

Niacin-Induced Cystoid Macular Edema

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INTRODUCTION

Cystoid macular edema is a retinal change caused by an accumulation of fluid in the fovea.¹ Retinal and choroidal abnormalities that develop because of untreated, chronic cystic macular changes may result in progressive loss of vision.² Several cases of niacin-induced cystoid macular edema have been reported.²⁻⁵ This article reports a case of this condition that was reversed upon discontinuation of niacin therapy.

CASE REPORT

A 58-year-old man had a documented history of carotid artery stenosis and elevated total and low-density-lipoprotein cholesterol. As a result of these risk factors for coronary artery disease, a regimen of niacin (nicotinic acid) was started to control the hyperlipidemia. A dosage of 2 g daily was used for nearly 1 year. The patient then increased the dosage to 3 g daily. Concomitant medications included acetylsalicylic acid, vitamin E, vitamin B₆, vitamin B₁₂, and occasionally chlorpheniramine maleate (4 mg) for allergic rhinitis. No medications were added after the patient started taking niacin. Approximately 2 months after increasing the dosage of niacin, the patient noticed that his vision had become blurry. Ocular examination in July 1999 revealed that the patient's visual acuity had decreased to OD 20/50 and OS 20/200; previous readings, obtained nearly 8 years earlier, were OD 20/25 and OS 20/20. There was mild anterior nuclear haze in the crystalline lenses and macular edema in each eye. The patient was referred to an ophthalmologist, who diagnosed binocular cystoid macular edema. The ophthalmologist suspected that the niacin had contributed to the cystoid macular edema. Niacin therapy was discontinued in July 1999. The patient noted gradual improvement in his vision. A follow-up examination with an optometrist in November 1999, 4 months after discontinuation of the niacin, revealed that visual acuity had improved to OD 20/25 and OS 20/40, and no cystoid macular edema remained in either eye.

DISCUSSION

The occurrence of niacin-induced cystoid macular edema is rare. One study of 300 patients followed over 9 years reported an incidence of 0.67%.² Most of the reported cases have been in men (ratio of males to females 10:1) in their third to fifth decade of life.³ Reports from the literature²⁻⁵ suggest that the onset of maculopathy ranges from 1 to 36 months after initiation of relatively high-dose therapy (3 g or more daily). There have also been reports of this condition with lower dosages (1.5 g daily).² This patient had increased the dosage of niacin to 3 g daily nearly 2 months before documentation of cystoid macular edema.

A validated causality assessment tool, the adverse drug reaction probability scale of Naranjo and others,⁶ was used to determine the likelihood of high-dose niacin therapy causing cystoid macular edema in this patient. The onset of symptoms coincided with the increase of niacin dose in a pattern similar to that reported in the ophthalmology literature.²⁻⁵ Although this patient had a history of carotid artery stenosis, he had not disclosed any history of venous occlusion or other vascular disorders that are known to cause cystoid macular edema.¹ None of the patient's other medications have been implicated as a cause of cystoid macular edema.^{1,7} Upon discontinuation of niacin therapy, the blurring of vision resolved and visual acuity improved. Unfortunately, fluorescein angiography was not performed. According to the scale of Naranjo and others,⁶ the sequence of events, niacin de-challenge, and lack of other potential causes of cystoid macular edema in this patient suggest a probable adverse drug reaction.

Aphakic cystoid macular edema has been reported in 30% to 77% of patients who have undergone cataract surgery.^{1,8} Vascular disorders such as diabetes mellitus, hypertension, collagen-vascular diseases, and vaso-occlusive diseases can lead to cystoid macular edema,^{1,9} as can inflammatory disorders such as toxoplasmosis, sarcoidosis or intermediate uveitis, tumours, and hereditary disorders such as retinitis



pigmentosa.¹ Niacin, epinephrine compounds, and latanoprost have been identified as toxic inducers of cystoid macular edema.^{1,7} There is some suggestion that the presence of pre-existing vascular or inflammatory disorders places patients undergoing cataract surgery at greater risk of postoperative cystoid macular edema.¹

The exact mechanism of niacin-induced cystoid macular edema is unknown. Several hypotheses have been proposed to explain the origin of the macular changes, which result in blurred vision, retinal thickening, or alteration of the foveal reflex (or any combination of these features).¹ In patients with vascular or inflammatory disorders, cystoid macular edema has been attributed to a prostaglandin-mediated process, which compromises the blood-retinal barrier.¹⁰ Breakdown of this barrier usually results in leakage, which can be observed on fluorescein angiography. The reported cases of niacin-induced cystoid macular edema suggest a different mechanism, as indicated by the lack of leakage observed on fluorescein angiography.²⁻⁵ Niacin-related maculopathy exhibits a distinctive appearance, with the inner retina wrinkled into a miniature sunburst and the foveola, at its centre, taking on a bright yellow hue.² Although Gass⁵ has described this bright yellow hue as an exudate, others believe that it more likely indicates accumulation of intracellular fluid.² One hypothesis suggests that some unknown derangement of intracellular metabolism leads to the intracellular accumulation of fluid, which results in cystoid spaces.¹¹ Cysts usually occur in a regular pattern around the rays of the sunburst in the foveal region and are smaller than those associated with cystoid macular edema of inflammatory or surgical origin.²

Alternatively, niacin has been proposed as having toxic effects on Müller cells,^{1,10} glial cells forming a framework that holds retinal tissue together.¹ The toxicity of niacin could cause swelling of the Müller cells and subsequent formation of cystic spaces between the glial spaces, without disruption of the blood-retinal barrier.¹ Because the exact mechanism of niacin-induced cystoid macular edema is unknown, it is unclear whether patients with pre-existing vascular or inflammatory disorders would be at greater risk of cystoid macular edema while taking niacin therapy.

Prophylactic ophthalmologic monitoring is not necessary for all patients receiving high-dose niacin therapy. It should be undertaken only for patients experiencing visual symptoms, such as blurred or decreased vision.²

First-line treatment for cystoid macular edema of toxic origin, such as that induced by niacin, is removal of the offending agent.⁴ Most reports indicate resolution of symptoms and of fundus findings about 4 to 8 weeks after the discontinuation of niacin therapy.² In milder cases of maculopathy, symptoms have resolved within a few days of drug discontinuation.²

Treatment for cystoid macular edema from other causes includes topical, systemic, or periocular corticosteroids or nonsteroidal anti-inflammatory drugs.¹ Immunosuppressive agents and surgery are also options in selected cases, depending on the cause of the cystoid macular edema.

Pharmacists can play a significant role in identifying niacin-induced cystoid macular edema by asking patients taking high doses of niacin about specific symptoms such as blurry or decreased vision.

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