Case Report

Amaurosis Fugax: A Rare Oxaliplatin-Induced Ocular Toxicity – A Report of Three Cases

Mutahar Ali Tunio^a Karen Phillips^b Peter Baker^c

^aColorectal Division, Swansea Bay University Health Board, Swansea, UK; ^bColorectal Division, Hywel Da University Health Board, Carmarthen, UK; ^cClinical Pharmacy, Hywel Da University Health Board, Carmarthen, UK

Keywords

Oxaliplatin · Toxicity · Ocular · Amaurosis fugax

Abstract

Oxaliplatin, a third-generation platinum-based agent, is a constitutive part of systemic treatment for colorectal cancer in adjuvant and metastatic settings. Ocular toxicity is an extremely rare adverse effect of Oxaliplatin. Ocular toxicities have been documented in the form of (a) common ($\geq 1/100$, $< 1/10$) which include the conjunctivitis, unexpected lacrimation, blurry vision, blepharoptosis, and (b) uncommon ($\geq 1/10,000$, $< 1/1,000$) which compromise the tunnel vision, idiosyncratic color perception, transient bilateral visual loss, and rarest phenomenon of Amaurosis fugax. Amaurosis fugax implies to any cause of transient, painless, unilateral visual loss; with the possible underlying mechanism of thrombo-embolic carotid plaque, hypoperfusion, or vasospasm of retinal vessels, due to hyperviscosity, and atherosclerotic vascular disease. To date, only a few case reports of Oxaliplatin-induced Amaurosis fugax have been published. We here-in report 3 cases who experienced Amaurosis fugax while receiving Oxaliplatin in our one of health board-based four hospitals.

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Introduction

Oxaliplatin is a third-generation platinum analogue, which is commonly prescribed in combination with fluorouracil/folinic acid, or capecitabine during adjuvant treatment in stage III, and as the first-line treatment in metastatic colorectal cancers [1]. An Oxaliplatin-induced

Correspondence to:
Mutahar Ali Tunio, mutahaar.ali@wales.nhs.uk

ophthalmic adverse event is extremely infrequent with only a few related cases have been reported. This toxicity is often short-lived, reversible, and may manifest with a range of symptoms [2]. During a retrospective assessment of 55 patients with Oxaliplatin-induced ocular toxicity, Noguchi et al. [3] explored that a total of 18.2% experienced Oxaliplatin-induced eye toxicities. Blepharoptosis was the most common event that occurred in 9.1%, followed by visual field defects including tunnel vision in 3.6%, decreased visual acuity in 3.6%, eye pain in 1.8%, conjunctival congestion in 1.8%, excessive lacrimation 1.8%, and blurred vision in 1.8% [3].

Amaurosis fugax is repeatedly used interchangeably to narrate transient visual loss and refers to transient, unilateral, and painless loss of vision. Possible underlying mechanisms for Amaurosis fugax are thrombo-embolic carotid plaque, hypoperfusion, or vasospasm of retinal vessels, due to hyperviscosity in hematological disorders, and atherosclerotic vascular disease [4]. Oxaliplatin-induced Amaurosis fugax is the rarest ocular adverse event; to date, only a few case reports of Oxaliplatin-induced Amaurosis fugax have been published [5]. We here-in report 2 cases, who experienced Amaurosis fugax while receiving Oxaliplatin in one of our health board based four hospitals.

Case Report/Case Presentation

Case 1

In May 2021, a 52-year-old man presented with rectal bleeding, which he had for the last 3 months associated with abdominal pain and weight loss of 10 kg over the same period. During colonoscopy, he was found to have a rectal mass 10 cm from the anal-verge. Histopathology confirmed moderately differentiated adenocarcinoma. Magnetic resonance imaging (MRI) pelvis showed a semicircular growth of 4.3 cm in a cranio-caudal direction in length in mid rectum with signs of extra-mural venous invasion with some peri rectal nodes more than 8 mm away from the mesorectal fascia. CT thorax, abdomen, and pelvis were negative for distant metastasis. The radiological stage was cT3N1M0. No significant previous medical history. He underwent anterior resection in July 2021. Histopathology showed grade 2 adenocarcinoma infiltrating the bowel wall to reach peri-colic fat, 4/12 nodes were involved, R0 resection, evidence of lymphovascular invasion, and extra-mural venous invasion. The final pathological stage was made pT3N2aMx. After a multidisciplinary team meeting, it was decided to propose four cycles of CAPOX (capecitabine/Oxaliplatin) adjuvant chemotherapy. Two days after Oxaliplatin infusion, he experienced acute right eyesight loss episodes occurring about 7–9 times initial lasting for a few minutes, but the last episode remained for more than 20 min. The left eye was completely normal. The immediate ophthalmological assessment was carried out, which confirmed no obvious damage to the retina and optic nerve. MRI brain with orbits showed no abnormalities in the brain parenchyma, or any stenosis or aneurysm in carotids and ophthalmic arteries. CT angiogram was also found normal. A diagnosis of Amaurosis fugax was made by combined ophthalmology and neurology experts, without any further follow-ups or any specific treatment. Two weeks later, he was assessed in the oncology. He denied any further episodes of ocular events. Further adjuvant chemotherapy was stopped upon his request as he was quite concerned about the ocular events. Surgical follow-ups were requested as a continuation of care.

Case 2

In March 2021, a 26-year-old man presented in the emergency department with severe recurrent abdominal pains with significant loss of weight. CT thorax, abdomen, and pelvis revealed ascending colon circumferential thickening with enhancement, along with mesenteric nodes

and extensive bilobar liver lesions. Liver biopsy confirmed adenocarcinoma of colon origin (CK7 negative, CK20 positive), MSI stable, RAS wild type. Serum carcinoembryonic antigen was 109 µg/L. After a multidisciplinary colorectal, and hepatobiliary meetings, it was decided to treat with FOLFORINOX (flourouracil/folinic acid/Oxaliplatin/irinotecan) chemotherapy, with dose modifications due to deranged liver function tests (alkaline phosphatase 593, AST 70). One day after the third cycle of Oxaliplatin infusion, he initially observed blurred vision for a few hours followed by complete loss of vision of the right eye, which remained for at least 10 min without any pain. Ophthalmological and neurological assessment was unremarkable. Radiological images were negative for any abnormalities. He was discharged from the hospital without any specific treatment. Ocular events were never reported again from him till his cycle 6th cycle, where his disease progressed further in the liver, and was transferred to the palliative care department upon his wishes.

Case 3

A 54-year-old lady who was treated for locally advanced rectal adenocarcinoma T3N1M0 with neoadjuvant chemoradiation in March 2019. Immediately after completing her chemoradiation, she developed isolated lung metastasis. She underwent anterior resection in June 2019, followed by wedge resection for right upper lobe lung metastasis. Histopathology confirmed ypT3N0 (0/16 lymph nodes), M1 (lung metastasis). After a multidisciplinary meeting, she consented for 8 cycles of CAPOX in December 2019. During the second cycle, 3 days after Oxaliplatin infusion, she had blurred vision followed by right eye visual loss for 30 min, along with some peripheral neuropathy. After this brief episode, she was fully recovered. Ophthalmological and radiological assessments were unremarkable. Following this event, Oxaliplatin was discontinued, and she was treated with capecitabine monotherapy till cycle 5, when she had progression in the lungs, and was switched to irinotecan-based chemotherapy. No further ocular event was recorded.

Discussion/Conclusion

Ocular adverse effects of Oxaliplatin are rare. A questionnaire-based analysis about Oxaliplatin-related neurotoxicity mentioned approximately 10–15% experience ocular events in form of blurred vision, ptosis, eye pain, and visual field defects [6]. Oxaliplatin-induced Amaurosis fugax or sudden, transient, painless unilateral visual loss is exceptionally uncommon ocular toxicity. Table 1 has illustrated Oxaliplatin-based visual field defects, bilateral visual loss, and Amaurosis fugax. Although transient in nature, Oxaliplatin-induced Amaurosis fugax has a significant impact on the quality of life, as our first patient, who was extremely scared of this ocular event, and refused continuation of adjuvant chemotherapy.

The exact mechanism is not well understood. The postulated mechanism for Oxaliplatin Amaurosis fugax could be related to the vasospasm of retinal vessels (vasospastic); similarly to Type 1 acute neurotoxicity, which develops immediately following Oxaliplatin infusion, and is signified by transient paresthesia and muscular spasm, often aggravated by exposure to cold. Detailed Ophthalmic assessment with scanning laser Doppler flowmetry may be helpful in this scenario [9]. Atherosclerotic plaque of carotid or ophthalmic artery as a possible underlying factor was excluded to some extent by CT and MRI; however, the role of the angiogram is yet to be decided in such transient event [10].

The course of Oxaliplatin-induced Amaurosis fugax is similar to acute neurotoxicity; rapid, transient and may worsen with the continuation of Oxaliplatin, and fully resolves without recurrent episodes after the discontinuation of culprit drug [2, 7]. Treatment is supportive; as in our cases, no specific medication was given. Role of Aspirin in Oxaliplatin-induced Amaurosis fugax is not reported in the previous report [5] and is subject to further research.

Table 1. Oxaliplatin-induced visual field defects, visual loss, and amaurosis fugax

Reference	Age/gender	Chemotherapy regimen	Cycle	Ocular event	Treatment/outcome
O'Dea et al. [2]	Case 1: 45 years/female	Case 1: FOLFOX	Case 1: 3	Case 1: Bilateral visual loss	Oxaliplatin was discontinued, symptoms resolved fully without re-appearance
	Case 2: 57 years/male	Case 2: FOLFOX	Case 2: 1	Case 2: tunnel vision	
	Case 3: 52 years/male	Case 3: Oxaliplatin monotherapy	Case 3: 2	Case 3: tunnel vision	
	Case 4: 29 years/female	Case 4: FOLFOX	Case 4: 1	Case 4: visual loss lower half of visual fields	
Kubo et al. [5]	71 years/male	SOX	1	Amaurosis fugax right eye	Symptoms recurred in 2nd to 5th cycles 100% resolution of symptoms discontinuation of Oxaliplatin
Noor et al. [6]	71 years/male	FOLFIRINOX	1, 2	Complete loss of vision in the right eye followed by tunnel vision	Symptoms recurred in 2nd cycle, full resolution of symptoms discontinuation of Oxaliplatin
Mesquida et al. [7]	52 years/female	FOLFOX	3	Blurred vision and altered color vision	Fully resolved discontinuation of Oxaliplatin
Ah-Thiane et al. [8]	Case 1: 51 years/female	Case 1: FOLFOX	Case 1: 1	Case 1: bilateral visual loss	Case 1: complete recovery discontinuation of Oxaliplatin Case 2: fully resolved/discontinuation of Oxaliplatin
	Case 2: 57 years/female	Case 2: FOLFIRINOX	Case 2: 3	Case 2: Right eye visual loss	
Our cases 2021	Case 1: 52 years/male	Case 1: CAPOX	Case 1: 1	Case 1: visual loss right eye	Case 1: complete recovery / discontinuation of Oxaliplatin Case 2: complete recovery / discontinuation of Oxaliplatin at cycle 5 after disease progression Case 3: fully recovered. No recurrent episode Oxaliplatin was discontinued
	Case 2: 26 years/male	Case 2: FOLFIRINOX	Case 2: 3	Case 2: visual loss right eye	
	Case 3: 54/female	Case 3: CAPOX	Case 3: 2	Case 2: Blurred vision and right eye visual loss	

In conclusion, Oxaliplatin-induced ocular toxicity is rare; and Amaurosis fugax is rarest in patients receiving Oxaliplatin. Thus, clinicians should be aware of this transient but frustrating unusual toxicity to reach prompt diagnosis and management to avoid permanent damage.

Statement of Ethics

This case series was granted an exemption from requiring ethics approval from Swansea Bay University Health Board Ethical Committee. Written informed consents were taken from patients (cases 1 and 2), and next of kin (case 3) for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M.A.T., K.P., and P.B. contributed equally to the study as well as to the preparation of the manuscript for publication.

Data Availability Statement

Patient data are confidential and its access available to clinical oncology staff in our health boards.

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