Solitary choroidal metastasis of distal cholangiocarcinoma: A case report

YUKIO SHIMOJIMA[1,2], YUKI HIROSE[1,3], TATSUYA NOMURA[1], KABUTO TAKANO[1], HIROAKI HARA[4], TAKEO BAMBA[1], MASAKI AIZAWA[1], HITOSHI NOGAMI[1], ATSUSHI MATSUKI[1], SATOSHI MARUYAMA[1], YASUMASA TAKII[1], HIROSHI YABUSAKI[1], JUN SAKATA[3], TOSHIFUMI WAKAI[3], SHUNICHI SHIOZAWA[2] and SATORU NAKAGAWA[1]

[1]Department of Digestive Surgery, Niigata Cancer Center Hospital, Niigata 951-8566; [2]Department of Surgery, Tokyo Women's Medical University, Adachi Medical Center, Tokyo 123-8558; [3]Division of Digestive and General Surgery, Niigata University Graduate School of Medical and Dental Sciences, Niigata 951-8510; [4]Department of Ophthalmology, Niigata Cancer Center Hospital, Niigata 951-8566, Japan

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Abstract. Metastatic choroidal carcinoma is rare and generally has a poor prognosis. The present case report describes a case of choroidal metastasis from distal cholangiocarcinoma, which was successfully managed using stereotactic radiotherapy (SRT). A 67-year-old Japanese man underwent pancreaticoduodenectomy for distal cholangiocarcinoma. The pathological stage was T2N0M0 stage IIA, according to the Union for International Cancer Control 8th edition. After surgery, the patient received adjuvant chemotherapy with oral TS-1® for 1 month. A total of 2 months after surgery, the patient was readmitted to hospital due to decreased visual acuity. Fundoscopy revealed a macular hole in the right eye that accounted for the decreased visual acuity. Additionally, Goldmann three-mirror contact lens examination revealed a 4-mm choroidal mass with a yellowish color situated at a considerable distance from the optic nerve. Magnetic resonance imaging revealed an enhanced choroidal mass. Based on the findings of ophthalmologic examinations and the patient's history of cholangiocarcinoma, they were diagnosed with choroidal metastasis from distal cholangiocarcinoma. SRT was administered at a total dose of 40 Gy divided into 8 Gy fractions. A total of 1 year after SRT, the patient achieved complete remission without decreased visual acuity. The patient remains alive and in good health without recurrence, 4 years after the diagnosis of choroidal metastasis. To the best of our knowledge, this is the second reported case of intraocular metastasis from cholangiocarcinoma. In conclusion, SRT may provide an opportunity to control metastatic choroidal carcinoma without decreasing visual acuity.

Correspondence to: Dr Yuki Hirose, Division of Digestive and General Surgery, Niigata University Graduate School of Medical and Dental Sciences, 1-757 Asahimachi-dori, Chuo-ku, Niigata 951-8510, Japan
E-mail: y-hirose@med.niigata-u.ac.jp

Abbreviations: CT, computed tomography; CA19-9, carbohydrate antigen 19-9; PD, pancreaticoduodenectomy; MRI, magnetic resonance imaging; SRT, stereotactic radiotherapy; EBRT, external-beam radiotherapy

Key words: choroidal metastasis, intraocular metastasis, distal cholangiocarcinoma, biliary tract cancer, SRT

Introduction

Intraocular cancer metastasis is rare. The most common site of intraocular metastasis is the uvea, which includes the choroid, iris, and ciliary body. Choroidal metastases account for 62-88% of intraocular metastases (1). In a study of 420 patients with uveal metastases, the primary lesions were as follows: breast cancer (47%), lung cancer (21%), liver cancer (14%), gastric cancer (9%), and colorectal cancer (2%) (2). Meanwhile, biliary tract caner is quite rare as a primary lesion of intraocular metastasis. To date, there was only one case reported in 2003 who had choroidal metastasis from cholangiocarcinoma (3).

Several therapeutic options for intraocular metastasis have been reported, including chemotherapy, photocoagulation, radiation therapy, or enucleation. However, there exist no data showing the survival advantage among them (4,5). Thus, there is no consensus about the treatment modality for intraocular metastasis in terms of survival, while preserving visual acuity and keeping quality of life hold the priority in the treatment selection.

Stereotactic radiotherapy (SRT) is a noninvasive treatment modality, and potentially has advantage in preserving the normal function compared with other invasive treatment methods (6). Thus, SRT was initially applied for focal intracranial vascular lesions and small neoplasms (6). Recently, SRT has been applied for the treatment of intraocular tumors considering the ability to reduce tumor margins and to preserve critical normal structures around the tumor (6). Herein, we reported a case of choroidal metastasis from distal cholangiocarcinoma, which was successfully treated utilizing SRT without decreasing the visual acuity.

Case report

A 67-year-old Japanese man with elevated liver enzyme levels was admitted to Niigata Cancer Center Hospital (Niigata, Japan) in February 2017. Multidetector-row computed tomography (CT) revealed dilation of the biliary tree and a 10-mm enhanced nodule in the distal bile duct (Fig. 1). He underwent percutaneous transhepatic biliary drainage via the left segment III of the intrahepatic bile duct. Prior to surgical resection, tumor markers of serum carcinoembryonic antigen and carbohydrate antigen 19-9 (CA19-9) levels were within the normal range. Thereafter, the patient underwent pancreaticoduodenectomy (PD) and regional lymphadenectomy. Intraoperative frozen section examination of the proximal margin of the bile duct revealed an invasive carcinoma. The proximal margin was additionally resected, and the final pathological diagnosis of the proximal margin confirmed the presence of carcinoma *in situ*. The pathological stage of the distal cholangiocarcinoma was T2N0M0 Stage IIA, according to Union for International Cancer Control 8th edition (Fig. 2). Pathological examination revealed that the tumor was poorly differentiated adenocarcinoma measuring 45x20 mm, exhibiting lymphatic invasion and perineural invasion. Following the PD, the patient received adjuvant chemotherapy with oral TS-1® at 100 mg/day (Taiho Pharmaceutical, Tokyo, Japan) for 1 month. Subsequently, after 2 months of the PD, he was readmitted to our hospital due to decreased visual acuity. Fundoscopic examination revealed a macular hole in the right eye, which was determined to be the cause of the visual acuity decline. Furthermore, Goldmann three-mirror contact lens examination revealed a 4-mm, yellowish choroidal mass (Fig. 3). The tumor was considered unrelated to the decreased visual acuity due to its location far from the optic nerve. Magnetic resonance imaging (MRI) revealed a 4-mm enhanced choroidal mass (Fig. 4). Positron emission tomography CT exhibited no remarkable findings that indicated recurrence. Based on the results of these ophthalmological examinations and the patient's history of distal cholangiocarcinoma, he was diagnosed with choroidal metastasis from distal cholangiocarcinoma. Photocoagulation was initially performed for the choroidal lesion. However, this was insufficient due to the location of the tumor. Therefore, the patient underwent stereotactic radiotherapy (SRT) with a cumulative dose of 40 Gy administered in 8 Gy fractions. At the initiation of SRT, serum CA19-9 level was elevated to 55.2 U/ml. Following 1 year of the radiotherapy, the choroidal lesion became obscured, and a complete remission was successfully achieved with SRT (Fig. 5). Following SRT, serum CA19-9 level returned to the normal range. He had been regularly followed up every 6 months as an outpatient with ophthalmologic examinations, contrast-enhanced abdominal CT scans, and orbital MRI scans. The patient remains alive and in good health, showing no signs of recurrence, 4 years after the diagnosis of choroidal metastasis.

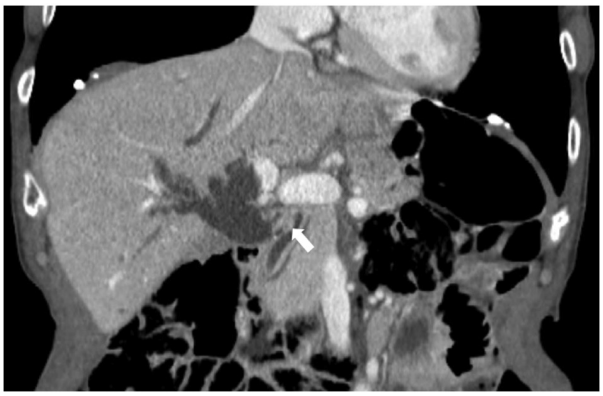

Figure 1. Image acquired from multi detector-row computed tomography revealing dilation of the biliary tree and a 10-mm enhanced nodule (arrow) in the distal bile duct.

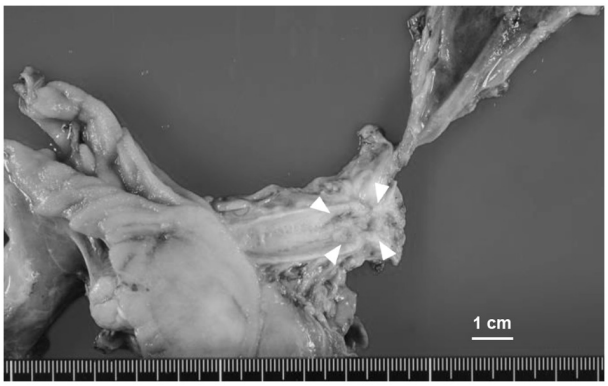

Figure 2. Surgically resected specimen showing a tumor (arrowheads) located in the distal bile duct.

Discussion

The occurrence of cancer metastasis within the intraocular region is rare. Choroidal metastases constitute a significant majority of intraocular metastases, ranging from 62 to 88% (1). Generally, patients with choroidal metastasis exhibit poor prognosis; median survival time of patients with choroidal metastasis is reported to be 4.2 months in pancreatic cancer, 11.5 months in lung cancer, 12.4 months in gastrointestinal cancer, and 22.2 months in breast cancer (7). To the best of our knowledge, this is the second reported case of intraocular metastasis from cholangiocarcinoma (3), and he exhibited no evidence of recurrence 4 years after the curative treatment for choroidal metastasis.

The chief complaints of patients with choroidal metastasis are blurred vision (81%), flashes and floaters (5-12%), and eye pain (5-14%); however, 9-11% of those with choroidal metastasis exhibit no symptoms (1). In the present case, the patient was referred to our hospital due to decreased visual acuity. However, the choroidal mass was considered to be unrelated to the patient's complaint because the tumor was distant from the optic nerve and a macular hole was suspected as the cause instead.

Most choroidal tumors are either malignant melanomas or metastatic tumors. Macroscopic appearance is valuable for clinically discriminating between the two types of tumors. Malignant melanomas typically exhibit a dark blackish color, whereas metastatic choroidal tumors tend to display a yellowish color. In the present case, Goldmann three-mirror contact lens examination revealed a 4-mm choroidal mass with a yellowish color, which supported the diagnosis of metastatic

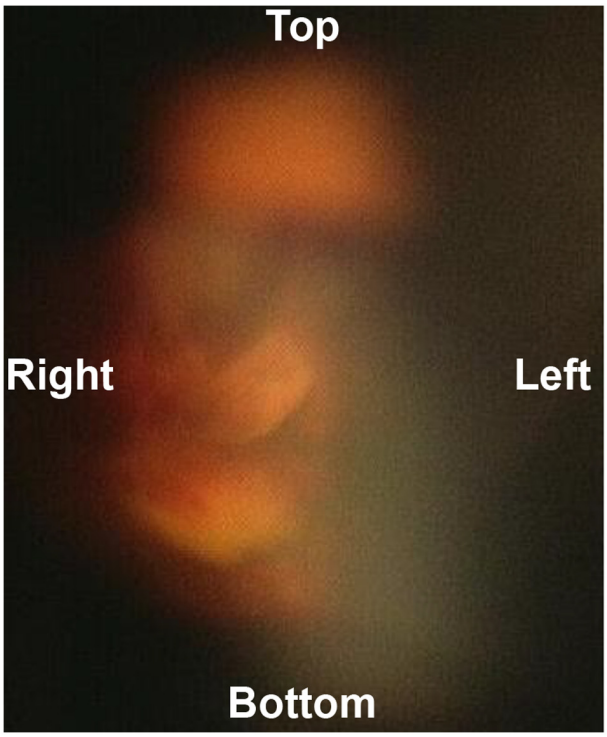

Figure 3. Image of Goldmann three-mirror contact lens examination revealing a 4-mm yellowish choroidal mass.

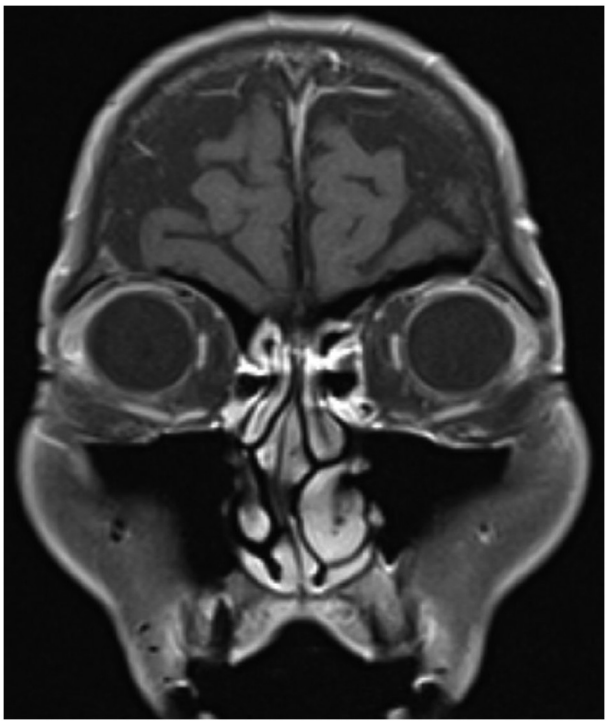

Figure 5. Image acquired from magnetic resonance imaging performed 1 year after stereotactic radiotherapy revealing metastatic choroidal tumor becoming obscured.

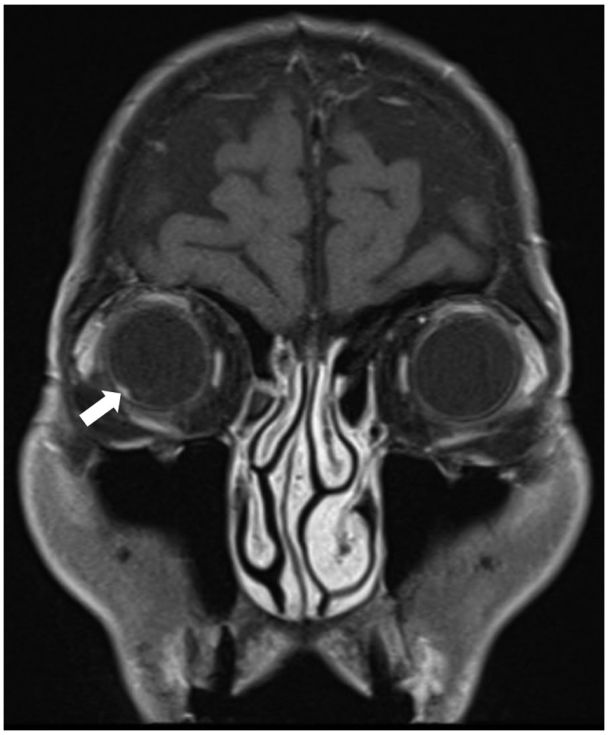

Figure 4. Image acquired from magnetic resonance imaging performed before stereotactic radiotherapy revealing an enhanced choroidal mass (arrow) measuring 4 mm in diameter.

choroidal tumor. However, it is important to note the existence of a variant of melanoma, known as amelanotic melanoma, which does not exhibit a blackish color but rather presents as pink, red, or brown lesion, thereby resembling a metastatic choroidal tumor in terms of gross coloration. In the present case, serum CA19-9 level, an established tumor marker for adenocarcinoma, was elevated at the initiation of SRT for the choroidal tumor. Considering the macroscopic characteristics of the choroidal tumor and the elevated serum CA19-9 level, the patient was diagnosed with choroidal metastasis from distal cholangiocarcinoma. Considering the aforementioned information, even for small choroidal masses measuring <5 mm, the macroscopic coloration of the choroidal tumor can serve as a useful feature in distinguishing between malignant melanoma and metastatic choroidal tumors. Nevertheless, in the absence of histologic examination, several clinical factors, such as gross observations, imaging findings, and tumor markers, should be considered to discriminate between the two.

No established standard treatment for choroidal metastasis is available (8). Treatment options for choroidal metastasis encompass chemotherapy, photocoagulation, radiation therapy, or enucleation. However, these treatment modalities do not result in significant variations in survival outcomes (4,5). Thus, prioritizing the preservation of visual acuity and enhancing quality of life is a crucial goal in the treatment of choroidal metastasis. Therefore, various radiation therapies have been employed.

One such approach is external-beam radiotherapy (EBRT), which is a conventional treatment for uveal metastasis that was first used in 1979 (9). The response rate to EBRT for choroidal metastases, defined as tumor shrinkage or visual stabilization, is approximately 80% (10,11). The recommended dose typically ranges from 26 to 46 Gy (median, 38.4 Gy) (12,13). Nonetheless, complications including cataracts, exposure keratopathy, iris neovascularization, radiation retinopathy,

and radiation papillopathy are relatively common with EBRT. Approximately 12% of patients experience complications over a median follow-up period of 5.8 months (11), and the incidence of these complications is dose-dependent: 0% at doses ≤30 Gy and 100% at doses ≥57 Gy (13,14). A disadvantage of EBRT is the need for daily treatment for 2-4 weeks (15).

SRT is a non-invasive treatment option for choroidal metastases. Meticulous computerized treatment planning and accurate repositioning based on high-resolution orbital CT can reduce tumor margins and preserve critical structures, such as the optic nerve, lens, and lacrimal gland (6). In addition, SRT provides low-dose radiation from multiple directions with high accuracy (16). Therefore, patients can receive treatment aimed at minimizing the adverse effects of radiation on surrounding normal tissues. Haidar *et al* (17) conducted SRT for choroidal metastases from breast cancer with a total dose of 25 Gy in 5 Gy fractions for 5 days. They reported that the patient's vision remained stable, and no recurrence was reported for 3 years following SRT of the choroidal metastases (17). Bellmann *et al* (6) treated 10 patients with unifocal choroidal metastases (3 breast carcinomas, 3 lung carcinomas, 3 colon carcinomas, and 1 cutaneous melanoma) using SRT with a single dose ranging from 12 Gy to 20 Gy or a total dose of 30 Gy over 10 days (3 Gy per session). They reported that local tumor control was achieved in all patients during follow-up periods ranging from 1 month to 34 months (median, 6.5 months) (6). In the present case of choroidal metastasis from distal cholangiocarcinoma, the patient underwent SRT with a total dose of 40 Gy administered in 8 Gy fractions over 5 days. The patient remains alive and in good health without any evidence of recurrence or signs of decline in visual acuity, 4 years after the diagnosis of choroidal metastasis. This suggested that SRT could be a viable treatment option for choroidal metastases, facilitating local tumor control while minimizing the adverse effects of radiation.

Even after curative resection for distal cholangiocarcinoma, 5-year survival rate ranges from 18 to 54% (18). This unfavorable prognosis can be attributed to the high recurrence rate after resection, with over 50% of patients experiencing distant metastasis within 5 years of curative resection (19). In the case of periampullary cancer, perineural invasion and lymph node metastasis have been identified as independent predictive factors for distant metastasis after curative resection (20,21). In the context of distant cholangiocarcinoma, Komaya *et al* (18) demonstrated that perineural invasion, pancreatic invasion, and lymph node metastasis were independent prognostic factors for time taken for recurrence after resection, while Kim *et al* (19) reported that poor differentiation and lymph node metastasis were predictors of distant metastasis. In the present case, the primary tumor exhibited poor differentiation and perineural invasion. Therefore, in cases of histologically-confirmed poor differentiation, perineural invasion, or lymph node metastasis following resection for distal cholangiocarcinoma, a close follow up utilizing tumor markers and imaging studies is recommended.

To the best of our knowledge, this is the second reported case of intraocular metastasis of cholangiocarcinoma. SRT may provide an opportunity to control metastatic choroidal carcinoma without decreasing the visual acuity.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

YS, YH, TN, KT, HH, TB, MA, HN, AM, SM, YT, HY, JS, TW, SS, and SN participated in the conception and design for the paper. YS and YH drafted and revised the manuscript, and are responsible for the paper. HH provided advice on ophthalmic findings and contributed to the writing of the manuscript. TN, JS, TW and SS critically revised the paper. TN, KT, and HH interpreted the imaging data. YS and YH confirm the authenticity of all the data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The patient provided written informed consent for the publication of the data.

Competing interests

The authors declare that they have no competing interests.

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