

Varicella-Zoster Viral Antigen Identified in Iridocyclitis Patient

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Background: The varicella-zoster virus (VZV) antigen has not been identified immunohistologically in iridocyclitis due to VZV.

Case: A 65-year-old woman diagnosed with iridocyclitis and secondary glaucoma underwent trabeculectomy. Samples of aqueous humor and juxtacanalicular and iris tissue were obtained for immunohistological and polymerase chain reaction (PCR) study.

Observations: Slit-lamp microscopy revealed ciliary injection, corneal epithelial edema, mutton fat precipitates, flare, cells, and progressive iris atrophy in the right eye. Subsequently, scant eruptions on her right upper eyelid appeared and disappeared within a week. Although a diagnostic increase in the complement fixation antibody titer to VZV was not observed, we started medical treatment for VZV, on suspicion of iridocyclitis due to VZV. Despite medical treatment, the ratio of peripheral anterior synechia was greater than 60% and iris atrophy progressed in parallel. The intraocular pressure in the right eye remained above 30 mm Hg at 6 months after the first visit, so trabeculectomy was performed. VZV-specific DNA was detected in the aqueous humor by the PCR study. Immunohistological examination demonstrated numerous VZV antigen-positive cells in the iris stroma, in particular, vascular endothelial cells.

Conclusion: To our knowledge, this is the first report of the detection of VZV antigen in the iris of an iridocyclitis patient. **Jpn J Ophthalmol 2002;46:70-73** © 2002 Japanese Ophthalmological Society

Key Words: Immunofluorescence method, iridocyclitis, varicella zoster virus, VZV antigen.

Introduction

Varicella-zoster virus (VZV) is known as an etiologic agent of iridocyclitis characterized by iris atrophy, mutton fat keratic precipitates, and secondary glaucoma. Zoster ophthalmicus without skin eruption is defined as zoster sine herpette.^{1,2}

Recent reports documented the usefulness of polymerase chain reaction (PCR) study in the diagnosis of zoster sine herpette.^{2,3} However, it has not been reported that VZV antigen was identified immunohis-

tologically in iridocyclitis due to VZV. We present the first report of detection of VZV antigen in the iris of an iridocyclitis patient.

Case Report

Iridocyclitis and secondary glaucoma of the right eye were diagnosed in a 65-year-old woman visiting our hospital in June 1998. At initial examination, best-corrected visual acuity was 0.3 in the right eye and 1.0 in the left eye. Intraocular pressure (IOP) was 33 mm Hg in the right eye and 14 mm Hg in the left eye. Slit-lamp microscopy revealed ciliary injection, corneal epithelial edema, mutton fat keratic precipitates, flare, and cells in the anterior chamber in the right eye. The left eye revealed no abnormal

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findings. For her right eye, 0.1% betamethasone sodium phosphate four times a day, 2% carteolol hydrochloride and 1% atropine sulfate, each two times a day, were prescribed. Seven days later, a few small vesicles appeared on her right upper eyelid. These were diagnosed as herpes simplex by a dermatologist; they disappeared without scarring within a week. Although a diagnostic increase in the complement fixation antibody titer to VZV in serum was not observed (1:16), iris atrophy had developed, raising the suspicion of iridocyclitis due to VZV. We added 1000 mg oral acyclovir daily for 2 weeks and 3% acyclovir ointment five times a day. Although the iridocyclitis gradually became inactive, and corrected visual acuity returned to 0.9, the ratio of the peripheral anterior synechia was greater than 60% and iris atrophy progressed in parallel (Figure 1). The IOP in the right eye had remained above 30 mm Hg and a nasal step appeared in her visual field at 6 months after the first visit, so trabeculectomy with 0.02% Mitomycin C was performed on her right eye. To identify the presence of VZV and to detect VZV antigen, samples of aqueous humor and juxtacanalicular and iris tissue obtained during the surgery were examined in the following manner. The aqueous humor was examined by PCR study using VZV primers with the following sequences: sense 5'-TCA CGA ACC GTT GAC AGG AC-3', and antisense 5'-CCA CTA CTC ATT GTA TCC GCG-3'. These primers were used to amplify a 216-base pair target sequence. The iris and juxtacanalicular tissue were examined immunohistologically using anti-VZV monoclonal antibody (Chemicon, Temecula, CA, USA) to detect the VZV glycoprotein I.

As a result, VZV-specific DNA was detected in the aqueous humor. Herpes simplex virus-specific DNA

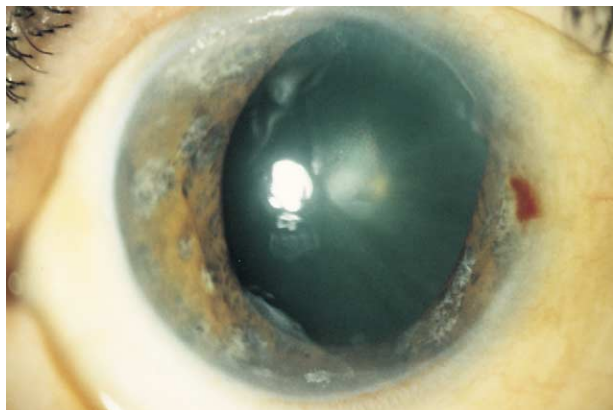


Figure 1. Right eye demonstrates marked iris atrophy.

was not identified by the PCR study (Figure 2). Hematoxylin-eosin staining showed neither marked inflammatory cellular infiltration nor vasculitis in the iris section (Figure 3). Immunohistological examination demonstrated numerous VZV antigen-positive cells in the iris stroma, in particular, vascular endothelial cells (Figure 4). However, VZV antigen-positive cells were not detected in juxtacanalicular tissue (Figure 5).

Postoperatively, IOP has been controlled in this patient between 15 and 25 mm Hg, and only mild reactivation of the iridocyclitis has occurred, although secondary cataract has progressed. Cataract surgery is planned in the near future.

Discussion

Herpes zoster ophthalmicus is usually accompanied by a typical rash, but cases of ocular zoster with no skin eruption, ie, zoster sine herpete, have been reported.¹⁻⁵ Cases of herpes simplex accompanying zosteriform eruptions are known as zosteriform simplex.^{4,5} It is important to distinguish between herpes

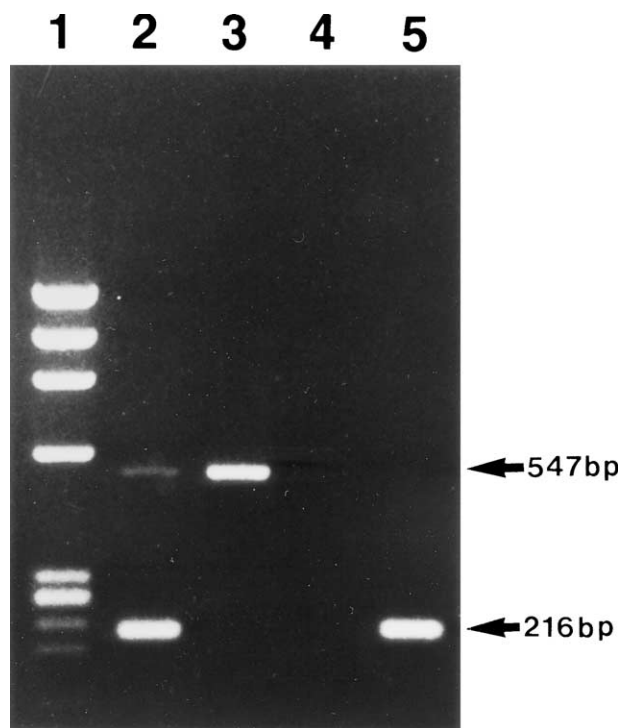


Figure 2. Detection of varicella zoster virus (VZV)-specific DNA in aqueous humor. Lane 1: X174 DNA/*Hae* as size reference, lane 2: band of 216-bp in length (VZV primer) from aqueous humor of this case, lane 3: negative control (human DNA), lane 4: negative control (Buffer), lane 5: positive control (VZV DNA). Band of 547-bp is internal control. bp: base pair.

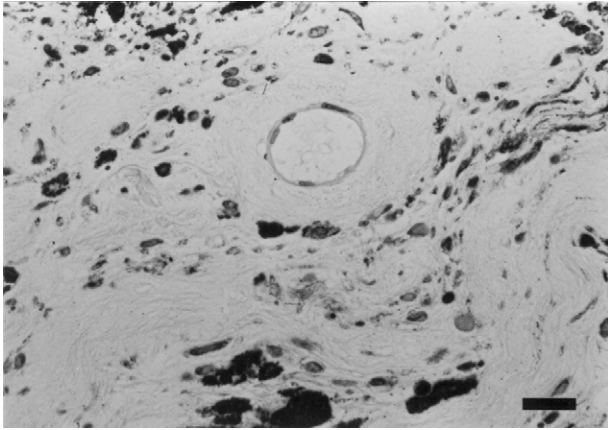


Figure 3. Hematoxylin-eosin staining showed neither marked inflammatory cellular infiltration nor vasculitis in iris section. Bar = 50 μ m.

zoster and herpes simplex to aid in the choice of appropriate medical therapy. In this case, the vesicles that clinically simulated those caused by herpes simplex virus disappeared without any scar formation within a week; because of this unusually rapid recovery, at first we were unable to determine the etiology of the disease.

Recently, PCR studies have been applied successfully to a variety of ocular samples to identify viruses in cases of intraocular inflammation. PCR studies have also been useful in the diagnosis of zoster sine herpette, and reports of VZV DNA detection in iridocyclitis have increased.^{2,3} Although VZV antigen has been detected in cells from vitreous aspirates⁶ and choroidal biopsies⁷ in acute retinal necrosis syndrome, it had not previously been identified immunohistologically from the iris in iridocyclitis. In this case, we not only detected VZV-specific DNA in the aqueous humor but also succeeded in detecting VZV antigen in the iris in a patient with iridocyclitis.

Iridocyclitis caused by VZV is characterized by iris atrophy and secondary glaucoma, as in this case. The pathogenesis of iris atrophy is thought to be due to either invasion of the pigment epithelium by the virus, a local vasculitis, or a neurogenic effect.⁸⁻¹⁰ Moreover, secondary glaucoma is thought to be due to a combination of several mechanisms, including trabeculitis and plugging of the trabecular meshwork by debris and cells, posterior synechia causing pupillary block, and anterior synechia causing angle closure.^{9,11} We detected VZV antigen-positive cells in the iris stroma, in particular vascular endothelial cells, but not in juxtacanalicular tissue. This suggests that herpes zoster is basically a

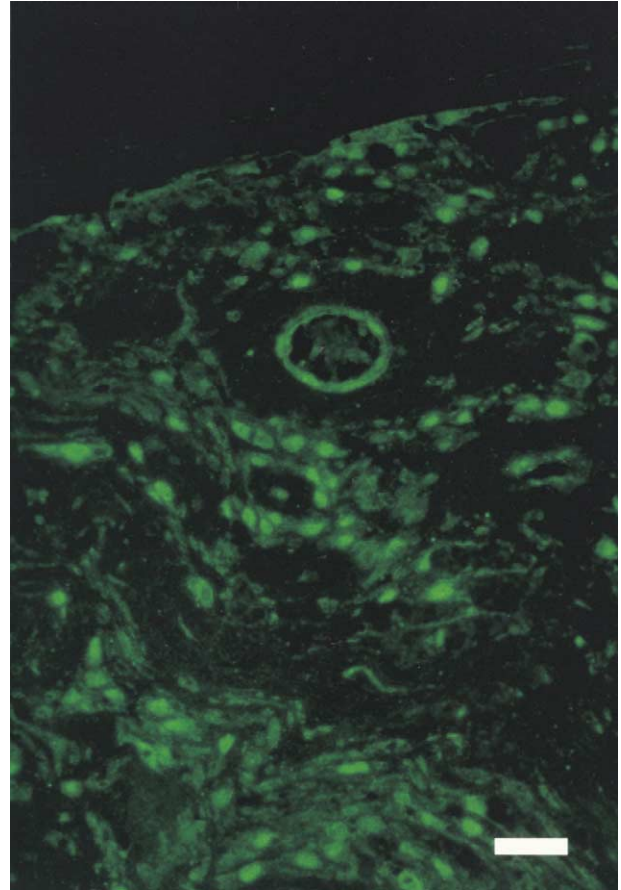


Figure 4. Numerous varicella zoster virus (VZV) antigen-positive cells in iris stroma, in particular, in vascular endothelial cells (indirect immunofluorescence method using anti-VZV monoclonal antibody). Bar = 50 μ m.

vascular disease. No marked cellular infiltration and vasculitis, however, were observed in the iris section. Though we have no exact answer to these findings, it may be associated with the stage of the disease at which we obtained the operative specimens. Therefore, in this case, in terms of clinical findings and histological findings, iris atrophy may have been due to invasion of the iris stroma by the virus itself, and secondary glaucoma may have been due to progressive anterior synechia causing angle closure. We cannot ascertain the pathogenesis of iridocyclitis from only this result, although this study may be helpful in improving our understanding of the mechanisms of iridocyclitis due to VZV.

To our knowledge, this is the first report of detection of VZV antigen in iris samples in iridocyclitis due to VZV.

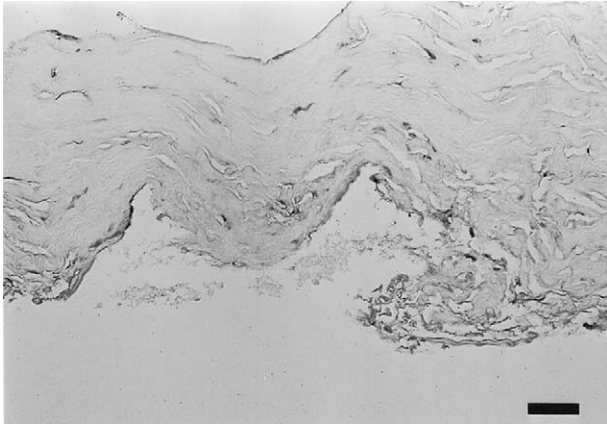


Figure 5. No varicella zoster virus (VZV) antigen-positive cells in juxtacanalicular tissue. (immunohistochemical method using anti-VZV monoclonal antibody). Bar = 100 μ m.

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