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Case Report

Case Report: Vision Loss Induced by Capecitabine in Patient with Preexisting Left Eyes Blind

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Keywords
Capecitabine · Vision loss · Antineoplastic agents · Rectal cancer · Toxicity

Abstract
Capecitabine is an orally administered fluoropyrimidine carbamate antineoplastic agent, widely used to treat different tumor types. Eye toxicity is not well established with this type of drug. Here, we report the case of a 57-year-old man with a low rectal cancer whose vision decreased 3 weeks after starting a daily treatment of capecitabine and radiotherapy. After eliminating all other diagnoses, toxicity of antineoplastic agents remains the most likely hypothesis, making it the first case of vision loss induced by this capecitabine.

Introduction

Capecitabine is an orally administered fluoropyrimidine carbamate, widely used to treat gastrointestinal tumors and metastatic breast cancer [1]. Capecitabine is metabolized to the active agent fluorouracil via a 3-step process, involving the enzymes carboxylesterase, cytidine deaminase, and thymidine phosphorylase [2].

The most frequently reported toxicity of this prodrug of 5-fluorouracil (5-FU) is diarrhea, hand-foot syndrome, and hematological toxicity [3–5]. Eye irritation has been reported in 10 percent of patients receiving capecitabine [6].

However, vision loss has never been reported with capecitabine. We only find 2 cases of ocular irritation, with reversible decreased vision and corneal deposits, but without vision loss [6]. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material at https://doi.org/10.1159/000530402.

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In this article, we report the case of a 57-year-old man with a low rectal cancer diagnosed in October 2019. He was blind of the left eye since childhood due to amblyopia. The patient was overweight (height: 188 cm, weight: 104 kg with a body mass index evaluated at 29) and had no other comorbidities, with no regular drugs at the diagnosis. Staging showed a T3N + tumor with a 6-centimeter-height lesion in contact with the anorectal junction, associated with significant adenomegaly within the mesorectum. The initial extension assessment did not show any secondary distance lesions. A local multidisciplinary board decided to offer him a conformational 3D external radiotherapy treatment of 50 Gy, associated with oral capecitabine at a dose of 800 mg/m^2/12 h (CAP50 protocol). The treatment was realized between November and December 2019. There was no other concomitant medication for rectal cancer treatment (except from paracetamol for pain and metoclopramide for nausea). The patient went to the emergency department for reduced vision symptoms, 3 weeks after beginning the daily treatment of capecitabine and radiotherapy. The patient was hospitalized in the internal medicine department for carrying out explorations. A papillary pallor with a normal macula at the fundus eye was observed, as well as normal intraocular pressure and a superior nasale quadrantanopia.

Cerebral MRI with magnetic resonance angiography found an optic atrophy in both eyes and eliminated the possibility of an inflammatory optic neuropathy (ON), as well as infiltrative or compressive neuropathies. The sella turcica aspect was compatible with an ancient pituitary macroadenoma. Endocrine testing was normal. The lumbar puncture was also normal. Optical coherence tomography confirmed the optic atrophy through the loss of ganglion cells and thinned old-looking retina. Visual evoked potentials showed severe conduction abnormalities of visual pathways consistent with very severe axonal bilateral ON. Autoimmune and infection testing were also negative and corticotherapy did not improve the vision loss.

Different assumptions were evoked. First, a vitamin deficiency ON but the supplementation with B1, B6, B9, and B12 did not improve the visual function and there was additionally no deficiency in the blood testing. Vitamin supplementation was administrated intravenously for 5 days in hospital and then continued orally at home (vitamins B1, B6, B9, and PP). Second, a paraneoplastic ON or retinopathy was considered and further eliminated thanks to a TEP TDM (usually, choroidal metastases are the recognition of characteristic solid yellow choroidal tumors with subretinal fluid [7]). Analysis of a panel of 88 genes and sequencing of the mitochondrial genome were performed and found to be negative. Therefore, the hereditary hypothesis was also eliminated. In the end, and after all other diagnoses had been eliminated, toxicity of antineoplastic agents remained the most likely hypothesis.

Discussion/Conclusion

Capecitabine-induced vision loss had never been described to the best of our knowledge. However, the antimetabolite 5-FU has been used to control proliferation of retinal pigment epithelial cells and fibrocytes and is currently the subject of a multicenter clinical trial of its value in the control of scarring after glaucoma operations [8]. There appeared to be some toxicity of 5-FU to the ocular surface epithelium in the form of persistent epithelial defects.

Ophthalmological toxicity is well documented with targeted therapies such as anti-VEGF drugs [9] or MEK inhibitors, and more rarely with traditional antineoplastic agents [10, 11], though it has been reported with irinotecan [12]. The most prevalent symptoms include blurred vision, photophobia, epiphora, and ocular irritation, but vision loss is extremely rare.

One year after the onset of symptoms, the optic nerve atrophy is stable and persistent, confirmed by a new cerebral MRI. Almost 2 years after the visual impairment, the patient did not regain his sight. Basic vision rehabilitation will be initiated to help the patient in his daily living activities.

Finally, eye toxicity is common with different pharmacological cancer treatment, and ophthalmological follow-up may seem interesting for patients treated for a long-term cancer. Advising the patients of this lesser-known toxicity is essential.

To conclude, vision loss induced by capecitabine is an extremely rare side effect of this antineoplastic agent. In this article, we report the first case of vision loss induced by this prodrug. The physiological mechanism is not known, and further studies are required to better characterize this toxicity.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. The Ethical Review Board of Gustave Roussy Institute waived the need for ethical approval of this case report.

Conflict of Interest Statement

The authors have no conflict to declare.

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Author Contributions

Investigation and data curation: Paul Matte and Michel Ducreux; writing – original draft preparation: Paul Matte; and writing – review and editing: Michel Ducreux.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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