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Case Report

Oxaliplatin-Associated Amaurosis Fugax

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Keywords
Oxaliplatin · S-1 + oxaliplatin · Amaurosis fugax · Ocular toxicity

Abstract
Oxaliplatin-associated amaurosis fugax has not been reported, and its clinical course and treatment remain largely unclear. A 70-year-old man with advanced gastric cancer was treated with the SOX regimen. After cycle 1 of oxaliplatin infusion, the patient realized that his right eye had visual field impairment, which he described as darkening of the right half of his visual field and loss of vision lasting about 1 min and occurring about 7 times a day. The daily frequency of this occurrence gradually decreased, and his visual field impairment improved in 1 week. However, as the same symptoms recurred from cycle 2 to cycle 5 of treatment, oxaliplatin was discontinued from cycle 6 and switched to S-1 monotherapy. Subsequently, the patient's amaurosis fugax improved. To our knowledge, this is the first report describing clinical course and treatment of oxaliplatin-associated amaurosis fugax.

Introduction

Oxaliplatin, a third-generation platinum analog, is widely used in the treatment of various cancers including colorectal and gastric cancers [1, 2]. While the most common adverse effects associated with oxaliplatin are neurotoxicity (acute, chromic, and persistent) and delayed hypersensitivity reactions [3], and ocular toxicity has been reported as an infrequent adverse event associated with oxaliplatin [4]. We herein report a case of oxaliplatin-associated amaurosis fugax.

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Case Report/Case Presentation

A 70-year-old man who complained of nausea, vomiting, and weight loss was referred to our hospital for examination and treatment. He had a history of hyperthyroidism, diabetes, hypertension, osteoporosis, infectious uveitis, and retinal detachment. Computed tomography revealed thickening of the gastric wall from the gastric body to the prepyloric region, as well as retention of food residues (Fig. 1). Esophagogastroduodenoscopy revealed friable and irregular mucosa, and a depressed lesion extending from the gastric antrum to the lower body (Fig. 2a). An esophagogastroduodenoscopy biopsy revealed poorly differentiated adenocarcinoma (por) (Fig. 2b). Surgery was performed for preoperative diagnosis of undifferentiated advanced gastric cancer. Total gastrectomy was initially planned but then was abandoned during the operation in favor of gastrojejunostomy because of a strong adhesion to the head of the pancreas. Systemic chemotherapy with the SOX regimen (S-1, 120 mg/day on days 1–14; oxaliplatin, 170 mg on day 1) was initiated as treatment because the patient tested HER2-negative in immunohistochemical staining.

After cycle 1 of oxaliplatin infusion, the patient realized that his right eye had visual field impairment, which he described as darkening of the right half of his visual field and loss of vision lasting about 1 min and occurring about 7 times a day. The daily frequency of this occurrence gradually decreased, and his visual field impairment improved in 1 week. No visual field impairment occurred in the left eye. Since the same symptoms recurred from the second to the fifth cycle of treatment, we consulted with an ophthalmologist. An ophthalmologic

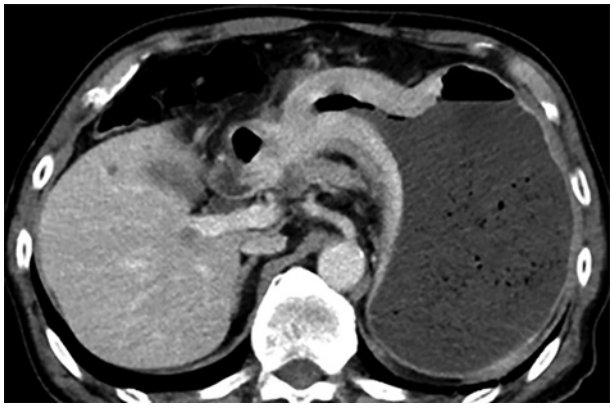

Fig. 1. CT findings. CT revealed thickening of the gastric wall from the gastric body to the prepyloric region as well as retention of food residues. CT, computed tomography.

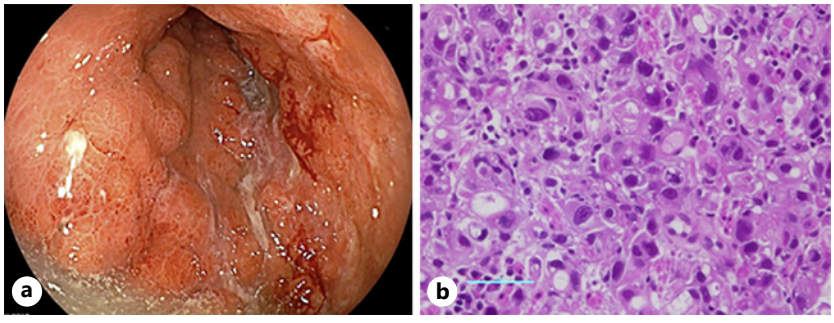

Fig. 2. Endoscopic findings and a histopathological examination of the biopsy specimens. **a** EGD revealed friable and irregular mucosa, and a depressed lesion extending from the gastric antrum to the lower body. **b** Histopathological examination of biopsy specimens showed poorly differentiated adenocarcinoma (por) (×400) (scale bar, 50 μm). EGD, esophagogastroduodenoscopy.

examination revealed no obvious damage to the retinal and optic nerves. The patient showed no abnormal findings in the brain or around the orbit on magnetic resonance imaging (MRI) (Fig. 3a, b), no stenosis or aneurysm in the internal carotid artery or ophthalmic artery on 3D-MRI (Fig. 3c), and no plaque or stenotic lesion in the bilateral carotid arteries on carotid artery ultrasound. Thus, the ophthalmologist arrived at the diagnosis of amaurosis fugax, but without mentioning its cause or recommending any specific treatment. His clinical course led us to suspect oxaliplatin-associated amaurosis fugax and to discontinue oxaliplatin and switch to S-1 monotherapy from cycle 6. Subsequently, the patient's amaurosis fugax improved.

After an improvement shown after cycle 6 in gastric wall thickening on computed tomography, total gastrectomy was performed with D2 lymph node dissection. The gastric lesion in the patient was diagnosed as tubular adenocarcinoma, well-differentiated type (tub1 > tub2), 45 × 13 mm, ypT3 (SS), ly0, v1, N0, M0, grade 1b, stage IIA. The patient underwent adjuvant chemotherapy with S-1 and has shown no recurrence for 6 months. In addition, no visual field impairment occurred since.

Discussion/Conclusion

Our case has 2 important clinical implications. First, amaurosis fugax may occur as an adverse event associated with oxaliplatin, while the clinical course and treatment of amaurosis fugax associated with oxaliplatin remain largely unclear, with no reports available in the literature.

Given that ocular toxicity associated with cancer chemotherapy has a great impact on quality of life, its timely recognition contributes to better patient management [5]. A study of oxaliplatin-associated neurotoxicity using an interview-based questionnaire reported blurred vision, ptosis, eye pain, and visual field cuts in 10–15% of all specific symptoms [6]. To date, 9 cases of oxaliplatin-associated ocular toxicity have been reported (males/females, 3/6; mean age, 56.9 years) (Table 1) [7–11]. Ocular toxicities included visual field impairment (n = 6) (tunnel vision, 3; visual loss in the lower half of visual field, 1; visual loss from the peripheral to central visual field, 1; and blurred vision, 1) and blepharoptosis (n = 3). Ocular symptoms are reported to have improved in all patients with the following treatments: oxaliplatin discontinuation (n = 7), prolonged oxaliplatin administration time (n = 1), and spontaneous improvement (n = 1). In the present case, visual field impairment affecting the right half of the right eye occurred after administration of oxaliplatin and improved after its discontinuation. In addition, visual field impairment did not recur after S-1 monotherapy. Therefore,

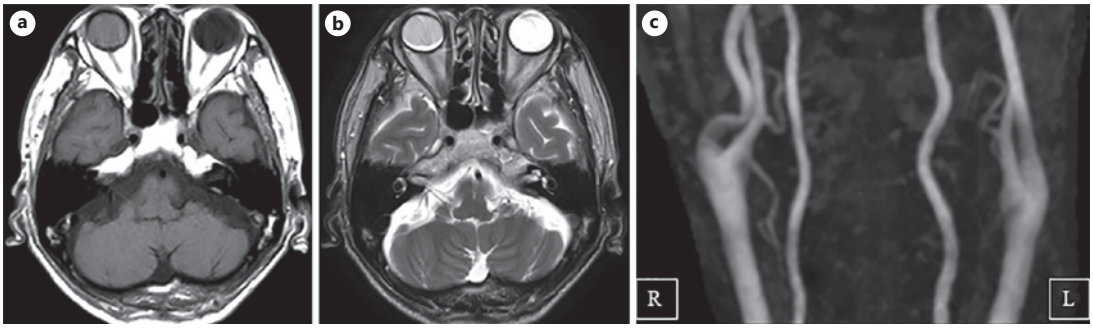

Fig. 3. MRI findings. **a**, **b** MRI showed no abnormal findings in the brain or around the orbit. **c** 3D-MRI showed no stenosis or aneurysm in the internal carotid artery or ophthalmic artery. MRI, magnetic resonance imaging.

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Table 1. Cases reported to date of oxaliplatin-associated ocular toxicities

No.	Ref.	Year	Age, years	Sex	Regimen	Cycle*	Ocular toxicity	Treatment
1	[7]	2006	45	F	FOLFOX	3	Visual loss affecting the peripheral to central visual field	Oxaliplatin was discontinued. After 4 months, ocular toxicity improved and oxaliplatin was restarted. There was no recurrence of the symptom
2			57	M	FOLFOX	1	Tunnel vision	Oxaliplatin was discontinued from cycle 4, and the symptom improved
3			52	M	Oxaliplatin monotherapy	2	Tunnel vision	Oxaliplatin was discontinued, and the regimen changed, and the symptom improved
4			29	F	FOLFOX	1	Visual loss affecting the lower half of the visual field	Oxaliplatin was discontinued, and the regimen changed, and the symptom improved
5	[8]	2007	58	F	FOLFOX	2	Blepharoptosis	The symptom improved spontaneously Oxaliplatin was discontinued, and there was no recurrence of the symptom
6			72	F	Oxaliplatin monotherapy	1	Blepharoptosis	The symptom improved spontaneously Oxaliplatin was continued without recurrence of the symptom
7	[9]	2009	76	F	EOX	2	Blepharoptosis	The time spent administering oxaliplatin was extended from cycle 6, and the symptom improved
8	[10]	2010	52	F	FOLFOX	3	Blurred vision and altered color vision	The symptom improved progressively 3 weeks after chemotherapy was discontinued
9	[11]	2019	71	M	FOLFILINOX	1	Tunnel vision of the right eye	With change of the chemotherapeutic regimen, there was no recurrence of the symptom
10	Our case	2021	70	M	SOX	1	Visual loss affecting the right half of the visual field in the right eye	Oxaliplatin was discontinued from cycle 6 and there was no recurrence of the symptom

FOLFOX, oxalipatin + fluorouracil + leucovorin; EOX, epirubicin + capecitabine + oxaliplatin; FOLFIRINOX, oxaliplatin + irinotecan + fluorouracil + leucovorin; SOX, S-1 + oxaliplatin.

*Chemotherapy cycle number at appearance of symptoms.

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the patient was diagnosed with oxaliplatin-associated amaurosis fugax, based on the ophthalmologist's diagnosis.

The other implication was that carotid artery lesions were excluded in diagnosing amaurosis fugax. It has been reported that causes of amaurosis fugax include carotid artery lesions, heart disease, coagulation abnormalities, and vasculitis, 88% of which are closely related to carotid artery lesions [12], where microembolism in carotid artery stenosis or occlusion often leads to occlusion of the ophthalmic artery [13]. In the present case, carotid plaque and stenosis were excluded by MRI and carotid artery ultrasound. While oxaliplatin has been reported to lead to damage to the retinal pigment epithelium and the optic nerve [10], with no abnormalities found in the retinal and optic nerves in our case, the mechanism of oxaliplatin-associated amaurosis fugax remain unclear. To the best of our knowledge, this is the first report describing the clinical course and treatment of oxaliplatin-associated amaurosis fugax.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose in association with this study.

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Author Contributions

K.K., N.K., R.W., M.H., M.T., and M.K. contributed equally to the study as well as to the preparation of the manuscript for publication.

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