EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 4
04-10
Year: 2021

COMPARISON THE DIFFERENCE BETWEEN ACUTE RETINAL NECROSIS AND PROGRESSIVE OUTER RETINAL NECROSIS

Samia Iqbal[1*], Nawar Jan Anwar[2], Muhammad Mujahid[3] and Rashida Riaz[4]

[1]Senior Lecturer and Optometrist in UOL, Lahore, Pakistan.
[2,3,4]Institute Mayo Hospital Lahor.

***Corresponding Author: Samia Iqbal**
Senior Lecturer and Optometrist in UOL, Lahore, Pakistan.

Article Received on 22/01/2020 **Article Revised on 12/02/2021** **Article Accepted on 02/03/2021**

ABSTRACT
Necrotising retinopathies can be visually destroying. Generally it is related with the viral family Herpesviridae and observed in both immune-competent and immunocompromised hosts, potential inconveniencil of necrotising retinopathies include normal retinal dystrophy with or without macular inclusion, optic neuropathy and eventually, optional retinal detachment. Examples include progressive outer retinal necrosis, acute retinal necrosis and cytomegalovirus retinitis. If diagnosed early and treated aggressively, visual complications can be prevented; however, there is no current consensus on the most appropriate antiviral regimen for each of the different varieties of necrotising herpetic retinopathy. This paper reviews aspects of varieties of necrotising herpetic retinopathy, including pathophysiology, treatment and diagnostic testing.

Necrotising retinopathies are a group of uncommon posterior segment complications of herpetic viral aetiology. The herpetic viral family, Herpesviridae, contains many viruses, including varicella zoster virus (VZV), herpes simplex virus (HSV) types 1 and 2, and cytomegalovirus (CMV). Necrotising retinopathies caused by members of Herpesviridae include acute retinal necrosis (ARN), progressive outer retinal necrosis (PORN) and cytomegaloviral retinitis, the most common herpetic retinal necrosis being cytomegaloviral retinitis within an immune-compromised patient population.

ACUTE RETINAL NECROSIS SYNDROME
According to the previous studies it is stated that Acute retinal necrosis is a clinical syndrome that has been associated with either HSV or VZV infection. General features of ARN syndrome include a vaso-occlusive angiitis of both the retinal and choroidal vessels, a necrotizing retinitis that preferentially involves the peripheral retina, and significant intraocular inflammation and as a results Rhegmatogenous retinal detachment is a major late sequela.[1]

As I studied a report in which it was stated that ARN was originally described in Japan in 1971 by Urayama and coworkers, in this report studied about six healthy patients with acute onset of a unilateral panuveitis and retinal arteritis which ultimately resulted in widespread peripheral, confluent retinal necrosis and as a result eventual retinal detachment.[2] Willerson and associates reported this entity in 1977 and was first reported in English medical literature, in this report two patients are with bilateral necrotizing vaso-occlusive retinitis.The term *acute retinal necrosis* (ARN or BARN, when bilateral), was coined by Young and Bird in 1978. As consulted different researches and according to such researches it is indicated that although this syndrome was initially described in healthy patients, it subsequently has been reported in individuals with compromised systemic immunity—most commonly in those individuals who have Human Immunodeficiency Virus (HIV) Infections.[3]

CLINICAL PRESENTATION
According to clinical investigation Acute retinal necrosis does not appear to have any racial predilection; however, it is indicated in many researches that it is more common in males. Although in many researches it is indicated that ARN typically affects individuals between 20 and 50 years of age, cases have also been reported in patients as young as 4 years and as old as 89 years of age.[4,5]

Initially, patients with such conditions may complain of mild to moderate ocular or periorbital pain accompanied by a red eye very often. Early visual symptoms may be rarely present or not present and sometimes insidious. When symptoms are present, these usually consist of floaters, blurred vision, or rarely, decreased peripheral vision.[6] A typical presentation is an Acute central visual loss because the posterior pole usually got spared from

the retinopathy as a late results in such cases.[7] Optic nerve involvement, retinal artery occlusion, and retinal detachment can affect central vision but usually are not manifest at presentation syndrome. Diffuse episcleritis, scleritis, or orbital inflammatory disease may got revealed as results of external examinations. In mild to moderate cases anterior segment cellular reaction is common, either granulomatous or fine keratic precipitates typically are present.[8,9]A condition of hypopyon is rarely or not present in such cases. Low IOP is also present in such cases in the absence of retinal detachment; however, elevated intraocular pressure occur as a results of secondary anterior segment inflammation. In healthy individuals concurrent herpes virus infection of cornea with dendritic or stromal keratitis is not a typical feature of ARN although it has been indicated or described in patients with HIV infection. According to a survey one case of simultaneous HSV Type 1 keratitis and ARN was reported in a patient with Ramsay Hunt Syndrome (RHS).[10]

ETIOLOGY AND HISTOPATHOLOGY

As it is indicated that immune compromised patients with HIV infection, autoimmune disorders, cancer, and organ transplants and it is concluded that ARN syndrome can be defined by its ocular features rather than by the immune status of the affected individual. In patients with HIV infection and ARN, the CD4+ T lymphocyte count generally is greater than 60 cells/µl, although ARN is sufficiently infrequent in these patients to allow any conclusions to be drawn regarding the CD4+ count. It is also indicated that HIV-infected patients are more likely to have simultaneous or recurrent VZV or HSV.[11,12]

Similarities between ARN syndrome and forms of viral retinitis such as neonatal HSV infections and CMV retinitis have been noted in this research. Early studies either failed to detect rising serum antibody titers to common viruses or failed to culture virus from the vitreous of patients with ARN, and as a result viral theory remained speculative.[13] In 1982, Culbertson and coworkers found viral particles consistent with a member of the herpes family of viruses in retinal tissue from an individual with ARN. Positive serum VZV titers and positive intraocular VZV antigen studies have been documented in some patients with ARN and VZV also has been cultured from the vitreous during the active phase of ARN along with VZV, it is now clear that HSV types 1 and 2 also produce ARN syndrome HSV has been cultured from the vitreous and HSV-DNA types 1 and 2 have been identified by polymerase chain reaction.[14,15]

DIAGNOSTIC EVALUATION AND ANCILLARY TESTS

The diagnosis of ARN is based on a clinical examination and a characteristic funduscopic appearance. Although the signs of ARN may vary in severity, the American Uveitis Society proposed the following clinical criteria for diagnosis of ARN syndrome, regardless of an individual's systemic or immune status: a discrete peripheral necrotizing retinitis that progresses rapidly and circumferentially without antiviral therapy; prominent vitreous and anterior chamber inflammation; and an occlusive vasculitis with arteriolar involvement. Other features supporting the diagnosis of ARN include optic neuropathy or atrophy, scleritis, and ocular pain.[16,17]

Diagnostic vitrectomy or retinal biopsy may be indicated in some atypical cases. However, evaluation of intraocular samples with various techniques, such as viral culture, serology, polymerase chain reaction, and histopathologic examination, do not always yield proof of a viral infection.[18] Intraocular antibodies in the vitreous or aqueous have been measured to determine the cause of necrotizing retinitis. In one study, intraocular antibody production to VZV or HSV was detected in 57% of patients with typical ARN syndrome.[19] The viral cause of ARN are often difficult to determine in an end-stage atrophic or detached retinal specimens, and may be more readily identified in ocular specimens obtained during acute stages of the disease.[20]

Optic nerve sheath enlargement on the side which is affected with ARN are often showed in computed tomography scans. In the presence of unilateral ARN bilateral optic nerve sheath enlargement has also been indicated as well as documented. . Concurrent lesions of the optic tract, optic chiasm and lateral geniculate body are also indicated in patients with ARN via Magnetic Resonance Imaging (MRI) which ultimately suggests that the infection may spread through the axons of the ganglion cells.[21,22]

TREATMENT

By studying various researches and underlying etiologies it is suggested that Intravenous acyclovir is the suitable medical treatment of choice for active ARN. Acyclovir works by selectively inhibiting herpesvirus DNA polymerase. It has antiviral activity against HSV type 1, HSV type 2, and VZV.[23] Most strains of CMV are resistant to acyclovir. The retinitis in ARN typically shows a rapid response to acyclovir therapy, in which progression of retinitis ceases in 3 to 5 days and eventual atrophy of the infected retina occurs. Untreated eyes tend to show regression of the necrotic lesions spontaneously over a period of 6 to 12 weeks. Acyclovir therapy speeds this regression and prevents new lesion formation. In unilateral cases of ARN, acyclovir reduces but does not completely eliminate the risk of fellow eye involvement. Initial treatment with a 10 day course of high dose intravenous acyclovir (10 mg/kg every 8 hours) is followed by oral acyclovir (800 mg taken 5 times a day) for up to 14 weeks.[24] The time interval for therapy is based on the observation that ARN in the second eye most often occurs within 6 to 14 weeks of the initial symptoms in the first eye. ARN in healthy patients does not generally recur in the same eye after antiviral

treatment. Long-term oral maintenance therapy may be required in immunosuppressed patients who develop recurrent lesions. Acyclovir has not conclusively been shown to decrease the incidence of subsequent retinal detachment. Ganciclovir and foscarnet are alternative intravenous agents that are effective against herpes viruses.[25,26]

Systemic and topical corticosteroids are advocated to suppress the speed clearing of the vitreous reaction and also the inflammatory component of ARN. According to my research it is indicated that systemic corticosteroids used alone have not demonstrated any beneficial effect in the early stages of ARN, and because of their immunoinhibitory effects, they should not be administered in active cases of ARN without concurrent acyclovir antiviral therapy.[27] Other antiviral medications such as vidarabine have been given to patients with ARN without a clear-cut beneficial effect. Cytotoxic agents were used in some early cases based on the similarity between ARN and Behcet's disease; however,[28] it is currently known that ARN is a viral retinitis and that cytotoxic therapy should not be used. If a patient with ARN syndrome is medically immunosuppressed, the immunosuppression should be reversed unless systemically contraindicated.[29] Associated anterior segment inflammation are successfully treated via topical steroids and cyclopegics thus these are useful in treating associated anterior segment inflammations.[30]

PROGRESSIVE OUTER RETINAL NECROSIS.

Progressive outer retinal necrosis syndrome is a really damaging for vision, acute necrotizing retinitis that occurs in patients those compromised by immune system. Further and associates initially identified PORN as a distinct entity and described 2 cases. It has been reported in patients with AIDS. PORN affects AIDS patients when their immune function is really come to terms, and life could be in danger zone also.[31] VZV is the only infectious agent that has been associated with PORN. Ocular features include multifocal, deep retinal lesions that progress rapidly to involve the entire full-thickness retina. The visual prognosis is extremely poor even with antiviral therapy directed at VZV.[32]

CLINICAL PRESENTATION

The whole scenario is not known, PORN syndrome not really happened. In past searches of 1007 patients with symptomatic HIV infection, four cases of PORN were severely find.It found in the late stages of AIDS and long-term survival after diagnosis normally is less than 1 year.[33] The CD4+ T-lymphocyte count in patients often is less than 50 cells/µl when PORN is diagnosed, with a median CD4+ count of 21 cells/µl in one study. Only one patient with PORN has been announced to have a CD4+ count greater than 100 cells/µl.PORN syndrome may be relative with other opportunistic retinal infections. It is reported that, Cases of PORN syndrome in one eye and CMV retinitis in the fellow eye have been firmed by polymerase chain reaction identification of VZV and CMV-DNA from the vitreous.[34]

Even though cutaneous VZV is delineate in 20% of AIDS patients, previous or active cutaneous VZV infection is famed in up to 67% of patients with PORN.This infection is present in any dermatome and may be temporally remote from the onset of PORN syndrome.[35] IN researches, Cutaneous VZV associated with ophthalmic division of the trigeminal nerve in 27% of patients from one study. A record of chronic oral acyclovir use may be responsible for the resistance and poor clinical response often remark during acyclovir therapy.[36] Basically, PORN syndrome may be associated with an increased risk of exaggerating VZV encephalitis in AIDS patients. Two patients with PORN syndrome and neurologic symptoms were confirmed to have radiographically demonstrable and histologically manifest VZV encephalitis.[37]

Engstrom and associates estimated that 38 patients with PORN and all patients firmed visual symptoms at presentation. A decrease or dimming of vision, constriction of visual fields, and floaters were frequently described, but still pain is not reported in such cases.[38] The visual symptoms may be unequal to the clinical findings early in the course of the disease. Asymptomatic disease often was reported in the contralateral eye in bilateral cases. Early visual acuity varies from 20/20 to loss of light perception, with a median acuity of 20/30.[39,40]

PORN can be unilateral or bilateral at outset and involvement of the contralateral eye eventually occurs in most patients. Bilateral involvement was noted in over 70% of patients at the time of their final examination. On other hand ARN, there is less or no clinically apparent inflammation in the anterior segment or vitreous with PORN. Fine white keratic precipitates have been observed in some eyes and posterior synechiae are rarely reported.[41]

PORN syndrome is a growing retinal infection with a definite early, middle, and late stage. The early stage is characterized by multifocal, homogeneous, opacified deep retinal lesions. These lesions lack a granular border, which is a feature of CMV retinal infection. Lesions measure from 50 µm to various thousand microns in diameter and can be found peripheral to the arcades or in the macula at presentation. Early macular lesions are noted in up to 65% of patients, often take shape as central cherry-red spots. Multifocal lesions rapidly progress to joining and to full-thickness retinal involvement, forming large yellow-white areas of retinal necrosis with minimal retinal hemorrhage.[42] In eyes with initial peripheral involvement, progression often extends into the macula, and the entire retina may be involved within days. Primary retinal vascular inflammation does not appear to occur, although retinal vasculopathy in the form of sheathing and occlusion may

be noted only within or adjacent to areas of retinal necrosis.[43]

ETIOLOGY AND HISTOPATHOLOGY

Varicella-zoster virus has been involved as the causative agent of PORN. This is based on a history of previous or active cutaneous zoster infection in many patients and laboratory verification of VZV in some Chorioretinal biopsy specimens.[44] VZV also has been recognized in some cases of ARN. While both PORN and ARN can be produced by VZV and have been described in individuals with HIV infection, they are clinically distinct syndromes.[45] The reason for a differential presentation of VZV in PORN and ARN is not clear, although it may represent a differential host immunologic response to the same etiologic agent or may be caused by different strains of VZV.[46] The degree of immunosuppression varies broadly in AIDS, and with progressive immune dysfunction the clinical characteristics of VZV infection may change from the ARN syndrome to the hyperacute fulminant retinitis seen in AIDS patients with PORN. Patients who develop PORN have critically impaired systemic immunity, which is illustrated by a very low CD4+ T-lymphocyte count that is usually less than 50 cells/µl.[47] These patients may not be able to generate an inflammatory response, so VZV infection progresses without intraocular inflammation. In contrast, HIV-infected patients with higher CD4+ counts are able to counter with intraocular inflammation when exposed to VZV and may develop typical ARN.[48]

DIAGNOSTIC EVALUATION AND ANCILLARY TESTS: The diagnosis of PORN is based on clinical manifestation and a fast-growing course and is courage by a history of marked systemic immunosuppression, HIV infection, prior VZV infection, or chronic acyclovir use. Chorioretinal biopsy to recognized VZV may be specify if the retinitis is atypical, although most specimens are acquired at the time of retinal detachment restore to confirm the diagnosis. VZV has not been exhibit in all cases of PORN because necrotic tissue specimens may no longer have viral particles and laboratory isolation of VZV may be difficult. VZV-DNA and VZV antigen have been recognized in vitreous biopsy specimens, but VZV has not been cultured from the vitreous. Blood culture was positive for VZV in one patient with end-stage PORN.[49]

Fluorescein angiographic features differ from depending on the stage of PORN, but exhibit involvement of the choroid, RPE, and multiple layers of the retina. In the early stages, peripheral retinal microvascular alterations are noted within and extending beyond deep retinal lesions. Retinal leakage is present in large areas of retinal whitening. With progression of PORN, pruning of the retinal vasculature as well as capillary loss, RPE destruction, and choroidal leakage occurs. Disease reactivation at the border of normal retina is noted by eminent brush-fire pattern of fluorescein leakage involving the retina, RPE, and choroid.[50]

TREATMENT

The optimal regimen for treatment of PORN and prevention of recurrences is not known. PORN produces rapid destruction of the retina with cleave and often bilateral visual loss, which can progress or reoccur in spite of antiviral therapy. Aggressive therapy of the progressive retinitis and any associated retinal detachments is essential to maintain vision. In start, an earliest response to acyclovir therapy emerged to delay visual loss, but this was not associated with a better visual manifestation at final examination.[51] Acyclovir is the drug of choice for treatment of VZV infection at other sites in immunocompromised patients. However, a poor response has been seen with intravenous acyclovir therapy alone for PORN. Previous chronic oral acyclovir use in many of these patients may help with the development of VZV-acyclovir resistance.[52] Decreased systemic immunity may prevent inhibition of VZV infection. In the murine model of herpes retinitis, animals depleted of CD4+ cells had minimal intra-ocular inflammation and poor clearance of the herpes virus. Spaide and associates noted that the CD8+ T lymphocyte was the predominant retinal cell infiltrate in PORN and hypothesized that a poor response to treatment may be related to a relative deficiency of CD4+ cells. Retinal ischemia secondary to retinopathy may prevent achievement of therapeutic drug levels in the retina after systemic administration.[53] This factor may be overcome by increasing the systemic dose or by using local intra-ocular therapy. An upgrade therapeutic response has been reported by using an increased dose of systemic acyclovir (10 to 20 mg/kg every 8 hours).[54]

Other antivirals agents, such as ganciclovir and foscarnet, have activity against VZV and have been used to treat PORN. Acyclovir-resistant VZV may be sensitive to foscarnet because of its different mechanism of action. High dose foscarnet (60 mg/kg every 8 hours) has been suggested by some authors for primary treatment.[55] The combination of ganciclovir and foscarnet may have additive or synergistic effects. Visual acuity of 20/100 or better was kept in at least one eye in six patients for the remainder of their lives with a combination of antiviral therapy (systemic foscarnet and either acyclovir or ganciclovir) and vitreoretinal surgical repair of retinal detachment as required. High doses of acyclovir (10 to 20 mg/kg every 8 hours) or ganciclovir (5 mg/kg every 12 hours) combined with foscarnet (60 mg/kg every 8 hours) have been suggested for earliest therapy of PORN.[56] Combination antiviral therapy shown to be effective, even though no clinical experiment have contrast with the efficacy of a single antiviral agent with combination therapy. Initial treatment is continued until existing lesions are inactive and no new lesions appear. Other antiviral agents effective against VZV, including famciclovir, cidofovir,

and sorivudine, have yet to be fully evaluated for treatment of PORN.[57]

DIFFERENTIAL DIAGNOSIS

The differential diagnoses of the ARN and PORN syndromes are listed in. ARN and PORN syndromes are differentiated by an individual's immune status and the intraocular inflammatory response to the virus. The ocular features of ARN include a peripheral retinitis, periarteritis, and vitritis. PORN is differentiated from ARN by initial outer retinal whitening, early involvement of the posterior pole, and the absence of intraocular inflammation and vasculitis. Only patients who are noticeably immunosuppressed, such as those with AIDS, develop PORN. ARN has been described in individuals with relatively intact systemic immunity, regardless of their HIV status.[58]

The other herpesviruses should be contemplated among the differential diagnoses. Although some initial reports suggested that CMV may produce ARN syndrome, this has not been shown in most studies.CMV retinitis occurs in immunosuppressed patients. CMV lesions are often granular and hemorrhagic and feature a slower clinical course than either ARN or PORN. The marked vitritis narrate in ARN is not a usual feature of CMV retinitis. PORN is diffrentiated from CMV retinitis by the deep, multifocal, retinal opacification; a relative absence of hemorrhage; and a very fast clinical progression. The differentiation of CMV retinitis is therapeutically relevant because CMV does not usually respond well to acyclovir, although other antivirals, such as ganciclovir, effectively control CMV infection. Late retinal detachment also has been reported in CMV retinitis. Tiedeman studied 10 patients with a diffuse, unilateral, or bilateral pan uveitis firmed with choroiditis that, evidence suggests, was secondary to EBV. In contrast to ARN and PORN, large areas of confluent retinal necrosis did not occur.[59]

Other types of posterior uveitis may be demented with ARN or PORN syndromes. Bechet's disease shares many similarities with ARN, including a diffuse uveitis, prominent retinal arteritis, and patches of retinal whitening. The presence or absence of associated systemic findings, such as aphthous and genital ulcers, rash, and arthritis should differentiate the two entities.[60] Uveitis and vascular sheathing may occur with ocular sarcoidosis; however, arteritis and broad patches of retinal whitening are atypical. Again, systemic evaluation is invaluable in separating sarcoidosis from ARN. Ocular toxoplasmosis presenting as a focal retinitis with overlying vitritis may be demented with ARN. Serum or ocular toxoplasma titers or polymerase chain reaction may be helpful for differentiation, but in some cases, especially in the case of an immunocompromised patient, careful monitoring with or without a therapeutic trial may be designated.[61]

REFRENCES

1. Culbertson WW, Blumenkranz MS, Haines H et al: The acute retinal necrosis syndrome. Part 2: Histopathology and etiology. Ophthalmology, 1982; 89: 1317.
2. Culbertson WW, Blumenkranz MS, Pepose JS et al: Varicella zoster virus is a cause of the acute retinal necrosis syndrome. Ophthalmology, 1986; 93: 559.
3. Lewis ML, Culbertson WW, Post JD et al: Herpes simplex virus type 1: A cause of the acute retinal necrosis syndrome. Ophthalmology, 1989; 96: 875.
4. Duker JS, Nielsen JC, Eagle RC Jr et al: Rapidly progressive acute retinal necrosis secondary to herpes simplex virus type 1. Ophthalmology, 1990; 97: 1638.
5. Cunningham ET Jr, Short GA, Irvine AR et al: Acquired immunodeficiency syndrome-associated herpes simplex virus retinitis: Clinical description and use of a polymerase chain reaction-based assay as a diagnostic tool. Arch Ophthalmol, 1996; 114: 834.
6. Holland GN, Executive Committee of the American Uveitis Society: Standard diagnostic criteria for the acute retinal necrosis syndrome. Am J Ophthalmol, 1994; 117: 663.
7. Urayama A, Yamada N, Sasaki T et al: Unilateral acute uveitis with periarteritis and detachment. Jpn J Clin Ophthalmol, 1971; 25: 607.
8. Willerson D Jr, Aaberg TM, Reeser FH: Necrotizing vaso-occlusive retinitis. Am J Ophthalmol, 1977; 84: 209.
9. Young NJ, Bird AC: Bilateral acute retinal necrosis. Br J Ophthalmol, 1978; 62: 581.
10. Fisher JP, Lewis ML, Blumenkranz M et al: The acute retinal necrosis syndrome. Part 1: Clinical manifestations. Ophthalmology, 1982; 89: 1309.
11. Carney MD, Peyman GA, Goldberg MF et al: Acute retinal necrosis. Retina, 1986; 6: 85. [published erratum appears in Retina 1986 Summer-Fall;6:168
12. Sternberg P Jr, Han DP, Yeo JH et al: Photocoagulation to prevent retinal detachment in acute retinal necrosis. Ophthalmology, 1988; 95: 1389.
13. Thompson WS, Culbertson WW, Smiddy WE et al: Acute retinal necrosis caused by reactivation of herpes simplex virus type 2. Am J Ophthalmol, 1994; 118: 205.
14. Clarkson JG, Blumenkranz MS, Culbertson WW et al: Retinal detachment following the acute retinal necrosis syndrome. Ophthalmology, 1984; 91: 1665.
15. Peyman GA, Goldberg MF, Uninsky E et al: Vitrectomy and intravitreal antiviral drug therapy in acute retinal necrosis syndrome: Report of two cases. Arch of Ophthalmol, 1984; 102: 1618.
16. Kometani J, Asayama T: A case of specific uveitis occurring acutely in the right eye. Folia Ophthalmol Jpn, 1978; 29:1397.
17. Saari KM, Boke W, Manthey KF et al: Bilateral acute retinal necrosis. Am J Ophthalmol, 1982; 93: 403.

18. Chambers RB, Derick RJ, Davidorf FH et al: Varicella-zoster retinitis in human immunodeficiency virus infection: Case report. Arch Ophthalmol, 1989; 107: 960.
19. Litoff D, Catalano RJ: Herpes zoster optic neuritis in human immunodeficiency virus infection. Arch Ophthalmol, 1990; 108: 782.
20. Sado K, Kimura T, Hotta Y et al: Acute retinal necrosis syndrome associated with herpes simplex keratitis. Retina, 1994; 14: 260.
21. Solomon MJ: Unilateral acute retinal necrosis syndrome with herpes simplex keratitis. Retina, 1995; 15: 359.
22. Okinami S, Tsukahara I: Acute severe uveitis with retinal vasculitis and retinal detachment. Ophthalmologica, 1979; 179: 276.
23. Culbertson WW, Clarkson JG, Blumenkranz M, Lewis ML: Acute retinal necrosis. Am J Ophthalmol, 1983; 96: 683.
24. Blumenkranz MS, Culbertson WW, Clarkson JG et al: Treatment of the acute retinal necrosis syndrome with intravenous acyclovir. Ophthalmology, 1986; 93: 296.
25. Hayreh MMS, Kreiger AE, Straatsma BR et al: Acute retinal necrosis. Invest Ophthalmol Vis Sci, 1980; 19(Suppl): 48.
26. Wang CL, Kaplan HJ, Waldrep JC, Pulliam M: Retinal neovascularization associated with acute retinal necrosis. Retina, 1983; 3: 249.
27. Altamirano D, Rochat C, Claeys M et al: Acute retinal necrosis: A result of immune dysfunction? Report of a case with subacute evolution and relapses in a patient with impaired cellular immunity. Ophthalmologica, 1994; 208: 49.
28. Sergott RC, Belmont JB, Savino PJ et al: Optic nerve involvement in the acute retinal necrosis syndrome. Arch Ophthalmol, 1985; 103: 1160.
29. Rungger-Brandle E, Roux L, Leuenberger PM: Bilateral acute retinal necrosis (BARN): Identification of the presumed infectious agent. Ophthalmology, 1984; 91: 1648.
30. Matsuo T, Date S, Tsuji T et al: Immune complex containing herpesvirus antigen in a patient with acute retinal necrosis. Am J Ophthalmol, 1986; 101: 368.
31. Sergott RC, Anand R, Belmont JB et al: Acute retinal necrosis neuropathy: Clinical profile and surgical therapy. Arch Ophthalmol, 1989; 107: 692.
32. Falcone PM, Brockhurst RJ: Delayed onset of bilateral acute retinal necrosis syndrome: A 34-year interval. Ann Ophthalmol, 1993; 25: 373.
33. Matsuo T, Nakayama T, Koyama T et al: A proposed mild type of acute retinal necrosis syndrome. Am J Ophthalmol, 1988; 105: 579.
34. Crapotta JA, Freeman WR, Feldman RM et al: Visual outcome in acute retinal necrosis. Retina 13:208, 1993
35. Culbertson WW, Brod RD, Flynn Jr HW et al: Chickenpox-associated acute retinal necrosis syndrome. Ophthalmology, 1991; 98: 1641.
36. Sternberg P Jr, Knox DL, Finkelstein D et al: Acute retinal necrosis syndrome. Retina, 1982; 2: 145.
37. Severin M, Neubauer H: Bilateral acute retinal necrosis. Ophthalmologica, 1981; 182: 199.
38. Minckler DS, McLean EB, Shaw CM et al: Herpes hominis encephalitis and retinitis. Arch Ophthalmol, 1976; 94: 89.
39. Bloom JN, Katz JI, Kaufman HE: Herpes simplex retinitis and encephalitis in an adult. Arch Ophthalmol, 1977; 95: 1798.
40. Gorman BD, Nadel AJ, Coles RS: Acute retinal necrosis. Ophthalmology, 1982; 89: 809.
41. Ludwig IH, Zegarra H, Zakov ZN: The acute retinal necrosis syndrome: Possible herpes simplex retinitis. Ophthalmology, 1984; 91: 1659.
42. Gass JDM: Stereoscopic Atlas of Macular Disease, p 490. Vol 2. St. Louis: CV Mosby, 1987.
43. Matsuo T, Koyama M, Matsuo N: Acute retinal necrosis as a novel complication of chickenpox in adults. Br J Ophthalmol, 1990; 74: 443.
44. Friberg TR, Jost BF: Acute retinal necrosis in an immunosuppressed patient. Am J Ophthalmol, 1984; 98: 515.
45. Chess J, Marcus DM: Zoster-related bilateral acute retinal necrosis syndrome as presenting sign in AIDS. Ann Ophthalmol, 1988; 20: 431.
46. Murray PI: Wegener's granulomatosis, pituitary adenoma and BARN. Int Ophthalmol, 1994; 18: 361.
47. Sellitti TP, Huang AJ, Schiffman J et al: Association of herpes zoster ophthalmicus with acquired immunodeficiency syndrome and acute retinal necrosis. Am J Ophthalmol, 1993; 116: 297.
48. Price FW Jr, Schlaegel TF Jr: Bilateral acute retinal necrosis. Am J Ophthalmol, 1980; 89: 419.
49. Hayasaka S, Asano T, Yabata K et al: Acute retinal necrosis. Br J Ophthalmol, 1983; 67: 455.
50. Pepose JS, Stewart JA, Grose C et al: ARN: Serologic studies and further characterization of the virus. Invest Ophthalmol Vis Sci, 1986; 25(Suppl): 12.
51. Soushi S, Ozawa H, Matsuhashi M et al: Demonstration of varicella-zoster virus antigens in the vitreous aspirates of patients with acute retinal necrosis syndrome. Ophthalmology, 1988; 95: 1394.
52. Sarkies N, Gregor Z, Forsey T et al: Antibodies to herpes simplex virus type I in intraocular fluids of patients with acute retinal necrosis. Br J Ophthalmol, 1986; 70: 81.
53. Margolis T, Irvine AR, Hoyt WF et al: Acute retinal necrosis syndrome presenting with papillitis and arcuate neuroretinitis. Ophthalmology, 1988; 95: 937.
54. Holland GN, Cornell PJ, Park MS et al: An association between acute retinal necrosis syndrome and HLA-DQw7 and phenotype Bw62, DR4. Am J Ophthalmol, 1989; 108: 370.
55. Rummelt V, Wenkel H, Rummelt C et al: Detection of varicella zoster virus DNA and viral antigen in

the late stage of bilateral acute retinal necrosis syndrome. Arch Ophthalmol, 1992; 110: 1132.
56. Davis JL, Feuer W, Culbertson WW et al: Interpretation of intraocular and serum antibody levels in necrotizing retinitis. Retina, 1995; 15: 233.
57. de Boer JH, Luyendijk L, Rothova A et al: Detection of intraocular antibody production to herpesviruses in acute retinal necrosis syndrome. Am J Ophthalmol, 1994; 117: 201.
58. Freeman WR, Thomas EL, Rao NA et al: Demonstration of herpes group virus in acute retinal necrosis syndrome. Am J Ophthalmol, 1986; 102: 701.
59. Pepose JS, Flowers B, Stewart JA et al: Herpesvirus antibody levels in the etiologic diagnosis of the acute retinal necrosis syndrome. Am J Ophthalmol, 1992; 113: 248.
60. Regillo CD, Sergott RC, Ho AC et al: Hemodynamic alterations in the acute retinal necrosis syndrome. Ophthalmology, 1993; 100: 1171.
61. Palay DA, Sternberg PJ, Davis J et al: Decrease in the risk of bilateral acute retinal necrosis by acyclovir therapy. Am J Ophthalmology, 1991; 112: 250.