Exacerbation of Zoster Interstitial Keratitis After Zoster Vaccination in an Adult

Two different forms of varicella-zoster virus (VZV) immunizations are available. Children are vaccinated with Varivax to reduce the risk of primary infection with VZV, and Zostavax is given to reduce the risk of VZV reactivation in adults. In a large prospective trial of adults older than 60 years, vaccination with Zostavax was shown to decrease the incidence of herpes zoster by 51.3% as well as to decrease the severity of the cases that occurred.1

Ocular complications of the childhood vaccine have been previously described,2,3 but the US Food and Drug Administration and the Centers for Disease Control and Prevention do not recognize a history of herpes zoster ophthalmicus (HZO) immunogenic stromal keratitis (interstitial keratitis [IK]) or iritis as a relative contraindication to adult vaccination. We describe a patient with marked worsening of VZV IK after receiving the Zostavax vaccine.

**Report of a Case.** A 50-year-old woman had left-sided HZO in 2002 that was initially treated with oral acyclovir at a dosage of 800 mg 5 times a day for 10 days. Four weeks later, she developed anterior stromal edema in the central and temporal cornea, trace cell and flare in the anterior chamber, and an intraocular pressure of 48 mm Hg. This was effectively treated with oral acyclovir at a dosage of 800 mg 5 times a day, topical loteprednol, 0.5%, 4 times a day, oral methazolamide at a dosage of 50 mg 3 times a day, topical brimonidine tartrate, 0.15%, 3 times a day, and topical bimatoprost, 0.03%, once nightly. Over the next 2 months, she stopped receiving all glaucoma medication and her treatment was tapered to oral acyclovir at a dosage of 400 mg twice a day and 1 drop of loteprednol, 0.5%, every other day.

Over the next 4 years, she had 7 mild asymptomatic episodes of IK detected on routine follow-up examination. In each case, the visual acuity was 20/30 or better; patchy infiltrates, 1 to 3 mm in diameter, were noted in the anterior, peripheral corneal stroma. Each episode resolved rapidly with frequent administration of topical loteprednol. Between episodes of stromal keratitis, she was managed on 1 drop or less of loteprednol. Each episode of stromal keratitis appeared to be unrelated to a recent taper of loteprednol. These episodes of stromal keratitis decreased in frequency over time.

In February 2007, 35 days after being vaccinated with Zostavax, she had a visual acuity of 20/80 OS, extensive epithelial edema, and diffuse stromal haze involving the lower two-thirds of the left cornea. The intraocular pressure was normal and there were no inflammatory cells in the anterior chamber.

Loteprednol administration was increased to 1 drop hourly, and treatment with oral valacyclovir hydrochloride at a dosage of 1 g 3 times a day was started. The cornea cleared rapidly with an associated improvement of visual acuity to 20/25. Loteprednol treatment was slowly tapered over 3 months and the patient was maintained on oral valacyclovir hydrochloride at a dosage of 500 mg twice a day and 1 drop of topical loteprednol every day until August 2008, when she had another asymptomatic and easily managed recurrence of IK in the left eye.

**Comment.** We report a case of severe worsening of HZO IK 35 days after vaccination with Zostavax. This exacerbation of the patient’s IK was much worse than prior episodes. Given the immune pathogenesis of HZO IK and the temporal association of this episode of IK with recent VZV vaccination, it is likely that the more severe recurrence of stromal keratitis was a consequence of the increased VZV immune response elicited by the vaccine. The interval between vaccination and reactivation of the immunogenic stromal keratitis is consistent with the time needed for antigen processing and immune response.

The Centers for Disease Control and Prevention do not recognize VZV ocular inflammatory disease as a relative contraindication to vaccination with Zostavax. However, we previously reported a case of immune reconstitution IK 35 days after vaccination with Zostavax. We have been concerned that VZV vaccination might worsen immune-mediated VZV ocular disease in patients with a history of HZO. In patients with a history of HZO with or without ocular involvement, we recommend careful monitoring after they receive the zoster vaccine, especially at approximately 4 to 6 weeks after vaccination.

Yousuf M. Khalifa, MD
Robert M. Jacoby, MD
Todd P. Margolis, MD, PhD

Author Affiliations: F. I. Proctor Foundation and Department of Ophthalmology, University of California, San Francisco (Drs Khalifa and Margolis); and Sansum Family Medicine, Santa Barbara, California (Dr Jacoby).

Correspondence: Dr Margolis, F. I. Proctor Foundation, Medical Sciences Bldg, Room S310, University of California, San Francisco, 513 Parnassus Ave, San Francisco, CA 94143-0412 (todd.margolis@ucsf.edu).

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Fluorescein Angiography of Recurrent Retinopathy of Prematurity After Initial Intravitreous Bevacizumab Treatment

Standard treatment for type 1 prethreshold retinopathy of prematurity (ROP) is laser ablation. A number of recent reports describe regression of ROP with intravitreous injection of the anti–vascular endothelial growth factor (VEGF) agent bevacizumab. We describe a premature boy diagnosed with type 1 prethreshold ROP who received bilateral intravitreous bevacizumab injections and demonstrated initial resolution. Two months later, clinical examination and fluorescein angiography demonstrated a circumferential vascular anastomotic pattern at the location of the initial stage 3 complex with radial vessels that continued peripherally toward a second, more anterior stage 3 complex. This was then successfully treated with laser photocoagulation.

Report of a Case. A 26-week-gestation boy weighing 675 g at birth and with multiple medical problems was transferred to our institution for treatment of presumed type 1 prethreshold ROP in the setting of prominent tunica vasculosa lentis. Although initial examination disclosed immature vessels in zone 2, he quickly progressed to stage 3 with plus disease by age 34 weeks. Given the patient’s critically ill health, the neonatology service recommended against prolonged sedation for laser therapy. Therefore, after an informed discussion with his parents, light intravenous sedation was administered to the infant and his eyelashes and conjunctival surfaces were prepared with 10% povidone-iodine topical solution. Intravitreous injections of bevacizumab (0.75 mg/0.025 mL) were administered bilaterally using a separate, sterile eyelid speculum for each eye. The infant was examined on postinjection day 1 and then weekly for 2 months. Within 2 weeks, examination identified regression of the lens-associated vessels, disappearance of extraretinal fibrovascular proliferation, and marked regression of plus disease. Subsequently, radial vessels grew anteriorly within the retina.

Two months after treatment, a second stage 3 complex developed anterior to the original stage 3 complex that had regressed, leaving a circumferential vascular anastomosis (Figure 1). Fluorescein angiography demonstrated anterior extraretinal fibrovascular proliferation with leakage and a more posterior circumferential vascular ring with associated telangiectasis but without leakage (Figure 2). Because the patient had become systemically stable enough for adequate sedation, conventional peripheral laser photocoagulation was administered to both eyes. Subsequent examination demonstrated bilateral cicatricial changes of the stage 3 complex over the next 3 weeks, with stabilization by 1 month after laser treatment without further vascular changes on follow-up.

Comment. Evidence indicates that ROP may be a biphasic disease with an initial oxygen-induced vascular obliteration phase, followed by hypoxia-induced vessel proliferation. Anti-VEGF therapy may be effective in the second phase and as a single dose because there is theoretically only 1 burst of VEGF. This is in contrast to other ocular neovascular conditions, such as age-related macular degeneration and diabetic retinopathy, where aberrant VEGF production often recurs as a result of long-standing disease.

Supporting this, Mintz-Hittner and Kuffel reported that a single bilateral injection of bevacizumab in 22 eyes of 11 infants induced regression of acute ROP and allowed vascularization of the peripheral retina to resume. In contrast, another report described a 41-week-old boy with zone 1, stage 2 plus disease that initially responded to bevacizumab treatment, but recurrence developed 11 weeks later. This recurrence responded to a second bevacizumab injection, but the patient died soon afterward of systemic illness.

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