RADIATION-ASSOCIATED CHOROIDAL NEOVASCULOPATHY, EXUDATIVE DETACHMENT AND NEOVASCULAR GLAUCOMA. A CASE REPORT.

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SUMMARY
Radiotherapy remains a controversial type of therapy for subfoveal neovascularization. Recently a peculiar pattern of neovascular growth of the irradiated choroidal neovascular membrane has been described. This evolution may be associated with extensive exsudative reaction. In one of our patients with this complication, the disease progressed to a total exudative retinal detachment and neovascular glaucoma.

RESUME
Le traitement par radiothérapie pour néovaisseaux rétro-fovéolaires reste controversé. Récemment, une évolution particulière des néovaisseaux sous-rétiniens irradiés a été décrite. Cette évolution peut être associée à une réaction exsudative étendue. Nous décrivons un patient avec cette complication, qui a évolué vers un décollement exsudatif de la rétine et glaucome néovasculaire successif.

SAMIENVATTING
Radiotherapie voor subfoveolaire neovascularisatie blijft een controversiële vorm van behandeling. Een ongewoon groepatoom werd onlangs beschreven bij geïrradiëerde choroidale neovascularaire membranen, waarbij een belangrijke exsudatieve reactie kan ontstaan. We beschrijven een patiënt, met deze complicatie, die verder evolueerde naar een totale exsudatieve retinolosilating en neovascular glaucom.

KEYWORDS
Age-related macular degeneration (ARMD), Exudative detachment, Radiotherapy, Neovascular glaucoma, Radiation-Associated Choroidal Neovascularopathy (RACN)

MOTS CLES
Dégénérescence maculaire liée à l’âge (DMLA), Décollement exudatif, Radiothérapie, Glaucome néovasculaire, "Radiation-Associated Choroidal Neovascularopathy (RACN)"

INTRODUCTION
The characteristics and progression of radiation retinopathy and optic neuropathy are well-known. Neovascular glaucoma has been reported as a complication of ophthalmic plaque brachytherapy and megavoltage external beam radiotherapy (EBRT) for choroidal melanoma, lymphoma, hemangioma, head and neck tumors. Radiation-associated choroidal changes have been studied since the introduction of indocyanine green angiography (ICGA) in clinical practice. Recently, attention has been paid to the side-effects of EBRT for age-related choroidal neovascularisation (CNV) (7,8,9). We observed an unusual pattern of CNV, an exudative retinal detachment and neovascular glaucoma in a patient treated by EBRT for subfoveal CNV.

CASE REPORT
In 1994 a 73-year-old man lost central vision of the LE from subfoveal CNV despite 5 ses-
sions of laser treatment. In January 1995 he complained of metamorphopsia in the right eye. Subsequently juxtafoveal neovascularization was diagnosed and laser treatment was given. However, in February 1995 a recurrence of the CNV was noted. Fluorescein angiography (FA) showed a small well-demarcated subfoveal CNV. Therapeutic options, including EBRT, were discussed. In view of promising results of pilot studies using EBRT (1,2,3), the patient accepted EBRT of the RE. Visual acuity before EBRT was 20/100 RE and 20/800 LE. Radiotherapy was delivered with 6 Mev photons of a Linear Accelerator, the patient's head being fixed with a thermoplastic mask. Irradiation was applied in a D-shaped field confined to the posterior pole of the affected eye(9). A dose of 20 Gy was given in 10 fractions in 2 weeks. Correct positioning of the radiation field was verified with gammaraphies taken with the treatment machines. The calculated dose under the protecting block to the anterior segment (at 4 mm posterior to the cornea) was 3.14% of the reference dose. One month after EBRT, VA of the RE was 20/200. Slitlamp examination showed a macular serous detachment in the RE with a few lipids and a small hemorrhage. FA revealed growth of CNV (Figure 1 Top left) to 1 MPS (Macular Photocoagulation Study) disc area. Three months following EBRT, VA was 20/300 and further growth of CNV was documented (Figure 1 Top right). Additional radiation of the posterior pole of the RE was suggested and planned in 8 sessions of 2 GY in July 1995.

Figure 1. Recurrent CNV in the RE after laser treatment. (Top left) FA 1 month after EBRT and (Top right) FA 3 months after EBRT show growth of the CNV. (Bottom left) Red free photograph 6 months after EBRT demonstrates a serous detachment, lipids, and hemorrhages. (Bottom right) FA shows intensive staining of bleb-like lesions around the border of the CNV.
After the second session of EBRT the patient complained of slight discomfort in the RE. Slit-lamp examination showed signs of chronic blepharitis. Although no superficial punctate keratitis was noted, the patient did feel relief with artificial tears. Ever since, the patient noticed a further loss of vision in his RE, which now was the eye with poorest vision. Six months after the first EBRT, VA was counting fingers RE and remained 20/800 LE. Biomicroscopy of the RE showed increased exudation with a prominent macular serous detachment, lipids, and fresh hemorrhages at the borders of the CNV (Figure 1 Bottom left). FA showed atrophic changes of the laser burn, mild leakage of the central part of the CNV, and intensive staining of bleb-like lesions around the border of the CNV (Figure 1 Bottom right). Repeated fluorescein angiograms did not reveal any signs of ischemia or radiation retinal effects in the periphery. These peculiar polypoidal lesions were more evident on the FA 1 yr after the first EBRT (Figure 2 Top left), and remained present on ICGA and FA for another year (Figure 2 Top right and Bottom). They were associated with pronounced and progressive exudation and with fresh hemorrhages (Figure 3 Top). In October 1997, two and a half year after the first EBRT, an exudative detachment of the inferior third of the retina and subretinal crystalline deposits were noted (Figure 3 Bottom left). In April 1998 the RE was blind and rubeosis iridis without glaucoma was diagnosed. Break-through vitreous hemorrhage blurred part of the CNV and
the retinal detachment was total (Figure 3 Bottom right). Signs of radiation retinopathy or central vein occlusion were never observed. Vitreoretinal surgery was considered in an attempt to restore some vision and to prevent neovascular glaucoma, but was not performed as the success rate was considered to be too low. In July 1998 neovascular glaucoma occurred. It was medically treated with atropine, timolol and dorzolamide eye drops. In October 1998, the RE was slightly painful. Biomicroscopy showed a relatively quiet eye with rubeosis iridis, synechiae, a mature cataract, and blood behind the lens, making visualization of the posterior segment impossible. On ultrasound B-scan, a total retinal detachment and a normal orbit were found. In the LE additional laser treatment for recurrences of CNV was given in June 1995 and March 1996. Later on, no new recurrences were noted in the LE (Figure 4) and the VA was 20/800. This patient had a history of arterial hypertension and mild cardiovascular problems, which was treated with aspirin, nifedipine and naftidrofuryloxalate. He had no history of transient ischemic attacks. Non-invasive evaluation of the carotid arteries revealed no abnormalities.

**DISCUSSION**

There is still no effective treatment for subfoveal age-related CNV with the exception of...
photodynamic therapy with recently published beneficial effect. The MPS recommends laser photocoagulation for small subfoveal CNV with well-demarcated boundaries. However, this treatment implies destruction of the overlying retina with immediate and often significant visual loss. EBRT was introduced as a less destructive treatment aiming to induce vessel obliteration of CNV (9), sparing the overlying retina. Unfortunately, the promising results of early pilot studies were not confirmed by studies from other centers (1,2,3). In 1994, 1995, and 1996 we have treated a total of 183 eyes with subfoveal CNV with EBRT. Five patients presented an associated retinal pathology e.g. angiod streaks and myopia. They were younger than 55 years of age. In all patients a fraction size of 2 Gy/day was used, which is commonly considered a standard safe fraction. Nearly all patients received a total dose of 20 Gy which is considered to be safe. Four patients, including the patient described in this report, had additional EBRT to a total dose of 30 Gy or 36 Gy. In 1996 we stopped with EBRT when it became evident that EBRT failed to control CNV growth and seemed to be ineffective to stabilize vision (9). However, all patients were encouraged to show up for further follow-up as there was a risk for side effects of EBRT (7). Indeed, 7% of our patients developed an unusual pattern of vascular growth of the neovascular complex with polypoidal lesions around the borders of the CNV (8). These patients often showed pronounced exudation and hemorrhages. This type of complication was also observed in patients treated with low doses of EBRT and was named radiation-associated choroidal neovascularopathy or RACN (8). Three of our patients with RACN progressed to a total or subtotal retinal detachment, and the patient reported in this paper had a further evolution to neovascular glaucoma. Laser photocoagulation appeared useful in other patients with RACN to induce regression of exudation and stabilization of vision. Radiation neuropathy or retinopathy were, up till now, not observed. Polypoidal lesions,
with a similar appearance as the peculiar vessels of RACN, are observed in idiopathic polypoidal choroidal vasculopathy, also known as the multiple recurrent serosanguineous retinal pigment epithelium detachment syndrome or the posterior uveal bleeding syndrome (4,6). The saccular dilatations of the choroidal vasculature causes recurrent serous and hemorrhagic detachments of the sensory retina and the retinal pigment epithelium, with extensive fibrovascular proliferation within the subretinal space and Bruch’s membrane. In one patient, the development of rubeosis and loss of useful vision in one eye has been clinicopathologically correlated with these findings (4). However, this patient was diabetic and showed diabetic background retinopathy, which is an additional risk factor for ischemic eye disease. Our patient had arterial hypertension, but no other underlying risk factors of evidence for developing ischemic conditions at the retina. He never presented signs of radiation retinopathy or vein thrombosis. Anterior irradiation may be another critical factor for the appearance of rubeosis iridis and neovascular glaucoma (5). However, in our patient the estimated total dose applied to lens and anterior chamber was only 1.13 Gy. Moreover, the patient was immobilized during EBRT with a thermoplastic mask, which makes errors in the treatment field unlikely. We consider the neovascular glaucoma in this patient to be a late complication of RACN.

CONCLUSION

EBRT remains a controversial form of therapy for AMD. Several studies have shown no beneficial effect on the growth of CNV and on stabilization of vision (9). With a longer follow-up of patients, side effects of EBRT on subfoveal CNV have been reported (7,8). Physicians who have treated patients with AMD with EBRT should be aware of these side effects and should urge their patients for follow-up. A high initial total dose or retreatment with an elevated total dose of radiation and a large irradiation field, are associated with an increased risk of side effects which may result in the total functional loss of the eye. RACN should be recognized in an early stage, as laser treatment appears effective in inducing regression of exudation and stabilizing vision.

REFERENCES


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