Molecular Diagnosis of Acute Retinal Necrosis Secondary to CMV in Vitreous Fluid

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Clinical Presentation

Chief Complaint (Jan. 2006)

- **blurring of vision**
- **floaters** in the left eye (OS)

History

- diabetes mellitus for 15 yrs
- **post-kidney transplant** in 1997

Medication

- **immunosuppresive agents** for 10 years

Clinical Presentation

Visual acuity

- OD 20/70 - improved to 20/30 on pinhole
- **OS 20/70** - **not improved on pinhole**

Slit lamp

- OD: normal
- **OS**: low grade **anterior segment inflammation** with few retrolental cells and 2+ vitreous cells

Fundus exam

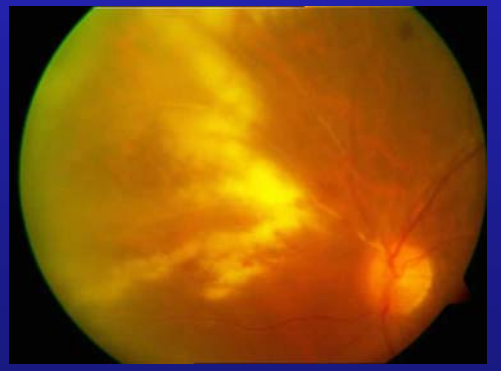
- OD: normal retina and optic nerve
- **OS**: massive arterial occlusion with sheathing of blood vessels; **retinal detachment** with necrosis

Initial Assessment

Acute retinal necrosis, left eye

Acute Retinal Necrosis

- first described in Japan in 1971
- **unusual ocular inflammatory syndrome**
- seen in both **healthy** and **immunocompromised**
- diagnosis is based on **clinical findings**



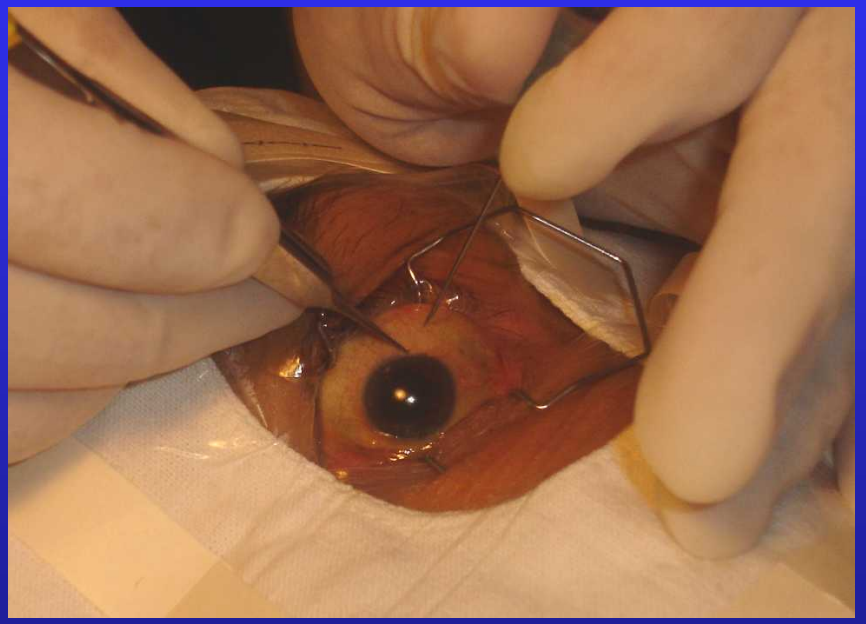
Diagnostic Hallmarks

- one or more foci of retinal necrosis in peripheral retina with **circumferential spread**
- evidence of **occlusive vasculopathy**
- inflammatory reaction in **vitreous and anterior chamber**

Holland GN *et al*. Standard Diagnostic Criteria for ARN Syndrome. Am J Ophthalmology. 1994.

Differential Diagnosis

- ocular toxoplasmosis
- syphilitic retinitis
- viral retinitis



Epidemiology

- slightly more common in men
- occur at any age (20 - 60 years of age)
- 1 case/1.6-2 million/year

Muthiah MN *et al.* ARN: A National Population-Based Study. Br J Ophthalmology. 2007.

Etiology

Ganatra JB *et al.* (2000)

- VZV DNA detected in 13 patients (48%)
- HSV-1 DNA detected in 7 patients (26%)
- HSV-2 DNA detected in 6 patients (22%)
- **CMV DNA detected in 1 patient (4%)**

Ganatra JB *et al.* Viral Causes of Acute Retinal Necrosis. Am J Ophthalmology. 2000.

Predisposing Factors

- AIDS
- hematologic disorders
- **immunosuppressive drugs**
- **organ transplant**

Incidence of CMV Retinitis

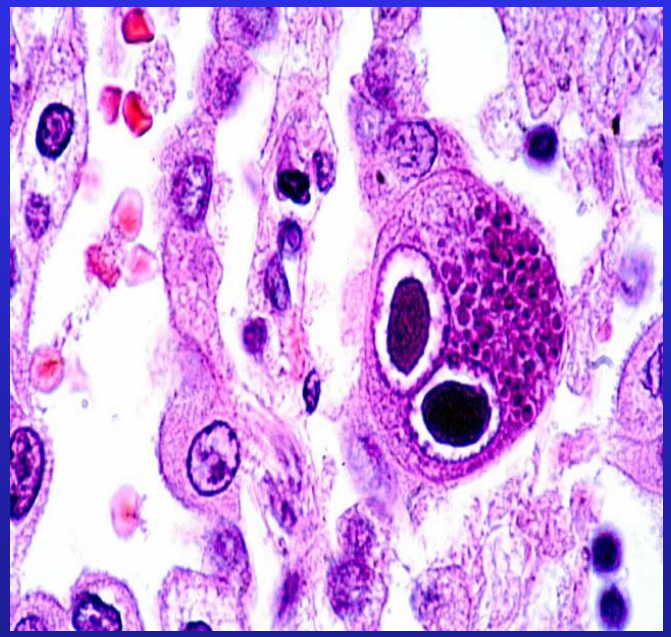
Mayo Clinic (1990 - 2004)

Kidney	**= 5**
Liver	= 2
Heart	= 1
Stem cell	= 1
Total	= 9

Eid A *et al* . Clinical Features and Outcomes of CMV Retinitis. Transpl Infect Dis. 2007.

Diagnostic Techniques

- electron microscopy
- histopathology
- immunocytochemistry
- serology
- viral culture
- **PCR**



Methodology

Sample collection

Viral DNA extraction

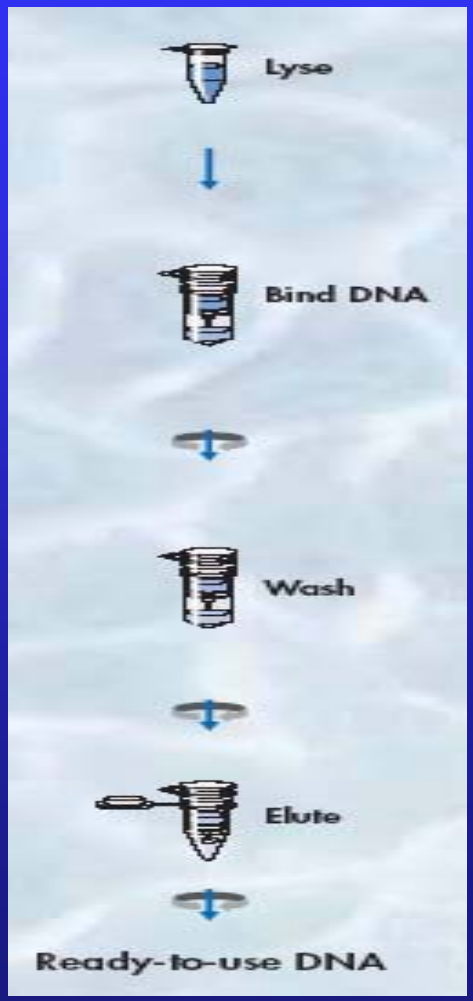
Nucleic acid amplification

Gel electrophoresis

Staining

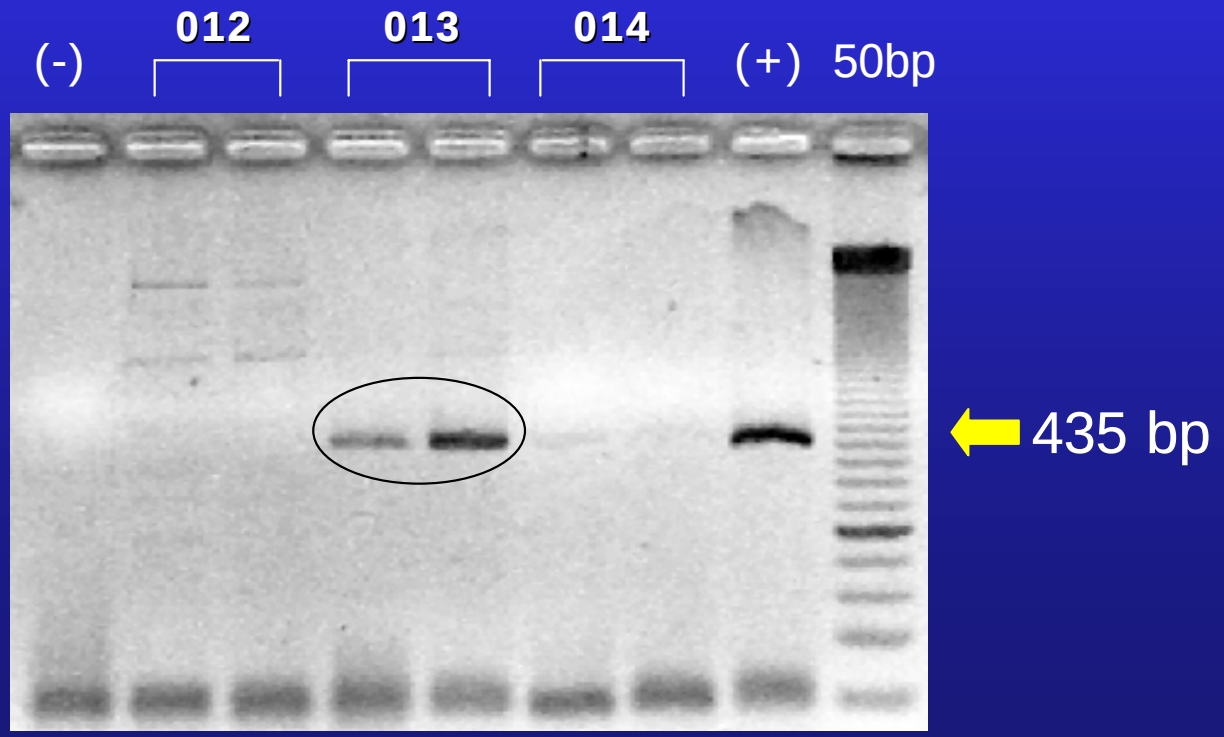
Viral DNA Extraction

- sample is **lyzed** to isolate DNA
- DNA **binds** to the membrane
- contaminants are **washed** away
- DNA is **eluted** in buffer



Nucleic Acid Amplification

Pathogen	Target Region	Amplicon	Reference
CMV	MIE	**435 bp**	Smith *et al*. 1993
HSV	Glycoprotein D	281 bp	Read *et al*. 1993



Current Techniques

- **Multiplex PCR**
  - **simultaneously screen** (CMV, HSV, VZV, *T. gondii*) for posterior uveitis in a single reaction, without loss of specificity

Dabil H *et al*. 2001

- **Real-time PCR**
  - rapid and sensitive detection and **quantitation** of infectious posterior uveitis pathogens

Dworkin L *et al*. 2002

Advantages of Molecular Methods

rapid detection

minimal sample

sensitive: 95%

specific: 98%

strain differentiation

slow growing organisms

unculturable pathogens

definitive diagnosis

Knox C *et al*. PCR-based assays of vitreous samples for the diagnosis of retinitis. Ophthalmology. 1998.

Final Diagnosis

Acute retinal necrosis 2° to CMV

Management

Treatment

- intravitreal injection of **ganciclovir**
- **pan-retinal photocoagulation**

Response

- vision **initially improved to 20/50** (two weeks post injection)

Outcomes

- progressive **visual loss**
- **retinal detachment** in 50-75% within 3 months
- final visual acuity **<20/200** in 76%
- visual **prognosis may be poorer**

Gartry DS *et al*. ARN Syndrome. Br J. Ophthalmology. 1991.

Conclusion

- ARN is a **rare syndrome** and only a **few cases** are due to CMV
- PCR is a **sensitive, specific** and **rapid** means of detecting small amounts of viral DNA in vitreous fluid
- Prompt **diagnosis** and **treatment** is crucial to reduce visual loss

Molecular Diagnostics Laboratory

Thank you