Surgical Treatment of Retinal Detachment Following Acute Retinal Necrosis Syndrome: Surgical Results in Four Patients

Chiun-Ho Hou, MD; San-Ni Chen, MD; Jau-Der Ho, MD; Cheng-Lien Ho[1], MD

Background: Acute retinal necrosis (ARN) syndrome is an uncommon but severe ocular disease that typically affects otherwise healthy individuals. It is frequently complicated with retinal detachment and the visual prognosis in such patients is usually poor.

Methods: We operated on four eyes in four patients from 1999 through 2001. Three ophthalmologists in our hospital did these operations, respectively. The surgical methods included pars plana vitrectomy, lensectomy, encircling scleral buckling combined with membrane dissection, air-fluid exchange, endolaser photocoagulation, and retinal tamponade with silicone oil or perfluoropropane gas.

Results: Three patients received one operation and the other one needed a second operation to release the retinal traction. One patient needed a lensectomy at the time of vitrectomy. Macular attachment was achieved in all four eyes (100%). Vision improved in two patients but none achieved visual acuity better than 20/200. The complications were cataract in three patients, macular pucker in three, and silicone keratopathy in one.

Conclusion: Our results suggest that modern vitrectomy techniques provide a very high retinal attachment rate in patients with retinal detachment following ARN syndrome.

(Chang Gung Med J 2003;26:835-42)

Key words: **acute retinal necrosis syndrome, retinitis, uveitis, vitrectomy.**

Acute retinal necrosis (ARN) syndrome is an uncommon intraocular inflammatory disease that is characterized by confluent peripheral necrotizing retinitis, occlusive arteritis, and vitritis. The spectrum of this disease varies from rapid onset of panretinal necrosis to an indolent vitritis with small areas of retinal necrosis that occur progressively over weeks.[1-4] The patients typically present with mild symptoms of anterior uveitis and blurred vision in an insidious onset. There is a triad of posterior segment changes. The changes include vitritis of mild to moderate severity develops early in the disease course, obliterative retinal and choroidal vasculitis primarily affects the arteries, and necrotizing retinitis develops multifocally in the peripheral retina area and may spread toward the posterior pole. Other findings include episcleritis, scleritis, elevated intraocular pressure, optic nerve head swelling and

From the Department of Ophthalmology, Chang Gung Memorial Hospital, Taipei; [1]Sunguard Eye Clinic, Keelung.
Received: Nov. 12, 2002; Accepted: Jun. 30, 2003
Address for reprints: Dr. San-Ni Chen, Department of Ophthalmology, Chang Gung Memorial Hospital. 5, Fushing Street, Gueishan Shiang, Taoyuan, Taiwan 333, R.O.C. Tel.: 886-3-3281200 ext. 8666; Fax: 886-3-3287798; E-mail: chensa@adm.cgmh.org.tw

macular edema. At presentation, the patients may complain of blurred vision, floaters, redness of the eye, or eye pain. This syndrome typically affects otherwise healthy individuals between 20 and 60 years of age and it causes devastating visual impairment in these productive individuals.[1-3] Urayama first reported ARN syndrome in 1971.[4] It is a self-limiting disease and spontaneous resolution occurs between 6 and 12 weeks following the onset of symptoms.[5] However, retinal detachment is a frequent late complication following ARN syndrome in up to 75% to 85% of the patients and they suffer from secondary visual impairment after the initial improvement. Medical treatment for ARN syndrome does not affect the high incidence rate of retinal detachment.[6] Surgical treatment of the retinal detachment following ARN syndrome includes scleral buckling alone, scleral buckling combined with vitrectomy, or vitrectomy alone.[5,6]

Here, we report our surgical results for the treatment of retinal detachment following ARN syndrome.

METHODS

We operated on four eyes of four consecutive patients with retinal detachment following ARN syndrome from September 1999 through November 2001. Three ophthalmologists in our hospital did the operations, respectively. These patients were all male and aged from 22 to 58 years (mean, 44 years; Table 1). The follow-up period ranged from 12 to 25 months (mean, 17.3 months).

All of the patients were immunocompetent. They received oral or intravenous acyclovir therapy combined with systemic corticosteroid 4 to 10 days after the onset of the symptoms (Table 2). Patient 1 received 2400 mg of intravenous acyclovir each day initially and the treatment was suspended for 7 days because he developed acute renal failure. The dosage of acyclovir was then reduced to 1000 mg per day. Patient 2 received 1500 mg of oral acyclovir each day for 14 days which was given by his local practitioner. He was referred to our hospital and received intravenous therapy with the maximal dose

Table 1. Summary of the Patients' Data

Case	Age (years)	Gender	Delay for Med Tx	RD after ARN	Preop vision	Extent of RD	PVR grade	Surgery	Postop vision	Macular attached	F/U (Ms)	Comments
1	58	M	7Ds	6 Ws	LP	100%	B	V+SB+MD+AFE+E+SO	HM	+	18	1. 2nd operation for tractional retinal detachment 2. Cataract developed and removed 3. Macular pucker
2	22	M	7Ds	3 Ws	CF	75%	B	V+SB+MD+AFE+E+C3F8	4/200	+	25	1. Cataract developed and removed 2. Macular pucker
3	54	M	4Ds	4 Ws	HM	100%	C P 2	V+SB+MD+AFE+L+E+SO	HM	+	14	1. Dense vitritis and RD noted in sonography 2. Silicone keratopathy
4	42	M	10Ds	9 Ws	20/50	75%	C P 2	V+SB+MD+AFE+E+SO	10/200	+	12	1. Cataract developed and removed 2. Macular pucker developed and removed

Abbreviations: Med Tx: medical treatment; Ds: days; RD: retinal detachment; ARN: acute retinal necrosis; Ws: weeks; Ms: months; LP: light perception; CF: counting fingers; HM: hand movement; PVR: Proliferative vitreoretinopathy; V: vitrectomy; SB: encircling scleral buckling; MD: membrane dissection; AFE: air-fluid exchange; E: endolaser photocoagulation; SO: silicone oil; C3F8: perfluoropropane; L: lensectomy

Table 2. Medical Treatments of Systemic Antiviral Agents and Steroid

Case	BW (kg)	Initial (per day)	Maintaining (per day)	Duration before tapering	Comment	Steroid (per day)
1	79	Acy IV 2400 mg	Acy IV 1000 mg	5 weeks	Dose reduction because of the onset of ARF	Pred 60 mg
2	60	Acy PO 1500 mg	Acy IV 1500 mg + Gan IV 450 mg	4 weeks	Transfer to our hospital after 2 weeks of therapy	Pred 120 mg
3	73	Acy PO 1000 mg	Acy IV 1050 mg	2 weeks	Transfer to our hospital after 5 days of therapy	Pred 60 mg
4	68	Acy IV 2100 mg	Acy IV 2100 mg	2 weeks		Pred 60 mg

BW: Body Weight; Acy: acyclovir; Gan: gancyclovir; IV: intravenous; PO: per oral; Pred: prednisolone; ARF: acute renal failure.

of 1500 mg of acyclovir per day and 450 mg of gancyclovir per day. Patient 3 received 1000 mg of oral acyclovir per day for 5 days at the beginning and then the maximal dose of 1050 mg of intravenous acyclovir per day. Patient 4 received 2100 mg of intravenous acyclovir per day for 12 days (Fig. 1).

There were no lesions involving the macula or the optic disc in our patients. All of the patients had unilateral disease, except for Patient 1. His left eye was involved 17 days after the onset in the right. We performed prophylactic photocoagulation therapy in two eyes, the left eye of Patient 1 and the left eye of Patient 4. Severe vitreous opacity in the others precluded the application of the laser therapy. Three to 9 weeks after the onset of the disease, the retinal detachments developed in the right eye of Patient 1 and those of the other three patients. The retinal detachments involved in 75% or more area of the retina. Patient 1 had multiple retinal breaks over four quadrants and the residual retina outside the major vascular arcades looked like a fish net. Patients 2 and 3 developed multiple retinal breaks over two quadrants. Patient 4 had honeycomb-like breaks over one quadrant. The maculae were detached in Patients 1, 2 and 3.

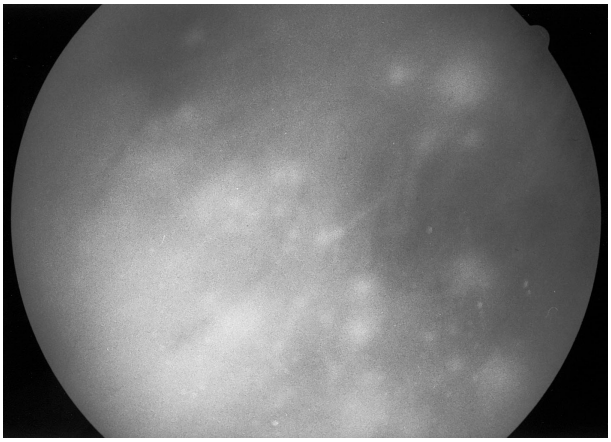

Fig. 1 Peripheral retina of the inferior-nasal quadrant in Patient 4 before medical treatment. Confluent yellowish white retinal lesions are visible.

We performed pars plana vitrectomy combined with encircling scleral buckling and endolaser in four eyes. Concomitant lensectomy was performed in Patient 3. The encircling scleral buckling was performed with the exoplants of Gortex bands. Vitrectomy was performed using the three-ports system with an attempt to remove as much of the vitreous cortex as possible, including the anterior vitreous base. The spontaneous posterior vitreous detachment over the posterior pole was noted in the four patients. The subretinal fluid was drained through the preexisting breaks in Patients 1, 2 and 3 and the planned retinotomy in Patient 4. The confluent endolaser photocoagulation was applied to the edge of the uninfected retina posterior to the area of retinitis. Finally, we substituted the vitreous with perfluoropropane gas in one eye and with silicone oil in three eyes. We examined the vitreous samples obtained during vitrectomy in Patients 2 and 3 using polymerase chain reaction (PCR) to identify the DNA of the causative agent.

RESULTS

The herpes simplex virus (HSV) DNA was detected using PCR in the vitreous samples of Patients 2 and 3. Macular reattachment was achieved in all four eyes after the surgical treatment (Fig. 2). In Patient 1, the peripheral fishnet-like retina exerted traction on the posterior retina and the inferior retina was detached 1 week after the operation. We performed the second vitrectomy with 360-degree retinotomy under silicone oil to release the

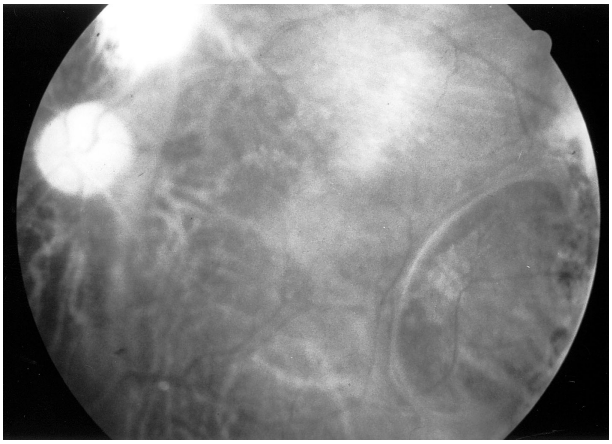

Fig. 2 Fundus photography of Patient 2 at 1 year after surgical treatment. The retina is well attached and the macular pucker is noted.

retinal traction. Macular puckers developed in Patients 1, 2 and 4 as late complications. Patient 4 received another vitrectomy for pucker removal but the other two refused further surgery because of the limited benefits. During the operation for pucker removal in Patient 4, we noticed that the fibrotic membrane was very thick and it was strongly adhered to the retina surface.

Cataracts developed in all patients, except for Patient 3, who received the concomitant lens extraction during the primary operation. Patients 1 and 2 received extracapsular cataract extraction with posterior chamber intraocular lens implantation months after the vitrectomy. Patient 4 had lensectomy during the secondary vitrectomy for pucker removal. Patient 3, who received silicone oil as the vitreous substitute, developed silicone keratopathy. Vision was improved in Patients 1 and 2 after the surgical treatment, but the visual acuity was below 20/200 in all four patients. Transient intraocular pressure elevation was noted in the days following the vitrectomy in two patients.

DISCUSSION

Previous studies have demonstrated that the herpes virus family, including herpes simplex virus (HSV) and varicella zoster virus (VZV), were causative agents of ARN syndrome. The evidence includes viral particles similar to the herpes virus family seen in an enucleated globe, VZV antigens within the intraocular fluid, culture growth of HSV and VZV from the intraocular fluid, and detection of DNA of the herpes virus family using PCR in the intraocular fluid.[7-11] We detected HSV DNA using PCR in the vitreous samples of Patients 2 and 3. The laboratory results helped us confirm the diagnosis of ARN syndrome, especially in Patient 2, who had poor response to acyclovir initially. Using PCR, Ganatra et al. demonstrated that the causative agents of ARN syndrome were age-related.[11] They detected VZV and type-1 HSV in the patients older than 25 years, and type-2 HSV in the patients younger than 25 years. Our laboratory does not have the facility to differentiate the DNA between type-1 and type-2 HSV. Occasionally, the patients with ARN syndrome might develop zoster lesions over face before the onset of ARN, but none of our patients had such a history.[12,13]

The rhegmatogenous retinal detachment usually develops within 2 to 3 months after the onset of ARN syndrome.[7] This complication plays a major role in patients' visual impairment. Laser photocoagulation applied posterior to the areas of active retinitis was recommended to prevent the retinal detachment in ARN syndrome.[14,15] However, the successful performance of photocoagulation requires clear media. Three eyes of our patients had severe vitreous reaction, which made this prophylaxis impossible.

It is difficult to repair the retinal detachment in ARN syndrome for three reasons.[16] First, the retinal breaks are often large in size, multiple in number and posterior in location. Second, proliferative vitreoretinopathy and vitreous traction is often present. And third, the inflammatory nature of the ARN syndrome usually results in the postoperative complications. With the advance of the surgical technique, the reported retinal reattachment rate was improved from 22% in the early studies to 100% in the later studies.[16-19] The pars plana vitrectomy with or without scleral buckling showed a better reattach rate than scleral buckling alone. We performed pars plana vitrectomy combined with scleral buckling in our four patients and the reattach rate was comparable.

The visual acuity improved in two patients (Patient 1 and 2), but no patient achieved visual acuity of better than 20/200. In previous studies,

approximately 80% of patients achieved visual acuity of 20/200 or better following vitrectomy alone.[17,18] The most frequent causes of vision loss were reported to be macular pucker and optic nerve dysfunction.[1,18] In our study, the incidence rate of macular pucker was high. Three of our patients had complications of macular pucker that required removal. Two patients refused further surgery to remove the pucker. Patient 4 received pucker removal but the visual improvement was limited. The high complication rate of macular pucker in our patients may be attributed to the severe inflammatory reaction. Three eyes of our patients had vitreous opacity so dense that made the prophylactic laser therapy impossible, and the opacity in one eye even precluded the fundus examination. During the vitrectomy, we noticed that the vitreous cavity was filled with fibrin and exudative substance. The posterior vitreous over the posterior pole detached spontaneously in every patient because of the long-lasting inflammation. In such a severely inflamed vitreous, the photoreceptors in the detached retina were most likely badly damaged, and the inflammatory cell and the debris induced the formation of epiretinal membrane. These effects prevented the visual recovery in our patients.

In general, the patients typically present with mild symptoms of uveitis and blurred vision in an insidious onset. There were several causes for the severe inflammatory condition in our patients. As a tertiary referral center, the patients referred to our hospital are usually in the relatively late phase of the disease, and the disease status is often more severe than in the average person. Prompt and adequate treatment is usually delayed. In our patients, the application of acyclovir was delayed for an average of 7 days. This delay could be one reason for the severe inflammation in our patients. In addition, suboptimal medical treatment in our study may have been another cause for the poor visual prognosis. The recommended medical treatment for ARN syndrome consists of antiviral agent of 1500 mg/m^2 of intravenous acyclovir per day for 10 days, antithrombotic therapy of 125 mg to 650 mg aspirin per day, and 60 mg to 80 mg systemic prednisolone per day.[1-3] In our patients, only Patient 4 received the dose of acyclovir that was close to what was recommended. Patients 2 and 3 were initially treated by a local practitioner with 1500 mg of oral acyclovir therapy per day for 14 days and 1000 mg of oral acyclovir therapy per day oral acyclovir therapy for 5 days, respectively. After admission, we added intravenous gancyclovir for Patient 2 because the disease continued to progress despite the 14 days of treatment with acyclovir. The laboratory examination of Patient 2 later revealed that he was immunocompetent and the causative agent was HSV. Patient 1 developed acute renal failure 2 days after the recommended dose of acyclovir. The medical therapy was then suspended for 7 days. In fear that there was racial difference in the therapeutic dosage, Patient 1 thereafter and the other two patients received only 50% to 60% of the recommended dose. This suboptimal treatment of acyclovir might have prolonged the disease course and intensified the intraocular inflammation. Crapotta et al. demonstrated that aggressive medical treatment provided better visual prognosis in patients with ARN syndrome when the disease extent was limited.[20]

None of our patients received antithrombotic therapy. It is possible that the absence of aspirin usage worsened the visual performance in our patients. However, no substantial clinical evidence supported the viewpoint that aspirin prevented the vascular obstruction in ARN syndrome, and therefore improved the visual outcome.[1,16] In the treatment of systemic corticosteroid, we gave the dose similar to what was recommended.

Blumenkranz et al compared the surgical results of vitrectomy alone and vitrectomy combined with scleral buckling.[18] Favorable visual outcomes resulted in the non-buckle group. Because our patients had multiple retinal breaks that covered large areas and severe intraocular inflammation, we chose vitrectomy combined with scleral buckling as the primary surgery. We believed that vitrectomy alone was not adequate to reattach the retina. During the operation, we did not perform cryotherapy with the scleral buckling. This was different from the study by Blumenkranz's in which the scleral buckling was always performed with cryotherapy. We avoided the complications of cryotherapy, but the buckling procedure itself might increase the ischemic and inflammatory reactions by compressing the vascular circulation. This might have impaired the visual recovery in our patients.

Racial differences may pose another reason for complications. Chung et al. reported on 10 Chinese

patients with ARN syndrome in 1993.[21] Seven of these patients were complicated with retinal detachment, and three received surgical treatment. The surgical procedures included pars plana vitrectomy, encircling scleral buckling, membranectomy and intravitreous gas tamponade. One had cryotherapy and two had endolaser photocoagulation. One patient achieved retina reattachment after the surgical treatment, but none of these seven patients achieved the final vision of 20/200 or better. We exhibited a better retinal reattachment rate in our study than that reported by Chung et al. This may have been due to the more delicate designs of the surgical instruments, and the use of silicone oil as vitreous tamponade. However, the visual improvement was limited in both groups. Delayed prompt medical treatment was the common reason. As a tertiary referral center, the seven patients in the study by Chung et al. were in the relatively late phase when referred. It was 1 to 4 weeks after symptoms before the proper treatment was given. Two of their patients were even complicated with retinal detachment when they first presented in the clinic. Because the initial symptoms are typically insidious in the diseased eye and the vision remains good in the other, it is possible that the patients in our population may not be alert enough to seek for medical help as early as possible. It is not known that racial differences or simply delays in prompt medical treatment impaired the visual prognosis in these patients of our population. Further case reports are needed.

Our experience demonstrated that the modern surgical techniques, which consisted of three-port bimanual vitrectomy, endolaser photocoagulation, and long acting retinal tamponade, is retina reattachment no longer a tough task in the surgical treatment of retinal detachment in ARN syndrome. There are some factors that explain the limited visual improvement after the surgical treatment in our patients. Delay in medical treatment, suboptimal medical therapy, combined scleral buckling, severer disease status, and racial differences all play a possible role. Prompt and adequate medical therapy seems to be a key point. It lessens the disease severity. The less severe vitritis makes the prophylactic photocoagulation practicable, and this reduces the changes of retinal detachment. The limited necrosis reduces the number of the retinal breaks and the areas to which they spread, and this makes it easier to reattach the detached retina by vitrectomy without scleral buckling. Finally, the damage of the photoreceptors in the detached retina is reduced under a condition of less severe inflammation. Though medical therapy itself cannot prevent the occurrence of retinal detachment in ARN syndrome, our results suggested that early recognition and adequate medical therapy were important in the visual prognosis in these patients.

REFERENCES

1. Duker JS, Blumenkranz MS. Diagnosis and management of the acute retinal necrosis (ARN) syndrome. Surv Ophthalmol 1991;35:327-43.
2. Morse LS, Mizoguchi M. Diagnosis and management of viral retinitis in the acute retinal necrosis syndrome. Semin Ophthalmol 1995;10:28-41.
3. Freilich JM, Ryan EA, Lou PL, Kroll AJ, Brockhurst RJ, Harooni M. Acute retinal necrosis syndrome: findings, management, and differential diagnosis. Int Ophthalmol Clin 1996;36:141-6.
4. Urayama A, Yamada N, Sasaki T, Nishiyama Y, Takei Y. Unilateral acute uveitis with retinal periarteritis and detachment. Jpn J Clin Ophthalmol 1971;25:607-19.
5. Fisher JP, Lewis ML, Blumenkranz M, Culbertson WW, Flynn JHW, Clarkson JG, Gass DM, Norton EWD. The acute retinal necrosis syndrome. I. Clinical manifestations. Ophthalmology 1982;89:1309-16.
6. Blumenkranz MS, Culbertson WW, Clarkson JG, Clarkson JG, Dix R. Treatment of the acute retinal necrosis syndrome with intravenous acyclovir. Ophthalmology 1986;92:296-300.
7. Culbertson WW, Blumenkranz MS, Haines H, Haines H, Gass DM, Mitchell KB, Norton EWD. The acute retinal necrosis syndrome. II. Histopathology and etiology. Ophthalmology 1982;89:1317-25.
8. Rungger-Brandle E, Roux L, Leuenberger PM. Bilateral acute retinal necrosis (BARN). Identification of the presumed infectious agent. Ophthalmology 1984;91:1648-58.
9. Culbertson WW, Blumenkranz MS, Pepose JS, Stewart JA, Curtin VT. Varicella zoster virus is a cause of the acute retinal necrosis syndrome. Ophthalmology 1986; 93:559-69.
10. Lewis ML, Culbertson WW, Post JD, Miller D, Kokame GT, Dix RD. Herpes simplex virus type 1. A cause of the acute retinal necrosis syndrome. Ophthalmology 1989; 96:875-8.
11. Ganatra JB, Chandler D, Santos C, Kuppermann B, Margolis TP. Viral causes of the acute retinal necrosis syndrome. Am J Ophthalmol 2000;129:166-172.
12. Yeo JH, Pepose JS, Stewart JA, Sternberg PJ, Liss RA. Acute retinal necrosis syndrome following herpes zoster dermatitis. Ophthalmology 1986;93:1418-22.
13. Browning DJ, Blumenkranz MS, Culbertson WW,

Clarkson JD, Tardif Y, Gourdeau A, Minturn J. Association of varicella zoster dermatitis with acute retinal necrosis syndrome. Ophthalmology 1987;94:602-6.
14. Sternberg P, Han DP, Yeo JH, Barr CC, Lewis H, Williams GA, Mieler WF. Photocoagulation to prevent retinal detachment in acute retinal necrosis. Ophthalmology 1988;95:1389-93.
15. Han DP, Lewis H, Williams GA, Mieler WF, Abrams GW, Aaberg TM. Laser photocoagulation in the acute retinal necrosis syndrome. Arch Ophthalmol 1987;105:1051-4.
16. Blumenkranz MS, Clarkson JG, Culbertson WW, Flynn HW, Lewis ML, Young GM. Vitrectomy for retinal detachment associated with acute retinal necrosis. Am J Ophthalmol 1988;106:426-9.
17. Clarkson JG, Blumenkranz MS, Culbertson WW, Flynn HW, Lewis ML. Retinal detachment following the acute retinal necrosis syndrome, Ophthalmology 1984;91:1665-8.
18. Blumenkranz MS, Clarkson JG, Culbertson WW, Flynn HW, Young GM. Visual results and complications after retinal reattachment in the acute retinal necrosis syndrome. Retina 1989;9:170-4.
19. McDonald HR, Lewis H, Kreiger AE, Sidikaro Y, Heckenlively J. Surgical management of retinal detachment associated with the acute retinal necrosis syndrome. Br J Ophthalmol 1991;75:455-8.
20. Crapotta JA, Freeman WR, Feldman RM, Lowder CY, Ambler JS, Parker CE, Meisler DM. Visual outcome in acute retinal necrosis. Retina 1993;13:208-13.
21. Chung YM, Liu JH, Yeh TS. Acute retinal necrosis syndrome. Chin Med J (Taipei) 1993;51:116-22.

急性視網膜壞死症併發網膜剝離之手術治療：對於四位病患的手術治療結果

侯鈞賀 陳珊霓 何昭德 何正廉[1]

背 景： 急性視網膜壞死症爲一不常見但嚴重之眼科疾病，其往往發生於健康個體。此症常併發視網膜剝離，造成病患嚴重視力缺損。

方 法： 我們於1999年到2001年對於四位病人的四隻眼睛施予手術治療，手術分別由本院三位眼科醫師實施。方法爲經平坦部玻璃體切除術、環狀鞏膜扣環術、增生膜分離、氣液交換、眼內雷射治療、以及使用矽油或膨脹氣體作視網膜填塞。

結 果： 一位病人於實施玻璃體切除術時，須伴隨水晶體摘除。而另一位病人因術後有視網膜牽引，須再次手術。四位病人的黃斑部均成功貼合 (100%)。兩位病人術後視力進步，但所有人的視力均低於20/200。三位病人術後併發白內障，三位病人併發黃斑部皺摺，及一位病人併發矽油性角膜病變。

結 論： 我們的手術結果顯示現今的玻璃體切除術之技術，對於急性視網膜壞死症併發網膜剝離之情形，有很高的手術成功率達到視網膜貼合。

(長庚醫誌 2003;26:835-42)

關鍵字： 急性視網膜壞死症，視網膜炎，葡萄膜炎，玻璃體切除術。

長庚紀念醫院 台北院區 眼科，[1]信光眼科中心
受文日期：民國91年11月12日；接受刊載：民國92年6月30日。
索取抽印本處：陳珊霓醫師，長庚紀念醫院 眼科。桃園縣333龜山鄉復興街5號。Tel.: (03)3281200轉8666; Fax: (03)3287798; E-mail: chensa@adm.cgmh.org.tw