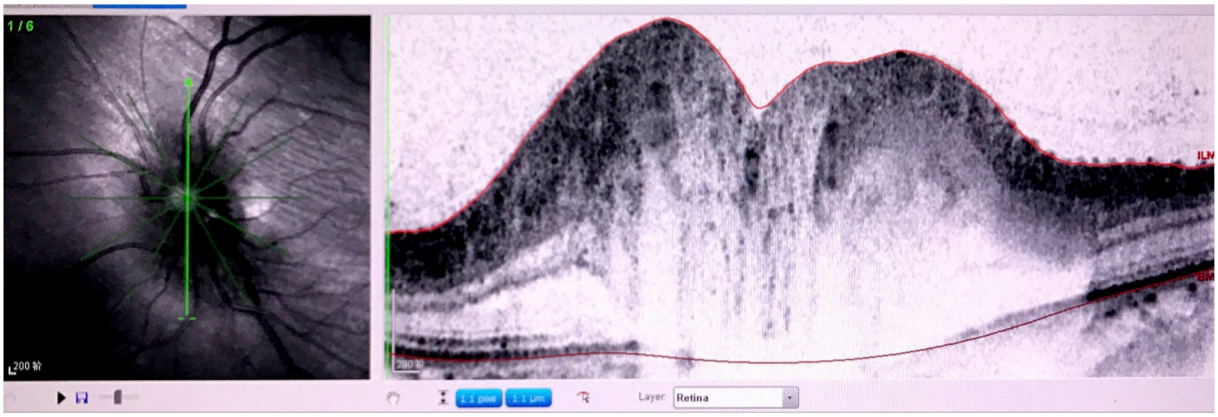

Fig. 3. Optical coherence tomography (OCT) vertical scanning showed optic disc and retinal edema.

of GIST metastasis to the anterior orbit. The patient had metastatic GIST involving the left orbit with a history of two separate GIST nodules involving the stomach 6 years earlier. CT scanning demonstrated a well circumscribed enhancing lesion confined to the anterior orbit.[4] In 2018, Roelofs et al. presented a case of bilateral orbital gastrointestinal stromal tumor metastasis, which was only the second histopathologically confirmed case of GIST metastasis to the orbit and the only case to develop bilateral orbital metastasis. The left and right eye metastasis interval was 8 months. The patient had taken Imatinib 400mg daily for about 6 years.[8] In comparison, our patient was admitted to the hospital with proptosis and vision loss. The patient underwent surgeries of the small intestinal stromal tumor and liver stromal tumor in 2009 and 2011, respectively. The recurrence intervals and the time described in the literature are the same. On MRI, the tumor involved the lacrimal gland. The lesion was hyperintense on T2-weighted and isointense to eye muscles on T1-weighted images. Coronal T1-weighted strengthened scanning images showed homogenous enhancement after contrast gadolinium injection. This is the first case to be confirmed with histopathology and immunohistochemistry of a GIST metastasis to the lacrimal gland. The same immunohistochemical results (taken twice) confirmed that the metastatic orbital tumors derived from GIST. CD117 positivity is used as one of the diagnostic criteria for malignant GIST, and has been reported as the gold standard for the diagnosis of GIST.[9] The 93.55% positive rate of CD117 was much higher than CD34, which was up to 83.26%, and was used as a surrogate for the biological behavior of the tumor.[10] In our case, the tumor cell expressed the c-KIT (CD117) and DOG-1 proteins. DOG-1 is a necessary complement to the diagnosis of GIST which has good sensitivity and specificity, and its expression is independent of KIT mutations under the negative expression of CD117. At present, there is no standard treatment for a metastatic tumor of the orbit, which has a poor prognosis due to resistance to both chemotherapy and radiation.[11]Both age and gender will impact the prognosis of GIST. Klaus et al. found that GIST patients older than fifty years showed significantly worse disease specific survival (DSS) compared to younger females.[12] This case patient underwent a local surgical treatment and achieved ocular symptomatic relief without recurrence as evidenced by orbital MRI during the six-month follow-up visit.

In summary, this case was confirmed as a malignant GIST that metastasized to the orbit as confirmed by immunohistochemical stain. Orbital MRI provided additional GIST images and the patient achieved symptomatic control after further surgery.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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Conflicts of interest

The following authors have no financial disclosures: (Yan Yu, Xiaoqian Ji, Wei Li, Changfan, Wu).

Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Authors' contributions

Yan Yu drafted the manuscript and collected data. XJ drafted and edited the manuscript. WL performed the clinical review of the patient and edited the manuscript. CW conducted the research. All authors read, reviewed and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2019.100528.

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