CASE REPORT

Bilateral Optic Disc Swelling Following Anastrozole Therapy

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ABSTRACT

A 56-year-old female with early-stage breast cancer, stage IA grade 1 endometrial cancer, and stage IC grade 1 ovarian cancer developed sudden-onset visual changes and right inferior visual field defect following anastrozole therapy. Examination revealed severe bilateral optic disc swelling and impaired visual acuity. Laboratory work-up was otherwise unremarkable. Anastrozole was discontinued and over the next month, patient had near-complete resolution of swelling in the right eye and improvement in the left eye. This is the only reported case of optic disc swelling following anastrozole therapy.

Keywords: Breast neoplasms, chemotherapy, optical coherence tomography, papilloedema, vision

INTRODUCTION

Anastrozole is a nonsteroidal aromatase inhibitor (AI), approved for use as adjuvant endocrine therapy in early-stage breast cancer in postmenopausal women. It acts by reversibly binding to the enzyme aromatase and interfering with steroidal hydroxylation, thereby inhibiting oestrogen synthesis.¹ We report a patient who was found to have bilateral optic disk oedema following initiation of anastrozole therapy. Despite widespread use of anastrozole, association with optic disk oedema has not been previously reported.

CASE REPORT

We report the case of a 56-year-old Caucasian female diagnosed simultaneously with oestrogen receptor

(ER)/progesterone receptor (PR)-positive infiltrating ductal carcinoma of the left breast, stage IA grade 1 endometrioid endometrial cancer, and stage IC grade 1 endometrioid ovarian cancer; status: post total abdominal hysterectomy and bilateral salpingo-oophrectomy (10/11), and four cycles of carboplatin and paclitaxel (completed 9 February 2012), and bilateral mastectomy (19 March 2012). She was started on anastrozole therapy on 16 April 2012. Her past medical history included hypercholesterolaemia, hypertension, and asthma, and other longstanding medications included atorvastatin, cetirizine, fluticasone, prnivil, montelukast, terbutaline, theophylline, levalbuterol, ondansetron, and prochlorperazine.

The patient developed subacute visual changes over the course of 2 weeks, noting crescent shapes in the right visual field. On 7 May 2012, she was seen by ophthalmology where she denied any visual flashes,

TABLE 1 Laboratory results.

Laboratory paramter	Value	Date obtained
PT	12.4	9 May 2012
PTT	24.9	9 May 2012
INR	1.0	9 May 2012
WBC	3.9	9 May 2012
Vitamin B12	822	11 May 2012
CSF Glucose	77	11 May 2012
CSF Protein	47	11 May 2012
CSF WBC	4	11 May 2012
CSF Oligoclonal bands	0	11 May 2012
NMO/AQP4-IgG	<1.6	14 May 2012
Anna-1,2,3 (serum)	Negative	14 May 2012
PCA-1,2,Tr (serum)	Negative	14 May 2012
Ampiphysin Ab	Negative	14 May 2012
CRMP 5 IgG (serum)	Negative	14 May 2012
Striational Ab	Negative	14 May 2012
Calcium channel Ab P/Q, N type	0.00	14 May 2012
AChR binding Ab (receptor)	0.00	14 May 2012
AChR ganglionic Ab	0.00	14 May 2012
Anti-glial nuclear Ab type 1	Negative	14 May 2012
Voltage-gated K channel Ab	0.00	14 May 2012
Ss-B	3	6 June 2012
RPR	Nonreactive	6 June 2012
CRP	11	6 June 2012
ESR	60	6 June 2012
ANCA IFA	<20	6 June 2012
Anti-nuclear IFA	160	6 June 2012
ACE-1	6.9	6 June 2012
Anti CCP IgG	4	6 June 2012
Anti-dsDNA Ab	<10	6 June 2012
Rheumatoid factors	8	6 June 2012
Ss-A	2	6 June 2012

curtain defects, or pain with eye movement. There were no focal neurological deficits on examination. Visual acuity (VA) was 20/100 20/25 OD/OS, fundus examination revealed 3+ 1+ optic disc oedema OD/OS without haem or cotton wools, and Humphrey visual fields (HVF) indicated a right eye central visual field defect. Magnetic resonance imaging (MRI) of brain and orbits was unremarkable without any evidence of enhancement or papillary protrusion. Anastrozole therapy was discontinued and the patient was referred to neuro-ophthalmology. Lumbar puncture on 11 May 2012 revealed a normal opening pressure of 20 cm H₂O and no evidence of malignant cells. Extensive work-up screening for autoimmune and infectious processes was unremarkable (Table 1). Optical coherence tomography (OCT) on 14 May 2012 was notable for severe bilateral swelling around the optic nerve (Figure 1). Global retinal nerve fibre layer (RNFL) thickness was 290, 196 µm (normal range: 82–111 µm) OD/OS. The patient was started on 60 mg prednisone for 1 week (14–20 May 2012), followed by a 1-week taper. Subsequent OCTs revealed improvement in RNFL values, and OCT on 11 June 2012 showed near-complete resolution of swelling in the right eye and improvement in the left (global RNFL

thickness = 99, 167 µm OD/OS). On 12 June 2012, the patient was started on 1 g intravenous (IV) Solu-Medrol for 3 days, followed by an oral steroid taper consisting of 3 days of 60, 40, 20, and 10 mg prednisone, and finished with 10 mg prednisone QOD (every other day).

On 17 December 2012, the patient was started on exemestane 25 mg daily, an oral AI, used as an adjuvant treatment in postmenopausal women with oestrogen receptor-positive early-stage breast cancer,² and was instructed to discontinue the drug if any visual changes occurred. On follow-up examination on 9 January 2013, OCTs revealed continued thinning of RNFL bilateral (global RNFL thickness = 52, 103 µm OD/OS), with VA 20/70 20/20 OD/OS, and the patient denied any new visual symptoms on current AI therapy.

DISCUSSION

We present the only reported case of optic disc swelling following anastrozole therapy, a serious adverse event possibly associated with a commonly used AI. Although both carboplatin and paclitaxel have been reported to be associated with papilloedema and macular oedema, respectively, the close temporal onset of visual symptomatology and OCT findings with initiation of anastrozole raises concern for anastrozole as the offending agent.^{3–5}

It is possible that the initiation of steroids could have contributed to the resolution of symptoms and improvement of the findings on OCT. Discontinuation of carboplatin and paclitaxel over 2 months prior to the onset of visual symptoms argues against either as the aetiology. Little is known about possible ocular affects of anastrozole; a cohort study has reported that it is associated with a larger optic disc cup size when compared with tamoxifen, although this was thought to be secondary to tamoxifen causing a reduction in disc cup ratio.⁶ In animal models, oestrogen deficiency has been reported to lead to an increased level of tumour necrosis factor-alpha (TNF-α) and endothelin-1, leading to a possible proinflammatory state in the vasculature.⁷ It is possible that the changes in oestrogen levels in our patient taking an AI led to changes in vasculature permeability and optic nerve swelling. Early recognition of this possible side effect may be crucial, as prompt discontinuation of the drug was associated with improvement of symptoms. In addition to adding to our understanding of a possible rare but serious side effect of anastrozole, our case also provides further evidence for use for OCT as a sensitive and noninvasive imaging technique that can help guide diagnosis in patients presenting with visual complaints.

FIGURE 1 Sequential OCT scans showing increased RNFL thickness and subsequent resolution. First row: 14 May 2012; second row: 11 June 2012; third row: 9 January 2013.

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Note: Figure 1 of this article is available in colour online at <http://informahealthcare.com/oph>.

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