Effect of the method of enucleation on the prognosis of choroidal melanoma*

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SUMMARY The prognosis following treatment of uveal melanomata depends not only on factors such as cell type and degree of mitotic activity, size and location of the tumour, and the age of the patient, but also on the method of enucleation, as surgical manipulation of the neoplasm may potentiate the shedding of malignant cells into the blood stream. One hundred and thirty-one patients treated by different methods of enucleation were reviewed and the mortality patterns assessed. The numbers of deaths over the first 5 years differed significantly between the different groups. A specific method of enucleation used for tumour-containing eyes is described and its importance emphasised.

Controversy has existed in recent years about the effect of enucleation on the prognosis of ciliary body and choroidal melanoma.¹⁻⁷ Surgical manipulation of the neoplasm may potentiate the embolisation of malignant cells into the blood stream⁵ with the subsequent development of metastases, but the prognosis following treatment of these tumours may well depend in addition on a combination of several other factors such as cell type and degree of mitotic activity, size and location of the tumour, and the age of the patient.

The specific method of enucleation described below, aimed at minimising the discharge of tumour cells into the circulation, has been adopted for many years by the surgeon-in-charge of the Oncology Clinic (Mr M. A. Bedford). The purpose of this pilot study is to compare the mortality rate of patients treated by this method with that of patients who underwent routine enucleations in other units, with the aim of assessing whether the method of enucleation bears any relation to mortality. Other factors which might influence the outcome of treatment will also be taken into account.

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Material and methods

One hundred and thirty-one patients with choroidal and ciliary body melanoma treated by enucleation between 1949 and 1980 were included in the study.

Tumours were clinically graded according to size: small=less than 10 mm maximum tumour diameter and up to 2 mm elevation; medium=larger than 10 mm but less than 15 mm diameter and up to 5 mm elevation; large=dimensions greater than the above. The site of the tumour was noted, being divided into those tumours anterior to the equator, posterior to the equator, involving the ciliary body, or with extra-scleral extension.

The neoplasms were classified histologically into spindle cell, epithelioid cell, and mixed groups, and the degree of pigmentation was noted. Duration of history—that is, whether symptoms were present for less than or greater than one year prior to treatment—and the patient's age at enucleation were also noted.

The treatment groups considered were those patients who underwent the specific 'tumour enucleation' by the method described below, those who underwent a primary enucleation at their local hospital, and those who had additional therapy prior to enucleation such as cobalt plaque or light coagulation.

The survival data were calculated from the date of operation. Current clinical evidence for or absence of

Fig. 1 Wire snare used for enucleation.

metastatic disease was noted, and, if present, the date when it was first noticed. The date of death or, if the patient was alive the date of last follow-up, was also noted.

Survival curves were constructed for the various factors studied.

METHOD OF ENUCLEATION

The surgical procedure is carried out under normotensive general anaesthesia. Precaution is taken to avoid excessive manipulation of the globe. After a 360° conjunctival peritomy the 4 rectus muscles are isolated in turn, traction sutures being placed through the muscle insertions, and each muscle severed from the globe by cutting cautery. The globe is then removed with a carefully placed Foster snare (Fig. 1). In particular, the snare is guided into position medially with a straight mosquito forceps, which is released just before the snare is fully tightened. This obviates inadvertently cutting into the eyeball, thereby releasing tumour cells into the orbit. This method prevents any bleeding from the Tenon's fascia or the ophthalmic and vortex vessels.

Results

Of the total of 131 patients reviewed 17 died during the interval studied from causes unrelated to their ocular disease, while 4 were excluded owing to

insufficient data. 87.2% of the patients survived from the date of their operation to the present time, giving a minimum follow-up of 2 years. All the deaths occurred within 9 years of surgery (Fig. 2). There were no deaths from the small posterior tumours (Fig. 3). As might be expected, because they tend to produce visual symptoms earlier and are therefore diagnosed early, almost all the small tumours were situated posteriorly (Table 1), and posterior melanomas were associated with a better survival than anterior (Fig. 4). The small tumours had a more favourable prognosis than the medium or large tumours (Fig. 5).

Because the majority of the melanomas in this series were classified as spindle cell type (Table 2), there being surprisingly few epithelioid or mixed cell tumours, the survival curve showed a slight trend in favour of the spindle cells, but this was not statistically significant ($p=0.11$). Neither was the amount of pigment contained in the cells found to be relevant to the prognosis.

The age of the patients and the duration of history were not statistically significant.

There were 31 patients who underwent a specific 'tumour enucleation,' 68 had their enucleations performed by the local ophthalmologist, 19 were initially treated with a cobalt plaque but subsequently required removal of the globe (this study does not include those tumours successfully treated by a

Fig. 2 Overall survival after date of enucleation.

Fig. 3 Small posterior tumours versus all others.

Table 1 Size versus site

	Anterior	Posterior
Small	2	22
Medium	11	40
Large	20	22

p=0.0011.

Table 2 Size versus pathology

	Spindle	Epithelioid and mixed
Small	17	4
Medium	35	6
Large	32	8

p=0.8038.

Table 3 Type of treatment

	Total no. of patients	No. of tumour-related deaths
Specific enucleation	31	1
Local enucleation	68	7
Plaque then enucleation	19	4
Others	9	1

plaque), while 9 had other forms of additional treatment such as photocoagulation prior to enucleation (Table 3). The effect of the method of enucleation on survival is shown in Fig. 6.

In the locally treated group the deaths occurred early, within 2 to 4 years, while the drop in percentage survival occurred later in the patients whose eyes were enucleated by the specific method.

Comparison of the number of deaths over the first 5 years showed there was a statistically significant difference between the locally enucleated eyes and all the others (p=0.01 by Fisher's exact test), while the specific enucleation procedure compared with those treated locally resulted in a p value of 0.09.

Fig. 4 Site of tumour.

Discussion

Therapy of a malignant tumour, to be effective, must alter the course of the primary lesion or prevent metastases. However, the relative efficacy of therapeutic methods at preventing metastases remains unclear, as it is not known at what stage in the natural history of uveal melanoma metastasis occurs. It has been shown⁷ that the 10-year survival in small enucleated tumours and those treated conservatively is very similar (81.4%:81.3%)—that is, enucleation may not be indicated for such tumours as a primary procedure while good visual acuity is retained.

In any tumour which carries the risk of metastasis complete removal of the tumour mass at an early stage should lessen this risk. Zimmerman and McLean,⁵ however, showed a relationship between mortality and enucleation and postulated that this was attributable to the dissemination of tumour cells into the blood stream during surgery or to a lowering of the host's immunological defence mechanisms, or a combination of the two.

Siegel *et al.*² questioned the validity of this observation, but mortality peaks following enucleation have also been found by other workers.⁷⁻⁹

Manipulation of the eye during the enucleation procedure may increase the dissemination of neoplastic cells owing to the attendant increases in intraocular pressure.¹⁰⁻¹³ The surgical technique described in this paper minimises unnecessary handling of or pressure in the globe during surgery until the snare has been tightened, thereby occluding all blood vessels. A cutting cautery is used to sever the rectus muscles, obviating any leakage of blood into the orbit. In fact the whole procedure is designed to maintain a blood-free operating field.

It is obviously impossible to know the exact surgical techniques in use in other eye departments, but all too often such an operation is entrusted to the least experienced member of staff, with the result that there is little refinement in the technique, which is

Fig. 5 Small posterior tumours versus all others.

Fig. 6 Type of enucleation.

often traumatic and bloody. It is therefore noteworthy that all the deaths in the group enucleated by their local ophthalmologists occurred at a relatively early stage after enucleation—i.e. between 2 and 4 years after surgery—compared with the group enucleated by the special technique, where the main peak in mortality was at 8 years.

The immunological response of the host may be affected by the removal of the tumour by enucleation. A fall in tumour-associated antibody levels has been reported after enucleation, while the titre rises after photocoagulation or the application of a cobalt plaque.¹⁴ Patients in this series treated first with a cobalt plaque and then later by enucleation after the tumour failed to respond show an increase in mortality at a later stage than the patients treated by primary enucleation of whatever type (Fig. 6). The lower final percentage survival must be considered in the light of the fact that these were the patients who failed to respond to the cobalt plaques and that enucleation was performed only because of the aggressive nature of the tumour. The relatively small number of patients makes this drop artificial. Patients treated initially by light coagulation and then later enucleation when further growth was noted showed uniformly good results, with no deaths, but it must be remembered that these tumours were relatively small and posteriorly situated to have made possible the initial treatment, and that the indication for enucleation was often loss of visual acuity rather than a massive enlargement of the tumour itself.

CONCLUSION

While a combination of factors needs to be taken into account when considering the mortality patterns fol-

lowing treatment for choroidal and ciliary body melanoma, the method of enucleation, aimed at minimising the shedding of malignant cells into the blood stream, is an important factor in influencing the final outcome of the disease. These preliminary data are a basis for further study.

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