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Favorable long-term results of primary pterygium removal by bare sclera extirpation followed by a single ^{90}Strontium application

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PURPOSE. *To describe and compare long-term (≥36 months) effects of patients with 86 primary pterygia treated with bare sclera extirpation (BSE) followed by β-RT or by sham irradiation.*
METHODS. *Prospective, multicenter, randomized, double-blind study. After BSE of their pterygium, patients were randomized to either β-RT or sham irradiation. In the case of β-RT, within 24 hours after the operation, a 90Sr eye applicator was used to deliver 2500 cGy to the sclera surface at a dose rate of between 200 and 250 cGy/min. Sham irradiation was given using the same type of applicator without the 90Sr layer. After treatment, both a masked ophthalmologist and a radiation oncologist performed follow-up examinations. These were continued until either a relapse occurred or at least 36 months had elapsed.*
RESULTS. *Adequate follow-up was available of 86 pterygia in 81 patients, treated between February 1998 and September 2002. Fifty-two (60%) patients were male. The mean age of the patients was 50 years (range: 24–77). After a follow-up of at least 36 months (mean: 40 months, SD:13.9 months), 5 out of 44 eyes (11%) treated with β-RT showed a recurrence versus 32 out of 42 eyes (76%) treated with sham-RT (after a mean follow-up of 22 months) (p<0.001). In the β-RT group, 80% were satisfied with the cosmetic result, whereas in the sham group this percentage was 41% (p<0.001). In the β-RT group, no scar or a white scar could be detected in 86% of the treated eyes, versus in 24% of the sham irradiated eyes (p<0.001). A change of keratometry (Javal) was seen in 5 patients (12%) following β-RT compared to 16 (38%) after sham irradiation (p=0.002). Complications were few: a granuloma was seen in three patients after sham irradiation, mild limitation of abduction in two β-RT patients versus in five after sham irradiation, and mild scleromalacia in one β-RT patient.*
CONCLUSIONS. *Bare sclera extirpation of a pterygium without adjuvant treatment has an unacceptably high recurrence rate and therefore should be considered obsolete. Bare sclera extirpation of a primary pterygium followed by a single-dose β-RT is a simple, effective, and safe treatment with lasting results and very few complications. (Eur J Ophthalmol 2008; 18: 327-31)*

KEY WORDS. *Primary pterygium removal, Bare sclera extirpation, β-RT, Sham irradiation*

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INTRODUCTION

The stream of publications dealing with the management of pterygium has been abundant for many decades, but – with a single exception (1) – not until the second half of the 1990s did properly designed controlled studies begin to appear (2). The commonly applied bare sclera extirpation (BSE) was then slowly being replaced by BSE plus mitomycin C application or by conjunctival autograft transplantation (CAT). Prior to the start of our study, three well-designed publications had demonstrated that mitomycin application or CAT lowered the incidence of prima-

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ry pterygium recurrence after BSE considerably (3-5). However, at the same time, it was stated that the use of mitomycin for pterygia remained controversial (6). At that time, few controlled studies regarding the effects of adjuvant CAT had been published. Only one group had studied the role of adjuvant β-RT in a randomized way, but the series in this study were small (7). Beta-irradiation for the treatment of pterygium has been advocated by Castroviejo and others since the early 1950s (8, 9). In our center, we applied a single-dose β-RT after BSE of a primary or recurrent pterygium since the 1970s and an internal evaluation had shown a recurrence rate of less than 10%. Therefore, it seemed appropriate to set up a prospective, multicenter, randomized, double blind study to evaluate the role of adjuvant β-RT after BSE. The outcome of this study showed 3 out of 44 recurrences after β-RT versus 28 out of 42 after sham-RT or a crude control rate of 93.2% versus 33.3%, respectively (10). After a mean follow-up of 18 months, no major side-effects had been observed. However, radionecrosis and subsequent bacterial or fungal infection of the recipient side long after β-RT has been reported (11). Therefore, we re- evaluated our results after at least 3 years of follow-up and describe ocular findings in more detail.

MATERIALS AND METHODS

Procedure

Included were patients between 20 and 80 years of age with a degenerative, fibrovascular wedge-shape lesion crossing the limbus (e.g., pterygium), who had not been treated for this condition so far except for local measures such as eyedrops. All patients underwent BSE under local anesthesia performed by ophthalmic surgeons of seven hospitals in the Utrecht region in the Netherlands. The following day, they visited the central radiotherapy department, where they received information about the trial. After providing informed consent, they were randomized for either β-RT or sham-RT. Treatment was given within 24 hours postoperatively under local anesthesia using oxybuprocaine. The technique has been described (10). Using a ^{90}Sr ophthalmic applicator with an active diameter of 12 or 15 mm, a single dose of 2500 cGy is administered to the surface of the conjunctiva at a dose rate of between 200 and 250 cGy/min. The only difference for those treated with sham irradiation was the absence of a ^{90}Sr source in the applicator. Neither the patient nor the ophthalmologist was informed about the real nature of the applicator being used until the end of the study period. Patients were checked 6 weeks and 6, 12, 24, and 36 months after treatment. At each check, they were asked to express their satisfaction or dissatisfaction with the treatment, whether the treated eye irritated, and whether they were using lubricants. The radiation-oncologist and the ophthalmologist together scored the condition of the treated eye (0 = no scar, 1 = white scar, 2 = red scar, 3 = elevated red scar confined to conjunctiva, 4 = recurrence of pterygium [e.g., crossing the limbus]). Finally, the ophthalmologist performed Javal keratometry (0 = no change, 1 = change of ≥1 diopter), measured the best visual acuity, which was compared to the preoperative best vision (0 = no change, 1 = drop of one or more lines on the Snellen chart), and tested the ductions in four directions and performed Javal keratometry. When a recurrence had been assessed, the patient and the masked ophthalmologist were informed about the nature of the treatment given and the study was terminated.

Statistical analysis

Using SPPS 12.01, clinical differences were calculated with the Pearson chi-square test ($p<0.01$ considered to be significant).

RESULTS

From February 1998 until September 2002, 91 patients with 96 pterygia were included in the study. The last control patient was seen on May 1, 2006. Ten patients were lost to long-term follow-up, resulting in 86 eyes accessible for final evaluation. Fifty-two patients were male and 34 female. The average age at inclusion was 50 years (range: 24–77). Four men and one woman had bilateral pterygia. All pterygia were mainly nasally located. Nine patients were Turkish, 11 Moroccan, and 55 from Dutch descent, while the others could not be grouped in one of these categories.

Forty-four eyes were randomized for β-RT. In this group, 28 patients complained about irritation of their pterygium; in addition, 14 had noticed growth of their pterygium and two experienced blurred vision caused by it. Of those pterygia (20 on the right and 24 on the left eye), seven just crossed the limbus, 10 extended as far as halfway be-

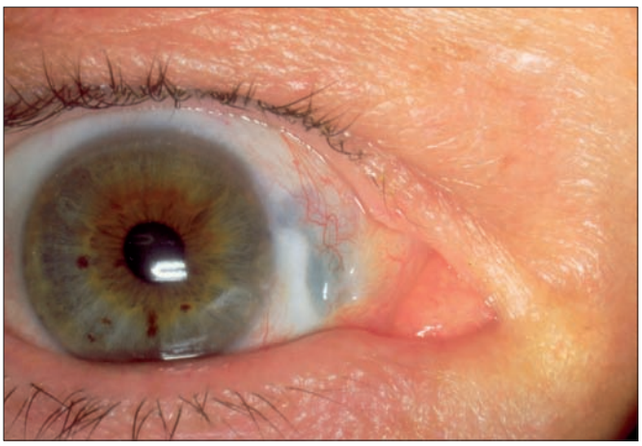

Fig. 1 - *Scleral thinning after beta irradiation.*

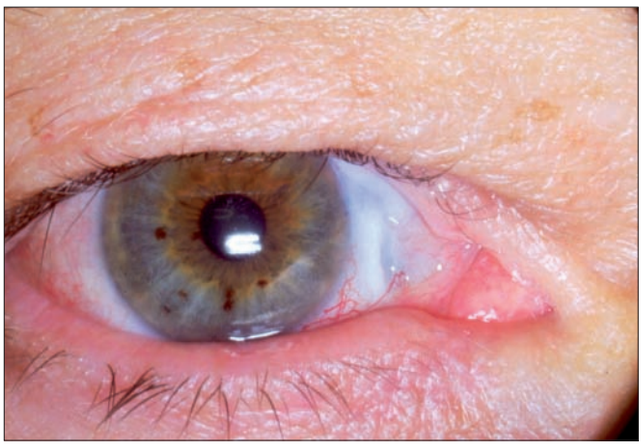

Fig. 2 - *Same eye 2 years later. The scleral thinning has become less obvious.*

tween the limbus and pupillary border, and 9 had crossed that border. In 18 patients, operated by ophthalmic surgeons outside the UMC Utrecht, this information was not available.

In the β-RT group, three pterygia recurred within 18 months. In addition, there were two recurrences after 28 and 39 months, bringing the total to 5 (11%). Thirty-five patients (80%) were satisfied with the final result. Twenty-four patients (55%) had no complaints anymore after treatment, 20 persons still experienced some kind of ocular irritation (photophobia and/or gritty feeling), for which 8 (18%) used a lubricant. No scar was detectable in 21 eyes, a white scar was seen in 17, a red scar in 1, and a recurrence in 5 eyes. A significant change of keratometry (e.g., ≥1 D) was found in 5 eyes (12%), causing a loss of one line on the Snellen chart in one eye. Two patients had a mild abduction limitation, of whom one also had a recurrence.

Forty-two eyes were randomized for sham irradiation. In this group, 31 patients reported irritation of the eye and 9 growth of the lesion, whereas in 2 information on the complaints was lacking. Of these pterygia (22 on the right and 20 on the left eye), six just crossed the limbus, 12 extended as far as halfway between the limbus and pupillary border, and 9 had crossed that border. In 15 patients this information was not available.

In the sham group, there were 32 recurrences (28 within 18 months), accounting for 76%. Nevertheless, 17 patients (40%) were satisfied with the final outcome. Twenty-two persons (52%) still experienced some kind of ocular irritation (photophobia and/or gritty feeling), for which 10 (24%) used a lubricant. No scar was detectable in 2 eyes, a white scar was seen in 8, and a recurrence in 32 eyes. A significant change of keratometry was found in 16 eyes (38%), causing a loss of one line on the Snellen chart in one eye. Five patients, all with a recurrence, had an abduction limitation, causing noticeable diplopia in two.

Of the five patients with bilateral pterygia, two patients were randomized for sham irradiation twice with both eyes experiencing failure, two patients for irradiation on both sides with both eyes achieving success, and one patient for irradiation on one side and sham irradiation on the other eye, both sides achieving success.

Pearson chi square test showed significant differences in recurrence rate (11% vs 76%, $p<0.001$), cosmetic outcome (86% vs 41%, $p<0.001$), and induced keratometry changes (12% vs 38%, $p=0.002$) between the β-RT group and the sham irradiation group. No significant difference between postoperative complaints of irritation of the eye or photophobia could be assessed.

Side effects were rare in both groups. A granuloma was seen in three sham irradiated eyes; scleral thinning (Fig. 1) developed in one patient 24 months after β-RT.

DISCUSSION

This randomized, double blind study, comparing BSE plus a single ^{90}Strontium application with excision plus sham irradiation, shows a recurrence rate of 11% versus 76% after a mean follow-up of 40 months. Our results are in

agreement with other studies and confirm that bare sclera extirpation as a single treatment should be considered obsolete (2). Far better results are obtainable when surgical extirpation is combined with application of mitomycin, with the use of a (limbal) conjunctival autograft or with ß-RT. (Less favorable results are reported after adjuvant amnion membrane insertion [12]). Randomized, blinded studies comparing BSE alone, BSE plus mitomycin-C, and BSE plus CAT (3, 4, 13-15) show recurrence rates for the latter two modalities varying from 3.3% to 38% for adjuvant mitomycin and 2% to 39% for autografting. Few and infrequent side-effects have been reported. Apart from temporary irritation and granulomata, scleromalacia and symblepharon after mitomycin in up to 10% and loose grafts after conjunctival autografting in a very low incidence have been assessed (4, 6, 14). Rubinfeld and Stein's prospective but not randomized study comparing different mitomycin administration protocols suggests that complications after the use of mitomycin are dose and technique dependent (6). Arguments not to perform conjunctival autografting are the more difficult and more time consuming technique. In terms of efficacy, adjuvant mitomycin, CAT, and β-RT seem comparable and the choice of treatment is determined by the facilities and experience of the surgeon and the side-effects of the various options.

Dusenbery et al, in 1992, assessed complications after ^{90}Strontium mainly in re-irradiated eyes (16). Moriarty et al, in 1993, in an 8-year database detected eight well-documented cases of severe intraocular infection complicating radionecrosis after a mean latency period of almost 15 years in patients treated with a mean dose of radiotherapy of 22.7 Gy and warned of a lifelong risk of intraocular sepsis and profound visual morbidity in patients with severe radionecrosis (11). Nishimura et al, in a series of 490 heterogeneous pterygia (452 primary, 17 recurrences after BSE, and 21 recurrences after BSE plus RT) treated with a total of 31–42 Gy ^{90}Strontium following surgical removal, described scleromalacia in four and a scleral ulcer in another two eyes (total 1%) after a mean follow-up of 61 months (17). Monteiro-Grillo et al using 30 Gy had five cases (5%) of scleral atrophy in a series of 100 heterogeneous pterygia (18). In the largest series to the present, Isohashi et al, in a series of 1320 heterogeneous pterygia treated with surgical removal plus 30 Gy ^{90}Strontium, noted no long-term serious side effects (19). The only important complication of β-RT we found was thinning of the sclera in a single eye (Fig. 1) in the field of irradiation of 3 x 2.5 mm seen 24 months after treatment. The patient had no complaints and after 2 years the area of thinning had reduced in size (Fig. 2).

In most studies, data were collected retrospectively, in many studies primary and secondary pterygia were grouped together, various surgical techniques have been combined with β-RT, and perhaps most importantly a variety of total doses and fractionation regimens have been used, resulting in different biological effects. In spite of these differences in techniques and evaluation methods, the outcome in terms of complications is consistent. The single most important but very rare complication mentioned is scleromalacia, which is synonymous with scleral thinning. Scleromalacia per se does not have to be a medical problem, but it makes the eye more susceptible to infection, which can be complicated–if not treated adequately and immediately–by intraocular infection with vision threatening sequelae. Except for the very small chance of scleromalacia, BSE plus β-RT can thus be considered an efficacious and safe technique to deal with primary pterygia.

However, since we started this study, several randomized, controlled clinical trials have shown that CAT is at least as effective and probably even safer (20). Moreover, limbal CAT may be even more effective in recurrent pterygia (21). Also, the initial arguments that CAT is a more difficult technique to perform and more time consuming have become obsolete since gluing techniques have been introduced (22, 23). The question now arises if we still need techniques other than CAT. The good results and the ease of application of β-RT as we have done, however, opens up the way to study the efficacy of β-RT as a single technique to deal with pterygia. Indeed, exclusive strontium/yttrium-90 β-RT has shown to be a promising technique to reduce early symptomatic manifestations of pterygia in a nonrandomized trial (24). Randomized trials, comparing corneal autografting with exclusive β-RT in several presentations of pterygia, are now required to assess which technique is most favorable in terms of efficacy, safety, speed, and cost.

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