Changing indications for enucleation and selected unusual pathologies

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Abstract

Purpose: To survey clinical indications for enucleations received within a single specialist ophthalmic pathology department over a 21-year period.

Methods: Cases were identified from the departmental records and categorised by indication type as well as by year.

Results: Over time, there has been a decreasing trend in eyes removed for end-stage indications such as phthisis, blindness or pain, as well as a decrease in eyes removed following trauma.

Conclusion: With the reducing number of eyes removed for end-stage disease and trauma, the majority of enucleations performed are now for malignancy. However, eyes are still removed for other indications. A selection of rarer pathologies is presented.

Keywords: Ophthalmic pathology, Enucleation, Epidemiology

Introduction

Eye removal is not a procedure that is carried out lightly. In addition to losing any residual visual function, the surgery can be disfiguring. Indications for eye removal include tumours, trauma, pain, cosmesis in a non-seeing eye and, occasionally, sacrifice of a normal eye because of adjacent disease.

Eye removal procedures comprise eviscerations, enucleations and exenterations. Exenterations—removal of the eye, surrounding orbital tissue (sometimes bone as well) and eyelids—are the most disfiguring procedure. They are usually performed for malignancy. Enucleation is removal of the globe including sclera, while in evisceration, the sclera is left behind in the socket.

Once the eye is removed, it may be submitted for histological examination. This helps the ophthalmologist audit preoperative diagnostic accuracy as well as being a safety net for any unsuspected pathology (such as occult tumours).

The Department of Eye Pathology, UCL Institute of Ophthalmology, London, is a specialist ophthalmic pathology laboratory. Approximately two-thirds of the specimens originate from the adjacent Moorfields Eye Hospital, a tertiary referral specialist eye hospital. Most of the remaining specimens are submitted from elsewhere within England although a few specimens are received from other UK organisations or the rest of the world.

Because of the specialist nature of the department’s work and volume of cases, review of specimens received may provide useful insights. We have not previously reviewed clinical indications for eye removal. Over the ten years I have worked within the department, I have developed an impression that the number of enucleations for non-tumour indications is...
decreasing. This retrospective case review will address the question.

This article will concentrate on enucleations. It will provide a brief survey of enucleations received in our department over a 21-year period with an emphasis on any change in indication. I will then provide examples of some of the less common pathologies.

Methods

The Department of Eye Pathology has a web-based database (EyePath) which holds pathology reports from 1997 onwards. EyePath was searched for enucleation specimens submitted to the Department of Eye Pathology during the calendar years 1997–2017 inclusive (a 21-year period).

Information was gathered as follows: case ID, geographic location of request (England, other UK, overseas), clinical indication for surgery, and histological diagnosis. This paper is not intended to assess accuracy of clinical vs histological diagnosis. “Histological diagnosis” was only used to identify unusual pathologies.

Eyes submitted for forensic examination or research (usually post-mortem donor eyes) were excluded from the survey. Eyes submitted from overseas were also excluded since the sporadic nature of their receipt might confound any trends.

Following data gathering, clinical indications were grouped into categories as follows: melanoma, retinoblastoma, tumour (either not specified or other than melanoma or retinoblastoma), end-stage eye (including blind painful eye, phthisis, rubeotic glaucoma), trauma, no information provided and “other”. Each case was assigned to a single category which was judged to be the most significant, although there is inevitable overlap.

Results

During the 21-year period from 1997 to 2017, a total of 1812 globes were identified on the EyePath search which met the survey criteria after exclusion of forensic, research and overseas cases.

A breakdown of cases by year and clinical indication is provided in Table 1.

The 1231 tumours formed the majority of specimens at 68%. 319 end-stage eyes and 152 trauma globes together made up another 26% of cases. The remaining 6% had either no information provided or were a mixture of indications as detailed below.

In 35 cases, no clinical indication was stated. 27 were given a histological diagnosis of tumour, 7 non-tumour and 1 was unclear.

75 cases fell into the “other” category. Clinical indications included: endophthalmitis, removal for orbital pathology, retinopathy of prematurity, staphyloma, Acanthamoeba, microphthalmia and an auto-enucleation.

Discussion

Indications for enucleation

It is unsurprising that blind painful eyes (subsumed into the “end-stage” category in this study), trauma and tumours are the commonest indications for enucleation. In an American study of 101 cases over 33 years, Erie found 62 blind painful eyes, 16 tumours and 12 trauma eyes. A larger study by de Gottrau in Germany included 1146 enucleations in an 11 year period and concluded that the commonest clinical indication was angle-closure glaucoma in 35%, with tumour coming second at 22%. Both these studies were published in the 1990s, before the time period covered by the current study. A 1998 study from Iceland reviewed 200 eyes (enucleations and eviscerations) removed over a 29-year period. 92 were removed for blind painful eye, 49 for tumour and 35 for acute trauma. A follow-up study covering 1992–2004 identified 56 enucleations, with the commonest indication being trauma followed by tumour. A Canadian study of 713 eyes received over a 10-year period (60% of which were enucleations)

Table 1. Enucleations by year and indication.

| Year | melanoma | RB* | tumour** | (Total tumours) | end stage eye | trauma | none provided | other | Total cases |
|------|----------|-----|----------|----------------|--------------|--------|--------------|-------|-------------|
| 1997 | 73       | 4   | (77)     | 25             | 12           | 4      | 5            | 123   |
| 1998 | 87       | 6   | (95)     | 25             | 15           | 1      | 5            | 141   |
| 1999 | 59       | 6   | (65)     | 36             | 18           | 5      | 4            | 128   |
| 2000 | 54       | 3   | (63)     | 36             | 26           | 4      | 2            | 131   |
| 2001 | 51       | 2   | (56)     | 22             | 14           | 1      | 2            | 94    |
| 2002 | 19       | 5   | (27)     | 24             | 14           | 1      | 3            | 69    |
| 2003 | 19       | 10  | (32)     | 30             | 8            | 5      | 4            | 79    |
| 2004 | 16       | 4   | (20)     | 24             | 7            | 2      | 1            | 54    |
| 2005 | 21       | 7   | (29)     | 14             | 5            | 2      | 2            | 50    |
| 2006 | 34       | 7   | (42)     | 24             | 6            | 1      | 7            | 72    |
| 2007 | 57       | 2   | (40)     | 14             | 6            | 1      | 2            | 63    |
| 2008 | 23       | 3   | (27)     | 3              | 3            | 1      | 3            | 37    |
| 2009 | 25       | 1   | (30)     | 3              | 3            | 3      | 5            | 41    |
| 2010 | 19       | 2   | (23)     | 8              | 3            | 3      | 3            | 37    |
| 2011 | 56       | 7   | (64)     | 6              | 2            | 2      | 6            | 80    |
| 2012 | 82       | 8   | (95)     | 5              | 1            | 2      | 5            | 108   |
| 2013 | 80       | 4   | (87)     | 7              | 3            | 2      | 5            | 104   |
| 2014 | 93       | 6   | (100)    | 6              | 3            | 1      | 10           | 120   |
| 2015 | 81       | 2   | (85)     | 2              | 1            | 2      | 2            | 92    |
| 2016 | 79       | 3   | (83)     | 2              | 1            | 1      | 5            | 91    |
| 2017 | 87       | 1   | (91)     | 3              | 2            | 1      | 1            | 98    |
| Total| 1095     | 93  | 43       | (1231)         | 319           | 152    | 35           | 75    | 1812        |

* RB = retinoblastoma.
** tumour = specified non-melanoma, non-RB tumour or non-specified tumour.
found the commonest indication to be blind painful eye (37%) with slightly fewer tumours (35%).

In this survey, infectious and inflammatory indications for enucleations are relatively rare although other studies (especially from low- and middle-income countries) have a higher prevalence of such indications. In a 2013 study of eye removals (including eviscerations) in Nigeria, infection was cited as the commonest indication. In a second Nigerian study, comment is made that ocular infections tend to be a common indication for eye removal in developing countries. In contrast, developed countries have a higher proportion of tumours. A study from Jordan found endophthalmitis to be among the top three indications for eye removal. Interestingly, anterior staphycoma is common enough in some studies to be given its own category. Vemuganti suggests that the relative prevalence of anterior staphycoma is related to poverty and trauma, especially in childhood.

Tumours

The number of retinoblastomas submitted was relatively small because paediatric ocular oncology specimens (i.e. retinoblastomas) are usually reported at another hospital rather than by the Department of Eye Pathology. The small proportion of retinoblastoma enucleations in this series is therefore not reflective of local ophthalmology practice.

Additionally, for a period of several years from about 2002 to 2010, adult ocular oncology specimens were also reported at a different hospital. The low numbers of melanoma globes during this time period are also not reflective of local clinical ophthalmology practice.

Because of the above two factors, it is difficult to meaningfully comment on any time trends regarding uveal melanomas or retinoblastomas.

Trends over time for non-tumour enucleations

Of the non-tumour cases, the numbers of both end-stage eyes and trauma globes has decreased from the beginning of the time period to the end. There are at least two possible explanations for this trend: improved treatment and therefore less need for eye removal, or increasing use of evisceration rather than enucleation. In order to explore the latter suggestion, EyePath was searched for numbers of eviscerations performed each year over the same time period. The numbers are presented in Table 2. The lowest number in a year was 10 in 1998, while the highest number was 80, in 2013. The four years at the start of the time period (1997–2000) had the lowest numbers of eviscerations per year as well as the highest number of enucleations per year. Otherwise, there is no apparent increase in evisceration numbers over time to balance the reducing enucleations for end-stage and trauma eyes. It is therefore plausible that fewer eyes are being removed for end-stage and trauma indications because prevention and/or treatment has improved.

Another possibility is that eyes are not being submitted for examination. In the UK, it is recommended that all removed eyes (globes, eviscerations and exenterations) are submitted for histopathological examination, but this does not always happen. Until fairly recently, even histopathologists might not view examination of globes or eviscerations as necessary.

The decrease in non-tumour cases is broadly in agreement with some prior studies. A similar trend was found in Iceland although in Saeed’s series (which included enucleations and eviscerations), the number of eyes removed for trauma increased while the number of eyes removed for glaucoma decreased. One American study covering a period from 1941 to the mid-1990s found the relative proportion of trauma cases to decrease over time, with a concomitant increase in tumour cases. In a more recent American review over 60 years, Setlur found a decrease over time for glaucoma as a surgical indication. Trauma formed 16% of cases in the 1960s, peaked at 31% of cases in the 1980s and decreased to 13% in the 2000s. The authors suggest that ‘‘end stage eye disease is being increasingly prevented by improved treatment.’’ A more recent study from India covering 1996–2018 has found a similar trend, with a decrease in atrophy/phthisis bulbii, painful blind eye and acute trauma as indications for enucleations. The authors suggest this reflects changing management practices.

It is difficult to rigorously compare this study with previous studies as they were carried out in different ways with different ways of recording information. Some included procedures other than enucleation. Others concentrated on diagnosis (whether clinical or histological) rather than clinical indication, or on histological findings. However, it does seem that in many units, tumours, trauma and painful blind eye feature among the top indications for enucleation. In some studies, trauma and painful blind eye have decreased as indications over time. Perhaps with time, tumours will also decrease further as non-surgical treatments improve.

Examples of rarer cases

In contrast to the early years of this survey, enucleations for non-tumour indications are now rare within the Department of Eye Pathology. That said, in the first three months of 2019, we have already received 6 non-malignant enucleations: three inflammatory cases, a globe removed while treating an orbital tumour, an eye with intraocular haemorrh-
rhage due to retinal vein occlusion and a choroidal haemangioma.

Here are a few case vignettes of pathologies which are rarely seen in our department although they may be more common elsewhere.

**Case 1 – Acanthamoeba**

A 57-year-old female was treated for Acanthamoeba keratitis which progressed to scleritis. Enucleation was performed because the eye was blind and painful. Macroscopic examination of the globe was notable for thickening of the sclera and choroid, fluffy retinal deposits and flattening of the anterior chamber.

On microscopy (Fig. 1), there were extensive corneal, scleral, ciliary body and vitreous abscesses with granulomata. PAS stain highlighted Acanthamoeba cysts within the cornea as well as a few more posteriorly. This was confirmed with Acanthamoeba immunohistochemistry.

**Case 2 – Granulomatosis with polyangiitis**

A 52-year-old female with known granulomatosis with polyangiitis suffered necrotising anterior scleritis leading to a blind painful eye and enucleation. Macroscopic examination was notable for the eye being shrunken and distorted with a crescentic yellow necrotic area at the limbus. No previous surgery had been performed.

Microscopy (Fig. 2) showed a fissural defect in the limbus/sclera with extensive necrosis. There was iris-lens adhesion, areas of necrobiosis and loose granulomata. The posterior segment was relatively spared although the retina was gliotic with epiretinal membrane formation.

**Case 3 – Retinal vein occlusion**

A 77-year-old female with previous retinal vein occlusion had complicated surgery and developed a painful blind eye.

Macroscopic examination (Fig. 3a) was notable for the eye being full of blood and barely discernable intraocular structures.

**Fig. 1.** There is a ciliary body (CB) and vitreous (V) abscess (A) with multinucleate giant cells (G) (Haematoxylin and eosin, x4 objective lens). The inset image shows confirmatory Acanthamoeba immunohistochemistry (cysts indicated with *).

**Fig. 2.** The anterior segment shows scleral necrosis (N), giant cells (G), disrupted Descemet’s membrane (DM) and iris adherent to lens (L) (Haematoxylin and eosin, x4 objective lens).

**Fig. 3a.** Macroscopic examination of the globe confirms the eye to be full of blood. The cornea (C) is indicated for orientation. The intraocular lens can just be discerned (L).

**Fig. 3b.** This is the anterior segment from the cornea (C) to the anterior vitreous (V). The profile of the IOL optic (IOL) and portions of residual lens cortex (L) are indicated. The anterior chamber is obliterated, with extensive iris-corneal apposition. Posteriorly, intraocular structures are obliterated by haemorrhage and proteinaceous exudate (Haematoxylin and eosin, x1.25 objective lens).
Microscopy (Fig. 3b) showed obliteration of most of the vitreous cavity and retina and flattening of the anterior chamber. Lens haptic and optic profiles were identified.

Case 4 – Choroidal haemangioma

A 63-year-old male with Sturge-Weber syndrome developed a blind painful eye, and enucleation was performed. Macroscopic examination (Fig. 4a) was notable for total retinal detachment. Additionally, the choroid was detached from the sclera with fluid in the suprachoroidal space (SCS).

Microscopy (Fig. 4b) showed early iris rubeosis with peripheral anterior synechiae. There was a pupillary and cyclitic membrane, and the crystalline lens was disrupted with foreign body reaction and considerable inflammation of the anterior segment. The choroid contained a haemangioma.

Conclusions

Within the limitations of this survey, there is no obvious upwards or downwards trend in numbers of enucleations over time for the 21-year period surveyed. Enucleations for end-stage eyes and trauma appear to be decreasing over time. However, even recently there are non-tumour indications for enucleations, with a few examples being presented here.

The number of eviscerations is not obviously rising to match the fall in enucleations for end-stage eyes and trauma, supporting the hope that non-surgical treatments have improved such as to reduce the number of eye removals.

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Declaration of Competing Interest

The author declared that there is no conflict of interest.

References

1. Erie JC, Nevitt MP, Hodge D, Ballard DJ. Incidence of enucleation in a defined population. Am J Ophthalmol 1992;113:138–44.
2. de Gottrau P, Holbach LM, Naumann GO. Clinicopathological review of 1146 enucleations (1980–90). Br J Ophthalmol 1994;78:260–5.
3. Sigurdsson H, Thórisdóttir S, Björnsson JK. Enucleation and evisceration in Iceland 1964–1992. Study in a defined population. Acta Ophthalmol Scand 1998;76:103–7.
4. Geirsdottir A, Aagnarsson BA, Helgadottir G, Sigurdsson H. Enucleation in Iceland 1992–2004: study in a defined population. Acta Ophthalmol (Copenh) 2014;92:121–5.
5. Chan SWS, Khattak S, Yücel N, Gupta N, Yücel YH. A decade of surgical eye removals in Ontario: a clinical-pathological study. Can J Ophthalmol J Can Ophthalmo 2017;52:486–93.
6. Ibanga A et al. Indications for eye removal in southern Nigeria. Int Ophthalmol 2013;33:55–60.
7. Musa KO, Aribaba OT, Onakoya AO, Rotimi-Samuel A, Akinsola FB. Indications for destructive eye surgeries at a Nigerian tertiary eye care centre: A ten-year review. Niger Postgrad Med J 2016;23:12-4.
8. Ababneh OH, AboTaleb EA, Abu Ameerh MA, Yousef YA. Enucleation and evisceration at a tertiary care hospital in a developing country. BMC Ophthalmol 2015;15:120.
9. Vemuganti GK, Jalali S, Honavar SG, Shekar GC. Enucleation and evisceration in Asian Indian patients: a histopathological review of 2009 cases. J Clin Pathol 2016;59:153–5.
10. Cheng GY et al. Review of 1375 enucleations in the TongRen Eye Centre, Beijing. Eye Lond Engl 2008;22:1404–9.
11. Thaung C. Ophthalmic service guidance: ocular pathology. https://www.rcophth.ac.uk/wp-content/uploads/2016/07/Ocular-Pathology-July-2016.pdf, 2016 accessed 18/03/2019.
12. Saeed MJ, Chang BYP, Khandwala M, Shivanegh A, Chakrabarty A. Twenty year review of histopathological findings in enucleated/ eviscerated eyes. J Clin Pathol 2006;59:153–5.
13. Spraul CW, Grossniklaus HE. Analysis of 24,444 surgical specimens accessioned over 55 years in an ophthalmic pathology laboratory. Int Ophthalmol 2017;21:283–304.
14. Setlur VJ, Parikh JG, Rao NA. Changing causes of enucleation over the past 60 years. Graefes Arch Clin Exp Ophthalmol 2010;248:593–7.
15. Kaliki S et al. Enucleation in Asian Indian patients: a histopathological review of 2009 cases. Eye Lond Engl 2019;33:120–8.