Two for the Price of One

How did a simple trip to the optometrist for a contact lens fitting turn into an eye-opening experience? For 57-year-old Doris Daisy—a Floridian, born and bred—the discovery of 2 corneal lesions prompted an initial referral from her optometrist to a cornea specialist and subsequently to our office.

We Meet the Patient

“Raised in the Sunshine State, I’ve lived in the sun all my life,” said Ms. Daisy. She had also traveled to other sunny areas, including Africa. In response to our questions, she reported no blurry vision, no photophobia, and no excess tearing. “A little morning redness is all I can think of—no pain, no irritation, nothing,” she recalled.

Ocular history. Ms. Daisy’s ocular history was significant for bilateral LASIK surgery 10 years earlier, which was successful, with no complications.

Medical history. She reported no chronic medical conditions and had no history of diabetes, hypertension, infectious disease (including HIV), or cancer. She had never smoked, and she drank alcohol occasionally.

The only abnormality she reported was an abnormal Pap smear.

What We Found

On examination, her best-corrected visual acuity was 20/20 in the right eye and 20/25 in the left eye. Her intraocular pressure was 10 mm Hg bilaterally. Her pupils, confrontation visual fields, and ocular movements were normal. The external exam was unremarkable. No cervical lymph nodes were palpated.

At the slit lamp. The slit-lamp exam of the right eye was notable for 2 lesions (Fig. 1A). The first was a diffuse white nodular lesion occupying the peripheral cornea at 2 to 3 o’clock, with resultant corneal opacification. The second lesion, which extended from the limbus at 3 to 5 o’clock, appeared gelatinous and leukoplakic, with slight neovascularization. Notably, this lesion stained positive with rose bengal. The conjunctiva and cornea of the left eye were normal.

All other anterior chamber and posterior pole findings were unremarkable bilaterally.

Differential Diagnosis

Ms. Daisy presented with 2 lesions, having similar yet distinct characteristics. When forming our differential diagnosis, we needed to consider whether these lesions represented the same or different entities.

Salzmann nodular degeneration. The first lesion we looked at, the upper lesion, presented a classic clinical picture of Salzmann nodular degeneration: an asymptomatic, avascular, white subepithelial nodule in a middle-aged woman. Although the condition is usually idiopathic, chronic irritation and/or a history of ocular surgery—such as Ms. Daisy’s LASIK—may predispose a patient to Salzmann nodular degeneration. However, this diagnosis alone failed to characterize the second lesion.

Ocular surface squamous neoplasia (OSSN). The second lesion appeared gelatinous and leukoplakic, with neovascularization, and it stained positive with rose bengal. Although Salzmann nodular degeneration may present as multiple lesions, the characteristics of
this second lesion were different from the upper one and were highly suggestive of OSSN.

Ms. Daisy had several risk factors we look for in patients with a corneal or conjunctival lesion suspicious for neoplasia: a history of a positive Pap smear, a history of chronic sun exposure, residence at a low latitude, and advancing age.

Pterygium. OSSN and pterygium share many risk factors, including extensive sun exposure and a positive Pap smear, both of which were reported by Ms. Daisy. Pterygium and OSSN can be present concomitantly.

Narrowing the possibilities. At this point, our differential included Salzmann nodular degeneration, OSSN, and pterygium. We ordered high-resolution optical coherence tomography (HR-OCT) to hone in on the diagnosis.

Making the Diagnosis
HR-OCT findings revealed 2 separate lesions with distinct characteristics (Fig. 1B):
• Lesion 1: thin, dark epithelium with subepithelial hyperreflective nodule. These features are consistent with Salzmann nodular degeneration.
• Lesion 2: thickened, hyperreflective epithelium with an abrupt transition from normal to abnormal epithelium. These features are consistent with OSSN. This was not a benign pterygium.

Definitive diagnosis. We determined that a diagnosis of Salzmann nodular degeneration with concomitant OSSN best fit Ms. Daisy’s clinical picture.

Discussion
A physician’s ability to solve clinical problems decisively and accurately is guided largely by clinical acumen, yet sometimes technology provides vital assistance.

Imaging modalities such as HR-OCT are important adjunctive tools to aid physicians in the diagnosis and management of ocular surface lesions. In this case, HR-OCT allowed us to accurately identify and compare 2 distinct ocular pathologies: Salzmann nodular degeneration and OSSN, both of which were present in the same patient.

Salzmann nodular degeneration.

OSSN. In contrast, the clinical appearance of OSSN may be gelatinous, leukoplakic, or papilliform, with prominent neovascularization. Rose bengal may reveal diffuse punctate staining.

Though biopsy remains the gold standard for diagnosis, HR-OCT can be used as a noninvasive adjunctive diagnostic tool for OSSN. On this imaging technique, OSSN appears as thickened, hyperreflective epithelium with an abrupt transition from normal to abnormal epithelium.¹

Pterygium. Clinically, pterygia are fibrovascular lesions that sometimes mimic OSSN. The transition between normal and abnormal epithelium is as abrupt as that seen in OSSN.

However, unlike OSSN, pterygium demonstrates nonthickened, mildly hyperreflective epithelium overlying a hyperreflective “stringy” subepithelial lesion on HR-OCT.

The key distinction is that pterygium is a subepithelial lesion, while OSSN is epithelial. Both pterygium and OSSN share UV light as a risk factor. Because pterygia sometimes precede the development of OSSN, the clinician should remain vigilant for signs of neoplastic disease.

Treatment
With the emergence of HR-OCT in the diagnosis of various ocular surface diseases, topical chemotherapy has become the preferred treatment for OSSN. Topical mitomycin C, 5-fluorouracil (5-FU), and interferon alfa-2b are all effective chemotherapeutic agents in the treatment of OSSN.²

Our patient elected to receive 5-FU, cycled 1 week on/3 weeks off. Cycling
helps diminish the irritating effects of 5-FU. Our patient completed 4 weekly cycles of 5-FU.

Continuing follow-up. Ms. Daisy received 1 final cycle of 5-FU, and she will be followed carefully.

Imaging after treatment. Slit-lamp photos and HR-OCT images were obtained after 2 cycles (Figs. 2A, 2B) and 4 cycles (Figs. 3A, 3B). As anticipated, the Salzmann nodular degeneration remained unaffected by the chemotherapeutic agent, while the OSSN lesion demonstrated marked clinical improvement.

And there’s more. Interestingly, once the OSSN lesion had resolved, a small pterygium head was visible at the origin of the cancerous lesion. Sunlight is a risk factor for both pterygium and OSSN, and careful monitoring of all pterygia for evidence of neoplastic disease is wise.

Final Thoughts
Role of HR-OCT. Ms. Daisy’s case demonstrates the value of HR-OCT in the management of ocular surface conditions. This imaging modality enabled us to establish the 2 separate diagnoses without biopsy. Further, it revealed complete clinical response and normalization of the epithelial hyperreflectivity and thickening, confirming the full resolution of the OSSN lesion with the topical 5-FU treatment.

Be vigilant. This is not the first, nor will it be the last, case of concomitant Salzmann nodular degeneration and OSSN. Therefore, it is important for clinicians to recognize that both lesions may be present in the same patient, and even in the same eye.

* Patient name is fictitious.


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