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Radiotherapy for choroidal neovascularisation of age-related macular degeneration

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Age-related macular degeneration caused by choroidal neovascularisation is an increasing problem in ophthalmology. The results of the therapy in the past were poor or associated with a number of side effects. Recently, some reports have shown a beneficial effect of low-dose irradiation. Therefore, we reviewed the data of our patients included in a pilot study to confirm the very preliminary data in literature. Fourty-three patients were irradiated with a linear accelerator (6 MV) at a total dose of 16 Gy. Six months after irradiation, 69% of our patients maintained or improved their visual acuity. We did not observe side effects or any acute or late sequelae within a median follow-up period of 12 months.

Key words: macular degeneration - radiotherapy, visual acuity

Introduction

Choroidal neovascularisation (CNV) is a major cause of severe loss of visual acuity in the patients with age-related macular degeneration.[1] Without therapy, the natural course of this disease would result in the loss of patient's sight.

In the past, laser photocoagulation was used as treatment method, but was, unfortunately, associated with further decrease in visual acuity.[2] In the treatment of CNV, interferon was used systemically, but, so far, the substance has not proved to be effective, moreover, it may be that it has severe side effects.[3]

Another approach is the surgical extirpation although the treatment results are not too encouraging.[4] Recently, some investigators have reported of a beneficial effect of low-dose irradiation of the subretinal neovascular membranes in the CNV.[5-13] The preliminary results are encouraging and the number of side effects is small.

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Patients and methods

Between September 1996 and July 1998, we treated 43 patients (25 women and 18 men) with radiotherapy for age-related macular degeneration. All patients gave their

informed consent before irradiation. The median age at the time of treatment was 74 years (range 60-88 years).

The right and the left eye were treated in 18 and 16 patients, respectively. In 9 patients, both eyes were involved. In all cases, the diagnose was set on the basis of visual examination (funduscopy) carried out by the ophthalmologist. All patients were diagnosed as having the exudative variety of macular degeneration. In 21 patients, angiography was used to determine the size of the neovascularisation.

Irradiation was carried out using a linear accelerator of 6 MV photons. A total dose per patient was 16 Gy and was given in normal fractionation with single doses of 2 Gy 5 times a week. When both eyes were involved, opposed portals were used and the dose was specifically adjusted to the middle of the scull. In case of unilateral neovascularisation, a single irradiation field was used. In all cases, we used a lens-sparing technique.

The median follow-up time was 12 months. Each patient was clinically examined before and immediately after the therapy and then every 3 months. All patients included in this study were questioned about their subjective experience of radiotherapy, treatment results and side effects.

Results

After the completion of irradiation, visual acuity improved in 5 patients (11%), in 35 patients (81%), it was the same as before irradiation and was worse in 3 patients.

Six months after the irradiation, 30 patients (69%) maintained their visual acuity while in 9 patients (21%), it was worse. Four patients were lost from the follow-up at the time of investigation.

Objective changes of visual acuity could be observed only to a limited extent (median difference 0.005). In 5 patients, the moist macular degeneration changed to a dry one without affecting the acuity. In 2 patients, the bleeding occurred again 3 and 7 months after the completed irradiation. As to the side effects, we have not observed any acute or late sequelae after irradiation.

In addition to the objective findings, the results of the interviews with the treated patients were the following results: 31 patients (72%) reported that irradiation had a beneficial influence on their acuity and 12 patients felt that irradiation did not improve their sight.

Discussion

Macular degeneration is an increasing problem in ophthalmology. Today, about 5% of the population in their sixties are affected.[1] The patients are handicapped by the loss of central vision and, therefore, their ability to read.

Often, both eyes are affected to various degrees and at different times.[14] Stage I shows a dry formation of senile membranes. A detachment of the pigment epithelium with retroretinar bleeding occurs within some weeks. In the exudative stage, disciform lesions are observed. They consist of choroidal neovascularisation and spread into the retroretinal space as a thin layer between the retina and choroid. At this stage, patients often report seeing only shadows. Regression of the exudative changes causes complete atrophy of the central part of the retina. The therapy is stage-dependant.[14]

In the early dry stage, no special therapy is recommended. The detachment of the pigment epithelium is treated with corticosteriods. Laser coagulation could be applied, but causes scars and decreases the acuity. [2,15-17] Neovascular membranes cannot be treated with laser. In these cases, radiotherapy can be applied as alternative treatment. Irradiation seems to be able to stop further progress of the disease.

Proliferating vascular cells have been

known to be relatively sensitive to low doses of radiation. Irradiation may prevent the proliferation of endothelial cells of newly formed subretinal capillaries and induce obliteration of the aberrant new vessels.[18] Some data that have appeared so far in the literature confirm the assumption that photon irradiation can be a beneficial tool in treating this disease. Chakravarthy *et al.* treated macular degeneration with a total dose of 10 or 15 Gy and recorded that the visual acuity was maintained or improved in 78% of all patients.[8] Hart and colleagues treated 41 patients with 10, 12 or 15 Gy and found no significant difference in the effect of treatment of 3 different dose regimes.[10] Bergking *et al.*[5] evaluated the patients in a study on doses ranging between 8 and 24 Gy. The first group received 8 Gy in a single fraction. In this group, only 30% had stable visual acuity. In the second group, 50% of patients having received a dose of 12 Gy had stable visual acuity after a follow-up of 18 months and in the third group having received a dose of 18 Gy, 40% of patients had stable visual acuity after the same follow-up period. In the group which had received 24 Gy, 80% of all patients had stable visual acuity.

Hence, it is possible that there is a relationship between total doses of irradiation and treatment results. But care should be taken not to exceed a total dose of 25 Gy in order to avoid an increase in side effects.

On the other hand, some data published in literature report of the positive treatment results using proton beam irradiation. Yonemoto *et al.*[13] reported that after a median follow-up of 11.6 months 58% of a total of 21 patients had an improved or stable visual acuity. So far, it has not been proved that, with regard to the treatment results, heavy particles such as protons are superior to normal photon therapy.

In our investigation, we recorded stable visual acuity objectively in 69% of all patients 6 months after irradiation. After interviewing the patients, it was estimated that the effect of treatment was beneficial in 72% of cases. As no acute or late sequelae and no changes in the number of stable diseases were observed within the median follow-up time of 12 months, we believe that low-dose irradiation can be a good treatment policy of the patients with progressive CNV. Nevertheless, the definitive role of radiotherapy in patients with CNV is still to be defined by a control phase-III study.

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