The Management of Childhood Intracranial Tumours and the Role of the Ophthalmologist

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Objective: This study looked at a single paediatric neuro-oncology centre's experience of childhood intracranial tumours seen in the ophthalmology clinic over an approximately five-year period. This was used to analyse the role of the ophthalmologist in their long term follow up.

Methods: A database was compiled of all children discussed at the neuro-oncology multi-disciplinary team (MDT) meeting between January 2012 and April 2017. All children who had an intracranial tumour determined by histology or suspected on neuroimaging, who had also been seen in the ophthalmology clinic, were included. A retrospective case review was performed to create a record for each child.

Results: The database contained 129 children of which 82 [64%] were boys and 47 [36%] were girls. Of these 89 [69%] had a histological diagnosis and 40 [31%] had a tumour suspected on neuroimaging. The most common tumour locations were the posterior fossa [n=54, 42%], diencephalon [n=20, 16%] and the visual pathways [n=17, 13%]. Papilloedema at first presentation was only found in 39 [30%] children. The most common other neuro-ophthalmic manifestations were non-paralytic strabismus [n=33], sixth nerve palsy [n=19] and seventh nerve palsy [n=12]. Non-paralytic strabismus was a presenting symptom in only one case. There were 13 ophthalmic surgical procedures required for these children, the most common being strabismus surgery.

Conclusion: We report the types and locations of paediatric intracranial tumours seen in the ophthalmology clinic as well as their neuro-ophthalmic manifestations. Only 30% present with papilloedema and approximately 10% will require an ophthalmic surgical procedure.

Keywords: *Brain tumour, Neuro-ophthalmology, Ophthalmic surgery*

Introduction

Brain tumours are the most common solid tumour type[1] in children whilst brain and central nervous system (CNS) cancers are the second leading cause of cancer death in those under 19[2-4]. Paediatric brain tumours are usually categorized according to histology or location[5,6] although more recently molecular parameters are also being incorporated[6-9]. Approximately 50% are found in the posterior fossa with the other 50% being supratentorial[10-12]. Another key distinction is whether they are benign which corresponds roughly to the old WHO grades 1-2 or malignant roughly corresponding to grades 3-4[13]. These factors greatly influence the presenting symptoms and prognosis[14,15] but also create different challenges for the ophthalmologist.

The management of childhood CNS tumours is complex and is best undertaken at a paediatric oncology centre by a multi-disciplinary team (MDT)[16,17] led by an oncologist or neurosurgeon[14]. The ophthalmologist however also plays an important role both in diagnosing[18,19] and managing secondary abnormalities of the visual, ocular, adnexal and oculomotor systems of children with intracranial tumours [17,20]. Whilst several studies have looked at the related neuro-ophthalmic manifestations[21-23] in children with brain tumours, these have typically been performed by oncologists or neurologists[24]. Other studies have looked at the neuro-ophthalmic manifestations at presentation[21,24-27] or the effect on quality of life[28]. There is however very little information in the literature regarding the neuro-ophthalmic manifestations of these tumours managed by the ophthalmologist over time[12,29] and none, of which we are aware, reporting the ophthalmic surgical interventions required.

Establishing exactly which neuro-ophthalmic manifestations and ophthalmic surgical problems are commonly encountered, demonstrates the specific skills required to manage these children, and helps to inform clinical planning and training requirements. This study therefore aims to determine the variety of paediatric brain tumours seen in the ophthalmology

clinic at a regional specialist referral centre as well as the neuro-ophthalmic manifestations encountered and which ophthalmic surgical interventions were required over an approximately five-year period.

Methods

We compiled a database of all children who had been discussed at the neuro-oncology MDT meeting between January 2012 and April 2017 at our centre. The record for each child was then checked and included in this study, if they had a tumour proven by histology or suspected on neuro-imaging. In addition, they had to have been seen in the ophthalmology clinic at the same centre which was determined through searching the electronic patient records.

This yielded 152 children, of whom 129 children had intracranial tumours and were included; the remainder having ocular or orbital tumours, which were excluded. A retrospective case review of the ophthalmology notes, clinic letters, radiology and histology reports as well as MDT outcomes was performed to create the record for each child. This was stored on a database created in Microsoft Excel and the clinical data was then analysed to determine relevant clinical characteristics of this cohort of patients as well as aspects relating to their ophthalmic management.

In our unit a specialist orthoptist attends the MDT and coordinates the ophthalmic input required for each child. All children were under the care of a single paediatric ophthalmologist with occasional input from other subspecialties.

This study was approved by the Research Governance and Ethics Committee of a Medical School Department of Postgraduate Medical Education and registered as an audit at the regional oncology centre where the database was compiled.

Results

The cohort consisted of 129 children (82 boys [64%] and 47 girls [36%]). The mean age at presentation was 5.8 years (range 0-17 years) which can be seen in Figure 1. Of these 89 [69%] had a histological diagnosis and 40 [31%] had a tumour suspected on neuro-imaging.

The tumour type based on histology for those 89 children who had a tissue diagnosis is shown in Table 1. 13 children died during the follow up period all of whom had a histological diagnosis the breakdown of which is also shown in Table 1.

The most common tumour location was the posterior fossa [n=54, 42%] followed by the diencephalon [n=20, 16%] and the visual pathways [n=17, 13%]. The full breakdown of tumour location is summarized in Table 2.

At initial presentation, 39 cases [30%] were found to have papilloedema, 78 [60%] did not, and 12 [9%] did not have a documented optic disc assessment. During subsequent follow up, 95 [74%] of children's optic discs were documented as normal while 33 [26%] showed atrophy or pallor and 1 [1%] showed non-glaucomatous cupping. Of the 33 with atrophy or pallor, only 12 [36%] had previously documented papilloedema and 15 [45%] had tumours of the visual pathways.

Other neuro-ophthalmic manifestations are shown in Table 3 the most common of which was non-paralytic strabismus [n=33] followed by sixth nerve palsy [n=19] and seventh nerve palsy [n=12]. Only one child presented with non-paralytic strabismus which was an exotropia in the context of poor vision in one eye secondary to an optic nerve glioma. One child had a longstanding esotropia and had previously undergone strabismus surgery. Of the remaining 31 cases of non-paralytic strabismus observed during the period of follow up, 21 cases were convergent and 10 cases were divergent. Tumours located in the posterior fossa were more likely to lead to palsies of cranial nerves III, IV & VI [n=16, 30%] and seventh nerve palsy

[n=11, 20%], when compared to supratentorial tumours and palsies affecting cranial nerves III, IV & VI [n=8, 11%] and seventh nerve palsy [n=0, 0%]. There was one seventh nerve palsy in a child with tumour locations in both the posterior fossa and supratentorial region. All 10 cases of internuclear ophthalmoplegia were in children with tumours located in the posterior fossa.

On review of the electronic patient records (but not the ophthalmology paper notes) eighty-four cases had reliable ophthalmic data at presentation and final follow up. Of these, 14 presented with a problem with eye movements (nystagmus, strabismus, diplopia), 26 had a headache, 21 had vomiting and 10 reported other visual symptoms. Fifty-four patients had a visual acuity of 6/9 or better at final follow up of whom 19 (35%) had neither visual or raised intracranial pressure symptoms at presentation. Similarly, for those children with vision worse than 6/9 in one eye at final follow up, 7 (27%) had neither visual or raised intracranial pressure symptoms at presentation.

Thirteen ophthalmic surgical procedures were required for these children of which there were 6 strabismus operations, 4 tarsorrhaphies, 2 cataract extractions and 1 enucleation. The enucleation was performed in a child with neurofibromatosis type 1 who had an intracranial glioma and a retinoblastoma.

In our centre, patients were seen in the paediatric ophthalmology clinic on average 3.4 times in the first year after diagnosis. It is however possible that some patients could have also been seen in an emergency setting which would not have been captured. Those diagnosed within the last 5 years were then seen on average twice per year, and those diagnosed over 5 years ago were seen on average 0.7 times per year. In our cohort most of these children remain under long-term follow up, with only 9 patients discharged, all of whom were originally diagnosed and treated over 5 years ago.

Discussion

This study looked at a particular cohort of children who had been diagnosed with intracranial tumours and were seen in the ophthalmology clinic at a single centre over an approximately five-year period. The aim of this study was to define the caseload encountered by the ophthalmologist working as part of the multi-disciplinary paediatric oncology team. Of particular interest was to determine which ophthalmic surgical procedures are required in this population as this has not to our knowledge been previously described.

The distribution in terms of sex and age at presentation (Figure 1) of children with intracranial tumours as well as the breakdown of histological diagnosis were similar to large case series described by oncologists and neurosurgeons[2,30,31] (Table 4). This implies that most children with intracranial tumours are also seen in the ophthalmology clinic. Of note, 31 tumours [24%] in our cohort were suspected to be low grade gliomas on neuro-imaging and did not undergo biopsy to obtain a histological diagnosis and therefore were not included in this table.

Large case series show tumour location to be roughly split with half in the posterior fossa and the other half supratentorial[10-12]. Our cohort mirrored this with 56% of tumours supratentorial and 42% infratentorial with 2% occurring in both locations. One difference is that the Central Brain Tumor Registry of the United States reported significantly fewer brainstem tumours at 11%[32]. This could reflect referral bias or that there were differences in how tumour origin was determined with most in our cohort based on the MRI report. This is however unlikely to affect management by the ophthalmologist with broad distinctions between posterior fossa, visual pathways and supratentorial being more relevant to the neuro-ophthalmic manifestations that arise. Papilloedema was seen at initial presentation in only 30% of children which is also similar to other reports in the literature[21,26] although as this was not a

prospective study it was not documented for all cases. Approximately half of the cases [n=20] were in children with tumours in the posterior fossa and half supratentorial [n=19]. Our study therefore highlights that a minority of children with brain tumours have papilloedema at presentation and therefore the absence of this sign should not delay neuro-imaging if a brain tumour is suspected.

Neuro-ophthalmic manifestations of paediatric brain tumours have previously been described at presentation[21,24,26] but there was only one study identified which looked at those that arose over the period of follow up in the paediatric ophthalmology clinic and consisted of 58 cases[12]. Our study therefore defines the neuro-ophthalmic manifestations that are caused not only by these tumours but also by the surgery, chemotherapy, conventional and proton beam radiotherapy used to treat them. An example of this is that the two cataract extractions identified in our study occurred in the same patient after radiotherapy which is a common complication of craniospinal irradiation[33]. This is therefore a manifestation that would not be seen at presentation and would occur sometime after treatment and affect the care and outcome for the child and family. This highlights the importance of careful monitoring in the ophthalmology clinic to detect later onset complications to those seen at presentation. Ongoing monitoring is also important to detect visual loss and signs that may indicate recurrence or raised intracranial pressure[29].

Palsies of cranial nerves III, IV & VI were more common in children with tumours in the posterior fossa [n=16, 30%] than the supratentorial region [n=8, 11%]. 11 of the 12 seventh nerve palsies were in children with a tumour in the posterior fossa with one in a child with a tumour in both locations; all internuclear ophthalmoplegia cases were in children with tumours in the posterior fossa. These neuro-ophthalmic manifestations are therefore more commonly encountered in posterior fossa tumours whilst papilloedema was roughly equal between posterior fossa and supratentorial tumours.

We could not identify in the literature any studies which specifically looked at the types of ophthalmic surgical procedures required in this cohort of children. Our study demonstrates that a range of surgical procedures are required ranging from lid and strabismus to intraocular surgery. After papilloedema, non-paralytic strabismus was the most common neuro-ophthalmic problem seen in this cohort and strabismus surgery was the most prevalent ophthalmic surgical procedure performed.

Our study has all the limitations of retrospective reviews: namely reliance on existing case records and absence of standardization of initial assessment at presentation. Many of the children did not have formal orthoptic review until after their initial decompression surgery. Therefore it is difficult to conclude at exactly what point children developed strabismus. Although we report 33 patients had non-paralytic strabismus during follow up, we suspect that many of these patients had resolved paralytic strabismus which has been previously reported[34]. There was only one case in which a child presented with non-paralytic strabismus which was an exotropia in the context of very reduced vision in one eye. One child also had a longstanding esotropia that had previously been operated on and so was incidental.

Unlike previous studies which have focused on neuro-ophthalmic signs at presentation we have aimed to define the role that the ophthalmologist plays in the long-term management of children with intracranial tumours. Our study suggests that the tumour types referred to the ophthalmology clinic broadly reflects the population of children with intracranial tumours as a whole, indicating there is unlikely to be a referral bias. They result in a range of neuro-ophthalmic manifestations either from presentation or that develop later during the course of their treatment with papilloedema, non-paralytic strabismus and cranial nerve palsies being the most common.

We recommend that all children diagnosed with an intracranial tumour should have an examination of eye movements, visual acuity assessment, and optic disc assessment at presentation where clinically possible. Subsequently, children should be reviewed in the ophthalmology clinic with a full orthoptic assessment and eye examination at each visit. Clear recording of visual acuity in the clinic letter and electronic patient record also helps all those involved in their care to identify problems and trends over time. The frequency of clinic review depends on the risk of developing complications, such as raised intracranial pressure or visual loss. In our study, visual or raised intracranial pressure symptoms at presentation were not a predictor for visual deficit at final follow up and so each case must be assessed individually. Depending on location, size and histology, we recommend 3-4 monthly review in the first year and then 4-6 monthly to year 5 as a reasonable guide in line with the practice in our department.

In conclusion the management of these children is complex and may require referral to other disciplines, monitoring, symptomatic management and in approximately 10% of cases, a range of ophthalmic surgical procedures. This demonstrates that the ophthalmologist requires versatility in order to provide optimum ophthalmic care to this cohort of patients as part of the MDT.

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Figure legends:

Figure 1: Shows the age at presentation for boys and girls

Table 1: Breakdown by histology for all tumours and for children who died

Table 2: Break down of tumour locations for the whole cohort

Table 3: Frequency of neuro-ophthalmic complications in the cohort

Table 4: Breakdown of tumours in our cohort with a histological diagnosis versus large cohorts taken from:

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