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LETTER TO THE EDITOR

Risperidone-related bilateral cystoid macular oedema

Kleanthis Manousaridis · Rajen Gupta

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Dear Editor,
We report the first known case of bilateral cystoid macular oedema related to treatment with risperidone.

A 65-year-old woman presented with a 5-week history of bilateral visual blurring. She had a history of depression and chronic obstructive pulmonary disease. Past ocular history was uneventful. She was on treatment with salbutamol and tiotropium inhalers for her chronic obstructive pulmonary disease, and had commenced risperidone 4 months previously. Initially compliance was intermittent, but recently she had regularly taken 1 mg twice daily over the past 2 months.

Best-corrected acuity was 6/18 right and 6/12 left eye. Anterior segment examination revealed normal findings bilaterally. Vitreous, optic discs, retinal vessels, and retinal periphery were bilaterally normal on funduscopy. Bilateral cystoid macular oedema (CMO) was noted and confirmed angiographically and on optical coherence tomography (OCT) (Fig. 1a, b). Full blood count, erythrocyte sedimentation rate, C-reactive protein, angiotensin-converting enzyme, luetic serology, blood pressure, and blood sugar levels were all normal. No systemic or ocular cause for the CMO was found. Risperidone-induced CMO was considered, and the drug was discontinued. She rapidly noted visual improvement, and 2 weeks after discontinuation acuity was 6/6 right and 6/9 left eye. The CMO resolved bilaterally on funduscopy and OCT (Fig. 2a, b).

A number of drugs have been described as potential causative factors for maculopathy. Anti-psychotic phenothiazine-derived drugs are among them, and long-term use can cause retinal pigmentary disturbances involving the posterior pole, and loss of retinal pigment epithelium and choriocapillaris [1]. Second-generation anti-psychotics (also called atypical anti-psychotics) are now available, including risperidone. Risperidone is used for the treatment of schizophrenia, bipolar disorder, depression and behavior problems. It is extensively metabolized in the liver mainly through hydroxylation to 9-hydroxyrisperidone, which has pharmacological activity similar to that of risperidone. Plasma concentrations of risperidone, 9-hydroxyrisperidone, and risperidone plus 9-hydroxyrisperidone are dose proportional over the dosing range of 1 to 16 mg daily. Risperidone and its metabolites are eliminated via the urine and, to a much lesser extent, via the faeces. The half-life for the "active fraction" (risperidone +9-hydroxyrisperidone) is approximately 20 hours [2].

Ocular side-effects attributed to its serotonergic (5- HT_{2A}) antagonism have been reported such as post hallucinogen-like visual disturbance and adverse effects on saccadic eye movements [3, 4]. Atypical central retinal vein occlusion and intraoperative floppy-iris syndrome during cataract surgery have been associated with use of the drug [5, 6].

To our knowledge, no cases of risperidone-induced CMO have been reported in the English medical literature. In addition to its high affinity for serotonin receptors, risperidone blocks a_1- and a_2-adrenergic receptors as well as dopaminergic receptors [6]. Experimental animal studies suggest that adrenoceptor blockade has a vasorelaxing effect on ocular arteries [7]. It is, however, unknown whether risperidone-induced adrenoceptor blockade could cause disturbances of the vascular tone regulation and permeability in human retinal vessels in vivo, or if other mechanisms such as a direct effect of the drug on human retinal vascular endothelium could be involved.

This case emphasises the possibility of idiosyncratic reactions secondary to systemic medication, and the importance of including this in the differential. To confirm our

K. Manousaridis (✉) · R. Gupta
Ophthalmology Department, Royal Victoria Infirmary,
Newcastle upon Tyne Hospitals, NHS Foundation Trust,
Queen Victoria Road,
NE1 4LP, Newcastle upon Tyne, UK
e-mail: kleanthis.manousaridis@googlemail.com

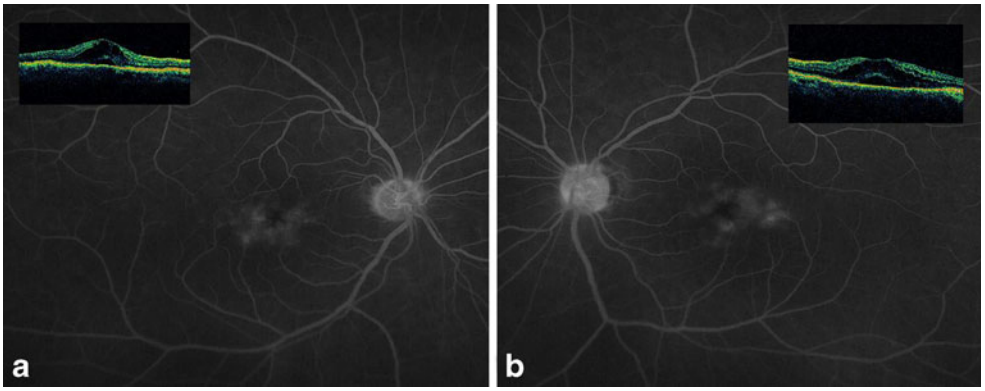

Fig. 1 **a**, **b** Fundus fluorescein angiography and OCT showing bilateral gross CMO

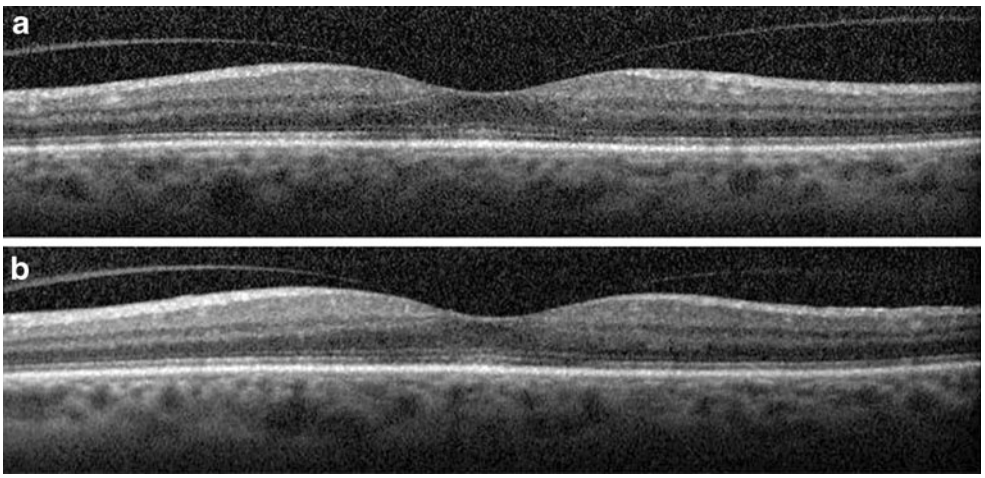

Fig. 2 **a**, **b** OCT 2 weeks after discontinuation of risperidone showing bilateral complete resolution of the CMO (**a**: right eye, **b**: left eye)

suspicions, ideally the patient would need to be re-challenged with risperidone. Clinically this was deemed inappropriate, and since no systemic or ocular cause was found and withdrawal led to CMO resolution, the cause was labeled as a probable adverse drug reaction using the criteria proposed by Naranjo et al. [8] to assess causality of adverse events by drugs. We recommend that in cases of CMO, clinicians should enquire about the use of risperidone, and consider discontinuation of treatment if no other cause is found.

Conflict of interest The authors declare no conflict of interest

References

1. Richa S, Yazbek JC (2010) Ocular adverse effects of common psychotropic agents. A review. CNS Drugs 24:501–526
2. Heykants J, Huang ML, Mannens G, Meuldermans W, Snoeck E, van Beijsterveldt L, Van Peer A, Woestenborghs R (1994) The pharmacokinetics of risperidone in humans: a summary. J Clin Psychiatry 55(Suppl):13–17
3. Lauterbach EC, Abdelhamid A, Annandale JB (2000) Posthallucinogen- like visual illusions (palinopsia) with risperidone in a patient without previous hallucinogen exposure: possible relation to serotonine 5-HT_{2A} receptor blockade. Pharmacopsychiatry 33:38–41
4. Sweeney JA, Bauer KS, Keshavan MS, Haas GL, Schooler NR, Kroboth PD (1997) Adverse effects of risperidone on eye movement activity: a comparison of risperidone and haloperidol in antipsychotic-naive schizophrenic patients. Neuropsychopharmacology 16:217–228
5. Agca A, Bayraktar Z, Cakr M, Bayraktar S, Ekinci O, Ylmaz OF (2008) Central retinal vein occlusion in a young adult during risperidone therapy. Retin Cases & Brief Rep 2:199–201
6. Ford RL, Sallam A, Towler HMA (2011) Intraoperative floppy iris syndrome associated with risperidone intake. Eur J Ophthalmol 21:210–211
7. Okamura T, Fujioka H, Ayajiki K (2002) Effects of nipradilol on alpha-adrenoceptor function in ocular arteries. Pharmacology 65:110–118
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ (1981) A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 30(2):239–245