A PREVIOUSLY UNDERRECOGNIZED BUT IMPORTANT SIDE EFFECT

By Stanley J. Berke, MD

I remember when Simmons Lessell, MD, stated the following during my glaucoma fellowship year (1985-1986) at the Massachusetts Eye and Ear Infirmary in Boston: “He who ignores the German literature discovers many new things.” His words rang in my head recently when a patient asked me, “Why is my left eyelid drooping?” My patient had a history of pseudoexfoliation glaucoma in his left eye only, and he had been using a prostaglandin analogue (PGA) drop in that eye only for more than 5 years (travoprost for 3.5 years, then bimatoprost for 1.5 years).

At first glance, the patient appeared to have marked ptosis of his left upper lid (Figure 1). On closer examination, however, he had only mild ptosis of the left upper lid but also exhibited marked deepening of the superior lid sulcus, relative enophthalmos (measuring 2 mm), inferior scleral show, periorbital fat atrophy, and involution of dermatochalasia. I subsequently observed these symptoms in the next few patients I saw who were using a PGA unilaterally (Figures 2 and 3). These changes were also present in most patients using PGAs bilaterally (Figure 4) but without the asymmetry.

I thought I had discovered a new side effect of PGAs, but a Google search led me to the page in Wikipedia about the fat-reducing properties of bimatoprost. Three articles listed in the reference section described my findings exactly,1-3 but they also revealed why I had not been aware of this complication. The first was written in German1; Dr. Lessell had been right. The second had appeared in an ophthalmic plastic surgery journal, and the third had appeared in an optometric journal. Further research led me to four more articles involving all three available PGAs by researchers in Korea, China, and England.4-7 I then found a good photographic example in a textbook coauthored by Wiley Chambers, MD, of the FDA. The figure was described as “allergic reaction to topical bimatoprost left eye.” It shows periorbital fat atrophy, deepening of the superior lid sulcus, ptosis, enophthalmos, and involution of dermatochalasia.8

IMPLICATIONS

Aside from the obvious cosmetic effects, prostaglandin-associated periorbitopathy (PAP) makes it difficult, if not impossible, to examine the eye or to perform applanation tonometry, surgery in the superior location, laser suture lysis, bleb needling, or argon/ selective laser trabeculectomy. In addition, some affected patients have undergone unnecessary medical and imaging workups to evaluate the visible asymmetry of their orbits and eyelids.

Topical PGA drops may play a role in the newly described tight orbit syndrome, which the article’s authors asserted is a cause of open-angle glaucoma.9 All six of the young patients were using one of the three currently available PGAs.

I myself have found that PAP is more apparent in young patients, probably because they have less dermatochalasia and orbital fat prolapse than elderly individuals. I therefore exercise and recommend caution in the prescription of PGAs for young patients and individuals with preexisting, anatomically deep-set eyes and tight lids.

The good news is that PAP seems to be reversible; I have seen its effects subside 1 to 3 months after patients discontinued using PGAs. It is also possible that PGA drops could benefit some patients with thyroid ophthalmopathy (medical decompression) or blepharochalasia (Figure 5).

Figure 1. A 62-year-old white man with pseudoexfoliation glaucoma in his left eye only had been treated with travoprost for 3.5 years and then bimatoprost for 1.5 years. In addition to the well-known side effect of longer eyelashes, he exhibited structural periorbital and lid changes consisting of mild ptosis, deepening of the superior lid sulcus, periorbital fat atrophy, inferior scleral show, relative enophthalmos, and involution of dermatochalasia.

Figure 2. A 60-year-old white woman had a well-functioning bleb in her right eye. She had been treated with latanoprost in her left eye only for 8 years.
A PREVIOUSLY UNDERRECOGNIZED BUT IMPORTANT SIDE EFFECT (CONTINUED)

REPORTS NEEDED

Since I posted my findings along with clinical photographs on the Web site of the American Glaucoma Society (AGS) on April 3, 2011, I have seen many more patients with PAP, either unilaterally or bilaterally. Many other members of the AGS have since made similar reports to the group. In early April, Dr. Chambers stated in an e-mail on the AGS.net that he was making a recommendation to all of the PGA manufacturers that they add the side effects of periorbital fat loss, deepening of the superior lid sulcus, etc., to their product labels.

It is important that clinicians report cases of PAP as an adverse event to all of the PGA manufacturers, the FDA (www.eyedrugregistry.com), and their medical societies. I would also encourage practitioners to share their cases with Louis Pasquale, MD, and me. Our goal is to increase awareness of PAP among physicians and patients.

Further research is needed to determine the frequency of PAP, how long it takes to occur, how long it takes to resolve after the discontinuation of topical PGAs, and any differences in PAP based on the patient’s age, his or her race/ethnicity, and/or the type of PGA used.

Stanley J. Berke, MD, is in private practice with Ophthalmic Consultants of Long Island in Lynbrook, New York. Dr. Berke is an associate clinical professor of ophthalmology and visual sciences at the Albert Einstein School of Medicine in Bronx, New York, and he is the chief of the Glaucoma Service at Nassau University Medical Center in East Meadow, New York. He is on the speakers’ bureaus of and has received research grants from Alcon Laboratories, Inc.; Allergan, Inc.; Merck & Co., Inc.; and Pfizer, Inc. Dr. Berke may be reached at (516) 593-7709, ext. 207; sberke@ocli.net.