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Clinical Study

Optimising treatment strategies in spinal ependymoma based on 20 years of experience at a single centre

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ABSTRACT

Spinal ependymomas are rare tumours, with total resection favoured where possible. Several case series assessing the outcome following neurosurgical treatment for spinal ependymoma advocate the usage of adjuvant radiotherapy in cases of subtotal resection, or in unencapsulated tumours. We assessed the outcome of 61 consecutive cases of spinal ependymoma in a single centre over a 20 year period using a variety of outcome measures. Sex distribution was equal, with a mean age at surgery of 43.6 years (range 5–76 years). Overall, most tumours occurred in the lumbosacral region (70.5%), with fewer in the thoracic (27.9%) and cervical regions (18.0%). Myxopapillary features were seen in 41.0% of tumours, and were more common when occurring in the lumbar region (51.2%). Gross total resection was achieved in 52.5%, subtotal resection in 37.7% and biopsy alone in 9.8% of patients and 31.1% received adjuvant radiotherapy. Two-thirds of patients achieved an excellent post-operative neurological outcome (Frankel grade E). Tumour recurrence was rare. Gross total resection and good preoperative neurological condition were most strongly predictive of good outcome. Post-operative radiotherapy did not seem to confer survival benefit in this case series, even in cases of incomplete resection, leading us to question its utility for all cases of spinal cord ependymoma.

1. Introduction

Ependymomas are central nervous system (CNS) tumours that arise from ependymal cells. Ependymal cells are glial cells that line the cerebrospinal fluid spaces of the CNS, including the ventricles of the brain, and the central canal of the spinal cord. Spinal ependymoma accounts for only 2–6% of all CNS tumours, but represents about half of all intradural spinal tumours in the adult population [1–4]. Spinal ependymomas present with similar features to other space occupying lesions affecting the spinal cord, and features are dependent on spinal level. However, the most common features include back pain (especially nocturnal and when lumbar levels are involved), radicular pain, hypoaesthesia, motor weakness, gait disturbance, and sphincter or sexual dysfunction [5–8].

Ependymomas are not capsulated, and usually have well-defined regular margins. On this basis, it is generally accepted that gross total resection (GTR) is possible is most cases, and is preferable when safe to do so, as it tends to confer a favourable neurological outcome. There is, however, a cohort of more invasive tumours. In these cases, the surgeon must balance the risk of post-operative neurological deficit against the risk of recurrence after partial resection [8–10]. The benefit of adjuvant radiotherapy after subtotal resection (STR) or in anaplastic ependymoma (AE) remains controversial, not least because of the morbidity that can be attached to spinal irradiation. Most large case series still advocate the usage of adjuvant radiotherapy in cases of incomplete resection [6,7]. The optimum interval and length of imaging follow-up is also debated [1,2,9,11].

These tumours can vary in histological grade (from World Health Organization [WHO] grade I myxopapillary ependymoma [MPE] to AE WHO grade III), can show multiple growth patterns (intra- or extra-medullary) and may also metastasise. Most extra-medullary ependymomas are myxopapillary, and tend to present in the conus medullaris or filum terminale [6,8]. In contrast, intra-medullary ependymomas are slightly more common in the higher spinal cord levels, but can occur at any level above the conus medullaris [5,7].

We aim to elucidate the optimum treatment strategy for spinal ependymomas. The question of the widespread usage of spinal irradiation following incomplete resection is important given its side-effect profile that includes radiation myelopathy with loss of

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function, wound breakdown and disruption of dissection planes for revision surgery, increased tumour adherence to the spinal cord and altered spinal cord microvasculature and mortality risk.

2. Methods

We conducted a retrospective study of 61 consecutive histologically confirmed ependymoma patients with primary presentation in the spine, treated at a single neurosurgical centre (Oxford, UK) between 1992 and 2012 (59 adults and two children). All patients underwent MRI and surgery. The standard technique was employed: laminectomy or laminoplasty followed by midline durotomy and microscopic resection then dural closure. Neurophysiological monitoring was not routinely used in this case series.

We aimed to identify surgical, radiological, or histological predictors of neurological outcome and risk factors for recurrence. We collected data on symptom interval, tumour extent, use of radiotherapy, and extent of surgical resection to determine their respective influence on clinical outcome. Patients were stratified according to WHO grade of the tumour. Neurological status was standardised according to the Frankel grading score prior to and following surgical intervention [12] (Table 1). Sphincter and erectile dysfunction were registered separately. Tumour extent was assessed by MRI.

Statistical analysis was performed with the Statistical Package for the Social Sciences version 21.0 (IBM, Armonk, NY, USA). Outcome was analysed with Kaplan–Meier plots and log rank test. Data were compared using Student's *t*-test, χ^2-test, and Cox multivariate regression models. Results are presented as mean ± standard deviation. p-values <0.05 were considered statistically significant.

3. Results

3.1. Patient cohort

All 61 patients (30 female, 31 male; mean age 43.6 years, 59 adults) received surgical treatment at a single centre (Table 2). The mean follow-up time was 55.9 ± 60.9 months with a significantly longer follow-up for intramedullary tumours compared to extramedullary conus tip or cauda equina tumours (73.1 ± 83.3 and 47.4 ± 45.2 months, respectively, p-values <0.05 were considered statistically significant) ranging from 0 to 256 months.

There were 34 cases of classical ependymoma (CE; 55.7%), 25 (41.0%) MPE and two cases of AE (3.3%) (Table 2).

Tumour extent was generally two spinal levels, with a maximum extent of nine levels (Fig. 2). Pre-operative MRI showed 19 cases of intramedullary tumours and 42 cases of conus tip or cauda equina tumours, with L2 being the most frequently affected spinal level (Fig. 2). In four cases the tumour was multifocal and disseminated throughout the subarachnoid space. In two cases, there were two separate levels of intramedullary tumour foci and there was one case of subcutaneous growth out through the sacrum. Histopathological assessment determined 34 CE (WHO grade II), 25 MPE (WHO grade I) and two AE (WHO grade III).

Mean symptom interval was 17.0 ± 14.5 months, as shown in Table 2. Neither tumour location nor histology had a significant effect on symptom interval (intramedullary 18.6 ± 16.0 *versus* extramedullary [mostly filum terminale lesions] 16.5 ± 14.1 months, p = 0.607, CE 15.5 ± 13.0 *versus* MPE 20.2 ± 16.0 months, p = 0.221). Frankel score at diagnosis was not significantly better in patients with MPE compared to those with CE (χ^2 = 1.15; Fig. 1a). The two patients with anaplastic tumours showed rapid clinical deterioration with incontinence and leg spasm developing 3 days and 3 months respectively after the occurrence of localised back pain as the presenting feature.

Intramedullary tumours (n = 19) exhibited a worse Frankel grade at presentation and were more frequently associated with paresis of upper or lower extremities or hypaesthesia, than were extramedullary tumours. Non-radiating, often nocturnal, lower back pain was the typical presenting clinical symptom of lumbar ependymoma (Table 2). Patients with lumbosacral tumours were significantly more likely to have a Frankel grade of E at presentation (62% *versus* 36.9%, χ^2 = 8.7, significant; Fig. 1b).

Table 1
The Frankel graded scoring system of neurological status [12]

Score	Definition
E	No sensory or motor deficit
D	Mild motor deficit
C	Severe motor deficit i.e. the inability to walk
B	Only sensory function left
A	Complete motor and sensory deficit

3.2. Surgery

Procedures involved the lumbar (n = 43), thoracic (n = 17), cervical (n = 11) and more rarely the sacrococcygeal spine (n = 7). GTR was achieved in 52.5% of all patients, but was significantly lower in intramedullary tumours (χ^2 = 7.56, significant). Fewer MPE than CE tumours could be fully resected (Table 2). Anaplastic tumours could not be fully resected due to tumour dissemination at the time of surgery. The main reasons for STR or biopsy alone were: disseminated tumour; intramedullary location in the cervicothoracic region with a high risk of affecting neurological outcome; or conus tumours with adhesion to the spinal cord, nerve roots or dura.

3.3. Adjuvant therapies

55.2% of patients underwent adjuvant radiotherapy after STR or biopsy compared with only 9.4% of patients after GTR. Twenty-four percent of MPE (n = 6) and 32.4% of CE patients (n = 11) received radiotherapy (χ^2 = 0.49, no significant difference; Table 2). Both anaplastic cases received radio- and chemo-therapy.

3.4. Complications

Fifteen (24.6%) patients experienced, mostly minor, complications (Table 3). Transient neurological deterioration included sensory deficit (n = 3), urinary incontinence (n = 2) and incomplete motor deficits (n = 2). Permanent deterioration in Frankel score after surgery was rare (n = 3).

Dexamethasone was administered peri- and intra-operatively to ameliorate symptoms caused by nerve swelling and compression. Secondary dorsal stabilisation was necessary in an adolescent after laminectomy over three levels. Eighteen percent of patients reported chronic pain, being either sciatic or local back pain more than 3 months after surgery.

3.5. Follow-up

A neurologically stable state was reached generally within 2 to 4 months after surgery. An improvement in Frankel score was found in 16.4% (n = 10) of patients. The best clinical improvements were seen in lumbar tumours with mild impairment (grade D). Good neurological outcome depended primarily on a good preoperative neurological state (Fig. 3 and 4). A longer symptom duration until diagnosis did not correlate with a worse resection grade or neurological outcome (Fig. 3, Table 2).

Only two patients had a recurrence of the tumour after GTR, while 11/29 = 37.9% (n = 11) of non-GTR tumours recurred, mostly