Acute unilateral conjunctivitis after rubella vaccination: the detection of the rubella genome in the inflamed conjunctiva by reverse transcriptase-polymerase–chain reaction

N Kitaichi, T Ariga, S Ohno and T Shimizu

Br. J. Ophthalmol. 2006;90;1436-1437
doi:10.1136/bjo.2006.096008

vision in his right eye. His medical history was remarkable for classic Wegener's granulomatosis that had been in remission for the past year. His best-corrected visual acuities were 20/25 in the right eye and 20/20 in the left eye. No relative afferent pupillary defect was evident. A slit-lamp examination of the anterior segment was unremarkable. Fundus examination of the right eye showed a clear vitreous, hyperaemic optic disc, peripapillary retinal haemorrhages, cotton wool spots, and dilatation and tortuosity of the retinal venous system (fig 1A). Fluorescein angiography showed delayed and prolonged filling of the retinal vasculature, blocked fluorescence as a result of the retinal haemorrhages and mild vessel staining in a few areas in the late phases (fig 1B–D). Fundus examination of the left eye was normal. The patient was diagnosed as having a central RVO and was urgently referred to his rheumatologist for evaluation of a possible relapse of systemic Wegener's granulomatosis.

Comment

Retinal manifestations in Wegener's granulomatosis include chorioretinitis, macular oedema, retinitis with cotton wool spots, acute retinal necrosis, peripheral retinitis, central retinal artery occlusion and exudative retinal detachment.[4] Five cases of RVO in Wegener's granulomatosis have been reported in the literature, all occurring in patients with classic Wegener's granulomatosis.[1–3] These patients also showed relatively good visual acuity (the worst was 20/60). RVO is believed to be caused by focal necrotising vasculitis.[2] However, all five patients failed to show any intraocular inflammation or retinal vasculitis at presentation. One of the eyes was enucleated owing to intractable neovascular glaucoma and was evaluated histopathologically, showing patchy areas of chronic choroiditis with no evidence of inflammation in the retinal vessels.[2] It was proposed that RVO may be due to inflammation occurring in the laminar or retrolaminar portion of the optic nerve that may not be clinically evident.[3]

The observation of RVO only in patients with classic Wegener's granulomatosis suggests that the mechanism may be similar to that of renal pathology in these patients. Pauci-immune necrotising extracapillary granuloma formation is a common feature of glomerulonephritis in small vessel vasculitides, such as Wegener's granulomatosis, Churg–Strauss syndrome and microscopic polyangiitis.[5 6] No cases of RVO have been reported in patients with microscopic polyangiitis, but the two reported cases of RVO in Churg–Strauss syndrome also did not show any evidence of vitritis or retinal vasculitis.[7 8] In the first patient, a presumed hypercoagulable state and associated thromboembolism were purported to have led to RVO,[7] whereas in the second patient, RVO occurred while the patient was adequately anticoagulated.[8] Lack of granulomatous inflammation is the distinguishing feature of microscopic polyangiitis from both Wegener's granulomatosis and Churg–Strauss syndrome.[6] We postulate that compression of the central retinal vein (in a laminar or retrolaminar location) by such extracapillary granulomatous lesions may be the mechanism of RVO in such patients. This pathogenic mechanism can also explain the lack of clinical evidence of retinal vasculitis in these patients.

M Wang, R N Khurana, S R Sadda
Doheny Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, USA

Correspondence to: S R Sadda, Doheny Eye Institute, Keck School of Medicine, University of Southern California, 1450 San Pablo Street DEI 3610, Los Angeles, CA 90033, USA; SSadda@doheny.org

doi: 10.1136/bjo.2006.095703

Accepted 4 June 2006

Competing interests: None declared.

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Acute unilateral conjunctivitis after rubella vaccination: the detection of the rubella genome in the inflamed conjunctiva by reverse transcriptase-polymerase–chain reaction

The efficacy of long-term rubella vaccine is >90%, and the anti-rubella vaccination causes few side effects.[1] Some cases of anterior uveitis were reported after a combined vaccination for measles, mumps and rubella, but not when vaccination for rubella alone was administered.[2] Another study reported that, after smallpox vaccination, 16 out of 450 000 subjects vaccinated had ocular complaints including conjunctivitis, keratitis and eyelid oedema, and only 5 of those cases were confirmed positive for vaccinia by culture or PCR.[3] However, conjunctivitis after rubella vaccination with laboratory confirmation has never been reported.

Case report

A 43-year-old man was referred to the Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Japan, with a history of conjunctival redness in his left eye for 2 days (table 1, figs 1A,B).

The patient's vision was 20/20 with correction in each eye. He had received an attenuated live anti-rubella vaccine on his left arm (Biken, Tanabe, Japan) 4 days before the onset of his left neck lymphadenopathy. He showed a flare-up at the site of injection 6 days before his eye symptoms developed. He also had itching at the injected site on day 12 after vaccination. No fever symptoms were observed. Biomicroscopy showed normal eyelids and lachrymal system. He had conjunctival flush with follicles in the left eye, but not in the right eye. The anterior chamber and fundus were normal in both the eyes. Adenovirus was not detected with immunochromatography (Adenocheck, Santen, Osaka). The patient's conjunctiva was scraped to collect samples. The possible presence of rubella virus mRNA expression in the conjunctiva was examined by RT-PCR (Mitsubishi Chemical Bio-Clinical Laboratories, Tokyo, Japan) as described elsewhere.[4] The results were positive for rubella mRNA expression (fig 1C). The inflammation of the eye improved without treatment in a few days. His antiserum rubella dilution titre was reported to be negative before vaccination and positive (×64) after injection.

Comment

In this patient, it is assumed that the acute unilateral conjunctivitis resulted from an ocular infection with rubella, caused by an attenuated vaccine. However, another possibility is that the conjunctivitis was caused by a contiguous infection from other people. We interviewed the patient carefully, but none among his family and associates had contracted rubella. The next possibility was the contralateral eye. Samples from the contralateral eye were not collected; thus, it is unclear whether RT-PCR might result positive or negative in the contralateral eye. The final point is why and how conjunctivitis occurred unilaterally. If the viruses are transmitted by haematogenous spread, the contralateral eye may develop conjunctivitis. The reason for unilateral involvement remains uncertain.

This is the first report to our knowledge of an adult man who developed acute conjunctivitis after vaccination with a rubella vaccine, and the rubella genome was confirmed at the conjunctiva by RT-PCR. Such viral—for example, adenoviral ocular infections, ranging from mild to full-blown with marked morbidity, often cause epidemics of nosocomial infections. Thus, it is important for clinicians to identify the virus causing acute conjunctivitis. RT-PCR results in a straightforward diagnosis in the case of rubella or any other RNA viral infection in which a serological test is not available. A viral detection test after vaccination is also appropriate if the vaccination was done with a live vaccine.

Table 1 Clinical course of the patient

Days after vaccination	Symptoms
4	Left neck lymphadenopathy
6	Redness of injected skin
12	Left conjunctivitis/ itching of injected skin
13	Medical examination/ collection of samples
16	Improvement of symptoms

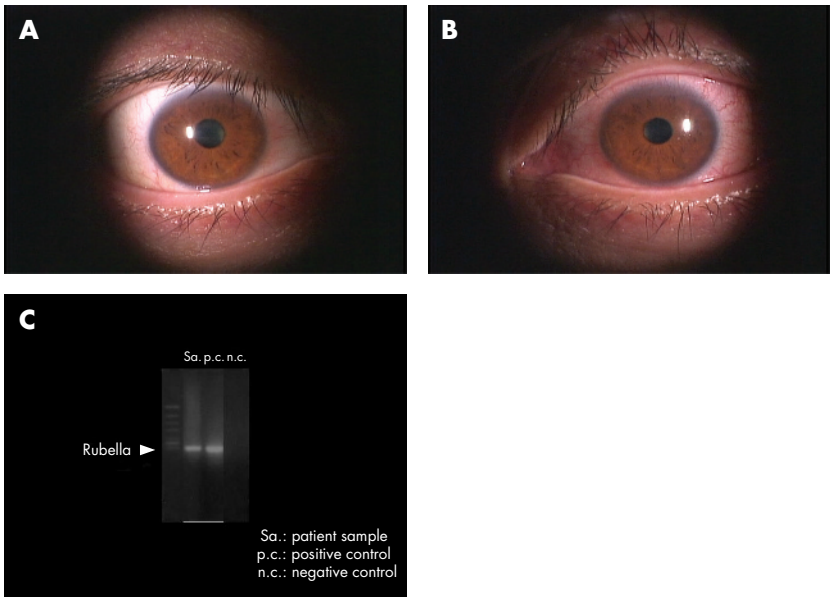

Figure 1 Photographs of right eye (A), left eye (B) and reverse transcriptase-polymerase chain reaction (RT-PCR) (C). Right eye is seen to be normal (A). Marked conjunctival hyperaemia is seen in the left eye (B). Rubella virus mRNA detected by using RT-PCR from the scrapings of the lower conjunctiva of the left eye (C). lane 1 (Sa) samples collected from the patient; lane 2 (pc), positive control (American Type Culture Collection (ATCC) VR-553); lane 3 (nc), negative control (distilled water for injections; Ohtsuka Pharmaceutical, Tokyo, Japan).

N Kitaichi, T Ariga, S Ohno
Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Sapporo, Japan

T Shimizu
Department of Dermatology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan

Correspondence to: N Kitaichi, Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, N-15, W-7, Kita-ku, Sapporo 060-8638, Japan; nobukita@med.hokudai.ac.jp

doi: 10.1136/bjo.2006.096008

Accepted 15 May 2006

Competing interests: None declared.

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Bilateral upper eyelid ectropion associated with blepharospasm

An unusual case of bilateral upper eyelid ectropion thought to be caused by blepharospasm is described. Botulinum A toxin injection yielded a good clinical response. A hypothesis for the pathogenesis of this condition is discussed.

Ectropion in adults typically affects the lower eyelid and is thought to result primarily from involution, paralysis and cicatrisation.[1 2] We report an unusual case of bilateral upper eyelid ectropion associated with blepharospasm in an elderly man who responded to treatment with botulinum A toxin.

Case report

A 73-year-old man was referred to our clinic with bilateral upper eyelid ectropion. The ophthalmic history showed that his symptoms started about 5 years earlier and that he had been treated unsuccessfully with lubricants and topical steroids. The patient reported that he sometimes tied a towel around his upper eyelid to raise the eyelid. There was no history of ocular surgery or treatment.

On clinical examination, the best-corrected visual acuity was 20/25 in both eyes, and the anterior and posterior segments were unremarkable except for senile cataract. Ectropion along the full width of both upper eyelids was observed, and the everted tarsal conjunctiva were inflamed and thickened (fig 1A). The eversion of the bilateral superior tarsi reoccurred immediately after the eyelids were manually repositioned, and severe blepharospasm was observed (fig 1B). The ocular surface was unaffected, and no epithelial damage was observed in either eye.

The patient was treated with injections of botulinum A toxin (Botox, GlaxoSmithKline, London, UK) into the bilateral orbicular muscles (six injections of 2.5 U on each side), the corrugator muscles (2.5 U on each side) and the procerus muscle (2.5 U). One week after the injections, the blepharospasm had almost resolved and the eversion of the bilateral tarsi had resolved (fig 1C).

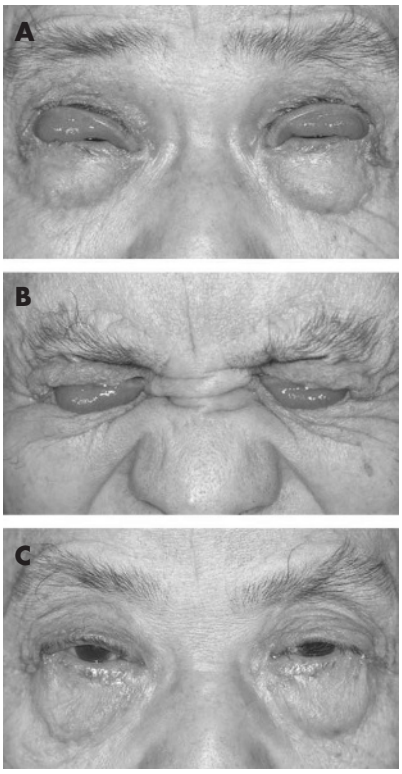

Figure 1 (A) A 73-year-old man with bilateral upper eyelid ectropion. The everted tarsal conjunctiva are inflamed and thickened. (B) Severe blepharospasm is seen on clinical examination. (C) One week after injection of botulinum A toxin, the bilateral ectropion and blepharospasm of the upper eyelid show marked improvement. Reproduced with permission.

Comment

Ectropion is due to an imbalance between the anterior and posterior lamellae, and usually develops in the lower eyelids.[1] Recently, rare cases of non-cicatricial upper eyelid ectropion have been reported.[3] The current case is unusual in that ectropion developed bilaterally in the upper eyelids and was associated with blepharospasm.

We theorised that the following mechanism may have caused the ectropion in this case. Because of the difficulty associated with eyelid opening caused by blepharospasm and blepharoptosis, the patient lifted the upper eyelids mechanically, which resulted in a functional shortening of the anterior lamellae. The patient might have naturally excessive posterior lamellae, or, because he has age-related aponeurotic ptosis, the tension of both the levator muscle and the superior tarsal muscle, which prevent tarsal prolapse, may have been weak.

Prolonged spasmodic contractions of the orbicularis muscle caused the upper tarsi to herniate. In addition, the thickening of the tarsal conjunctiva, caused by longstanding exposure, increased the conjunctival volume, resulting in the failure of the tissue to return to the normal position in the conjunctival sac, making the tarsal herniation chronic.

Blepharospasm is presumed to be the underlying cause in this case; therefore, injection of botulinum A toxin was effective.[4 5] Because the effect of botulinum toxin is transient,[4 5] the