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Original Article

Ependymomas of the filum terminale: The role of surgery and radiotherapy

Lars de Jong, Frank Van Calenbergh, Johan Menten[1], Johannes van Loon, Steven De Vleeschouwer, Christiaan Plets, Mehrnaz Didgar, Raf Sciot[2], Jan Goffin

Departments of Neurosurgery, [1]Radiation Therapy and [2]Pathology, University Hospitals Leuven, Belgium

E-mail: *Lars de Jong - ldjone@hotmail.com; Frank Van Calenbergh - frank.vancalenbergh@uzleuven.be; Johan Menten - johan.menten@uzleuven.be; Johannes van Loon - johan.vanloon@uzleuven.be; Steven De Vleeschouwer - steven.devleeschouwer@uzleuven.be; Christiaan Plets - christiaan.plets@online.be; Mehrnaz Didgar - mehrnaz.didgar@uzleuven.be; Raf Sciot - raf.sciot@uzleuven.be; Jan Goffin - jan.goffin@uzleuven.be
*Corresponding author

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Abstract

Background: Ependymomas of the filum terminale (EFT) form a specific and relatively uncommon subtype of spinal cord ependymomas. Most series in the literature are small, spanning a large time period. Up to date no consensus has been reached about the optimal treatment of these lesions. Some authors promote postoperative radiotherapy for all cases, others advocate postoperative radiotherapy only when a subtotal resection is performed or when metastasis are apparent.

Methods: We performed a retrospective analysis of 22 patients with an EFT (mean age at diagnosis of 35.6 years).

Results: In all patients (9/22) with lesions smaller than 4.5 cm no metastases were present and a complete resection could be obtained. No adjuvant radiotherapy was performed and at latest follow they had an excellent outcome. In our series, these initial tumor characteristics were more important regarding prognosis than either histology or treatment-related factors. For the larger tumors, total resection was obtained less frequently, more dissemination was diagnosed and a worse outcome was scored. Radiotherapy if indicated did lead to an acceptable disease control.

Conclusion: In every case of EFT, an individual treatment protocol has to be outlined, but if an EFT is relatively small and can be resected completely, we would advocate to withhold radiotherapy.

Key Words: Filum terminale ependymoma, intraspinal tumor, radiotherapy

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INTRODUCTION

Ependymomas of the filum terminale (EFT) form a specific and relatively uncommon subtype of spinal cord ependymomas: in contrast to the more common intramedullary ependymomas, EFT present macroscopically as an intradural extramedullary tumor surrounded by the cauda equina nerve roots. Compared to intramedullary ependymomas, most frequently seen in childhood and adolescence, EFT occur generally at a later age.[2,3,5,7,10,16-18]

Histologically, the majority are of the myxopapillary type (WHO grade I), although in a few cases, grade II tumors

also occur. Because the myxopapillary and the grade II ependymomas have a very similar clinical presentation, an indistinguishable appearance during surgery and a similar biological behavior, with the possibility of local recurrence and CSF metastasis occurring in both myxopapillary and grade II ependymomas,[5,12,16] we have analyzed these together, as was done by several other authors.[9,16,18]

Ependymomas in general have a reputation to be relatively resistant to radiotherapy and most chemotherapeutic regimens.[6,14] Surgery has therefore been considered the mainstay of treatment.[7,8] This is also true for EFT management where complete resection can lead to permanent cure in a large percentage of patients.[3,7] However, there is a significant risk of local relapse and of dissemination through CSF pathways leading to spinal cord compression above the level of the cauda equina and even of brain metastasis.[13] Recent publications have not been able to solve the controversy, some series advocating surgical removal as the only treatment except in selected cases,[3,7,16] others arguing in favour of adjuvant radiotherapy in all cases.[2,5,12,18] There is also substantial controversy about surgical technique: 'en bloc' without opening the capsule vs. piecemeal using ultrasonic aspiration.[5,10]

MATERIALS AND METHODS

All patients with spinal tumors presenting to the department of neurosurgery are prospectively identified and included in a database. From this database, we identified all cases with a new diagnosis of ependymoma of the filum terminale treated in our institution from 1992 until 2008. The files were studied retrospectively. Patients diagnosed before 1992 but still in follow up later were excluded, because diagnostic modalities (myelography and CT scan), surgical technique (e.g., availability of ultrasound aspiration) and guidelines for staging and radiotherapy were quite different in this early period, but have been much more standardized since the early 1990s.

We identified 22 patients. Age at diagnosis ranged between 7 and 81 years (mean 35.6 year, median 32 years), with 4 children and 12 patients in the third or fourth decade. Average follow-up was 107 months (median 91 months). At initial presentation, lumbar and/or sciatic pain was the most frequent symptom (20 cases). In five patients, some motor deficit was noted on clinical examination, while three patients had sphincter problems. In one case the tumor was causing pseudotumor cerebri with papilledema, an exceptional but well known association,[8] and in one case, the tumor was a fortuitous finding on imaging because of a traumatic sacral fracture.

All patients were operated shortly after diagnosis. Staging with cranial and whole spine MRI was performed either preoperatively or in the weeks following surgery.

In the absence of clear data in the literature, strict guidelines for the indication for adjuvant radiotherapy were not made prospectively. The indication to start or withhold radiation was discussed in an interdisciplinary meeting. The surgical impression of complete resection and the MR absence of residual tumor were the primary arguments for withholding irradiation.

Follow up was organized clinically and with MRI every 6 months in the first years, and annually after 3--5 years. Treatment of local recurrences or metastasis was performed at the time of diagnosis with MRI, not waiting for symptomatology to develop.

The dimensions of the primary tumor were estimated using a linear measurement of the length of the EFT along the axis of the spinal column. For the earlier cases, this was done using the measuring rule on the hard copy images, from 2001 onwards using the measuring tool in the DICOM images. Width was not considered. For statistical analysis the patient group was dichotomized: small tumors (up to 4.5 cm) and large tumors (larger than 4.5 cm). This limit of 4.5 cm is somewhat arbitrary but has surgical significance (less than 2 vertebral heights).

Possible prognostic factors (tumor dimensions, metastasis, surgical aspects and radiotherapy) were analyzed and statistical analysis was performed using Fisher's exact test for a 2×2 contingency table.

RESULTS

In five patients, metastases were found at diagnosis, in three only in the distal end of the dural sac, in two at higher levels. Surgery was complete in 18 (including two cases where the metastases could be resected) and partial in 4. Surgical technique was in 5 cases 'en bloc', in the 17 others piecemeal resection using biopsy forceps and ultrasound aspiration.

Histology showed myxopapillary type in 16 (4 with metastasis), grade II in 6 (1 with metastasis). Adjuvant radiotherapy (in 6 cases local field from T11 to S2-3, with a dose of 46-50 Gy and in 4 craniospinal irradiation with local boost) was performed after incomplete resection and/or metastasis in 6 cases and in 2 cases after complete resection. In 12 other patients, where the surgeon had the impression of complete resection, no radiotherapy was performed. The absence of residual disease was not in all cases confirmed by early MRI. Delayed radiotherapy was given in 5 cases: in 3 nonirradiated patients, 2 on a local recurrence and in 1 for distal sacral sac metastasis. In two locally irradiated patients delayed radiotherapy was performed on a proximal spinal cord recurrence.

At last follow up, 1 patient had died of progressive

disease and 2 of unrelated cause (1 tumor free and 1 with a stable residual tumor). Seven patients had been treated for recurrences with surgery, radiotherapy and in 2 cases with chemotherapy (temozolomide in both, and tamoxifen/etoposide in 1 patient). Of the 19 patients alive, 16 were tumor free at last follow up, in 2 there was stable disease for 2--5 years and in 1, distal metastasis, treated with repeated surgery alone, remain stable after 1 year.

After statistical analysis, the most important prognostic factor was initial tumor presentation [Table 1]: all 9 patients with a tumor smaller than 4.5 cm did not have metastasis or recurrence, were not irradiated and had excellent functional outcome. In patients with larger tumors, there were more metastases and recurrences, radiotherapy was performed and functional outcome was excellent only in 9/13.

DISCUSSION

General presentation and histology

Ependymomas of the filum terminale are relatively rare tumors and most series in the literature are small, spanning a large time period. The symptomatology at presentation is in most cases limited to pain, either lumbar or sciatic. The use of MRI allows early detection, since these tumors can be missed on CT scan, especially when CT scanning is limited to the lower disc levels. In a minority of patients, motor or sensory deficits can occur, and sphincter disturbances are also possible.

Because of the typical presentation, the similar image on MRI and during surgery, and the similar prognosis, we have elected to analyse the few cases of grade II EFT together with the more frequent myxopapillary ependymomas (WHO grade I) as has already also been done by other authors.[9,16,18] In our analysis, histological grade did not influence prognosis: in the 6 cases with grade II tumors, complete resection was possible (in 1 including resection of a sacral metastasis), radiotherapy was given in 2 and 5 of 6 were tumor free at the latest follow up.

Table 1: Disease-related characteristics dichotomized according to size

	<4.5 cm	>4.5 cm	*P* value
n	9	13	
Complete Resection	9/9	8/13	NS (0.053)
Metastases	0	6	0.046
Radiotherapy (adjuvant or late)	0	11	0.0002
Recurrence	0	6	0.046
Died	1 (unrelated)	2 (1 unrelated and 1of disease)	

Ependymomas are tumors that are prone to metastasize in the CSF. This holds true also for the apparently benign myxopapillary tumor. Some authors have even suggested that pediatric myxopapillary ependymomas are often already disseminated at the time of diagnosis.[13] At presentation, we found CSF metastasis in 5/22 cases, and later in the course of the disease, 1 patient developed new metastasis after an interval of 2 years. It is therefore important to do a complete staging with MR imaging of the CNS in all patients in whom an EFT is diagnosed.

Surgical technique

Surgical technique in smaller tumors is straightforward: the tumor can be resected "en bloc" after dissecting the tumor from the surrounding cauda equina nerve roots that are separated from the tumor capsule by an arachnoid plane. Transection of the filum terminale then allows removal of the tumor without opening the tumor capsule, without risk of seeding small tumor fragments in the CSF. In larger tumors, it usually is necessary to open the tumor capsule and debulk the mass using ultrasound aspiration, before one can safely dissect the nerve roots from the capsule. This implies a risk of dissemination of tumor cells. Controversy exists whether this risk of seeding occurs frequently.[5] This distinction in smaller and larger tumors is important from a surgical point of view, but not often described in the oncological literature. However, in our analysis these initial tumor characteristics, associated with the possibility to obtain a complete surgical resection, seem to be more important than either histology or treatment-related factors.

Radiotherapy

Radiotherapy for EFT has been shown to prolong progression-free survival in patients after less than total resection[1,5,9,15,18] and in patients with leptomeningeal metastasis or recurrent tumors first treated with surgery alone.[4,5,9] In a series of 85 patients from the Rare Cancer Network,[12] 45 % were initially treated with surgery alone and 55 % received adjuvant radiotherapy. After multivariate analysis, high dose radiotherapy was of benefit to prevent recurrence and prolong progression free survival.

On the other hand, radiotherapy of the spinal cord is associated with frequent early toxicity (nausea, vomiting, rectitis, hematologic toxicity), can lead to vertebral body osseous changes and growth disturbances and may be associated with potentially serious long term effects (e.g., radiation myelitis and second tumors), especially in younger patients.[11] A small series of seven children from Montreal suggests that disease control may be improved using adjuvant radiotherapy, even in children.[2] However, other authors find that pediatric patients have a worse prognosis due to higher risk of dissemination and local recurrence than adults.[3] Therefore, the role

of radiotherapy after complete resection in adults remains uncertain for these slow growing and rarely life-threatening tumors and some authors thus advocate only aggressive resection.[3,7,16]

Our protocol over the 16 year time period varied somewhat, but from our retrospective analysis, it can be seen that the guidelines for withholding radiotherapy after complete resection were in general well followed. Some patients needed radiotherapy for recurrent or disseminated disease. In those patients, until the present, the use of radiotherapy led to disease control except in one patient who died from the disease.

CONCLUSION

Although EFT has a tendency to metastasize in the CSF, there is still debate whether or not EFT needs to be treated adjuvantly after surgical resection. Some deliver postoperative radiotherapy for all cases, most authors advocate postoperative radiotherapy only when a subtotal resection was performed or when metastasis are apparent.

In the retrospective analysis of our series of 22 patients with EFT of the myxopapillary type (WHO grade I) and grade II ependymoma (which have a very similar clinical presentation, an indistinguishable appearance during surgery and a similar biological behavior) we used an arbitrary dichotomy of 4.5 cm (less or more than 2 vertebral bodies in height). This distinction is important from a surgical point of view, but not often described in the oncological literature.

All patients (9/22) with a tumor smaller than 4.5 cm had an excellent outcome at the latest follow up. So, in our series the tumors with these initial tumor characteristics were associated with the possibility to obtain a complete surgical resection, they seem to be more important than either histology or treatment-related factors.

They did not need radiotherapy after surgery and had an excellent long term prognosis without recurrence. For the larger tumors, total resection was obtained less frequently more dissemination was diagnosed and a worse outcome was scored. Radiotherapy if indicated did lead to an acceptable disease control.

In every case of EFT an individual treatment protocol has to be outlined, but if an EFT is relatively small and can be resected completely, we would advocate to withhold radiotherapy.

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