Letters to the Editor

The role of radiotherapy in the treatment of spinal chordomas: an integrative analysis of 523 cases

We read with great interest a recent paper by Meng et al on the clinical features and prognostic factors of patients with chordoma of the spine.¹ The authors performed a retrospective analysis of 153 patients in a single center. They found that tumor location of C3–L5, dedifferentiated chordoma, preoperative Frankel scores A–C, and total spondylectomy were independent prognostic factors for local relapse-free survival (LRFS), while total en bloc spondylectomy and KPS >80% were favorable factors for overall survival (OS).

We commend the authors for performing the largest study in the literature on spinal chordomas, as the disease is rare and previous published series were limited to a small number of patients. Meng et al argued that having a cohort of patients from a single center reduced the heterogeneity of the data. However, one disadvantage of this approach is that subgroup analysis, with its potential to reveal factors which could have affected LRFS and OS, cannot be performed due to the small sample size. We noted that Meng et al did not find radiotherapy to be an independent prognostic factor for spinal chordomas. This contradicts previous studies that showed the beneficial effect of adjuvant radiotherapy after tumor resection.^{2–4} Therefore, we aimed to further define the role of radiotherapy in patients

with spinal chordoma by performing an integrative analysis of 519 cases from the literature with 14 additional cases from our local institution.

We included papers from 1990 to 2015 that presented data on LRFS and OS for individual patients. Studies with incomplete patient information were excluded. We performed univariate and multivariate analysis of prognostic factors on our dataset according to the protocol described by Meng et al. Our cohort comprised 312 men and 179 women; gender was not reported for 42 patients. The mean age was 55 years (median, 57; range, 6–89). Of these patients, 364 presented with primary chordoma, while 37 presented with chordoma recurrences after initial surgical treatment. Three hundred chordomas were located in the sacrum, with 20 in C1–L2 and 82 cases in C3–L5. Out of 498 (96.0%) patients who underwent surgical treatment, 171 (34.3%) had positive margins; 327 (65.7%) had negative margins. The mean follow-up period was 60 months (median, 48 mo; range, 0–408 mo). Recurrence was detected in 253 (48.4%) patients, and 165 (31.5%) died in the follow-up period. The mean time from surgery to recurrence was 34 months (median, 24; range, 0.1–204). The mean follow-up for the deceased patients was 61 months (median, 50; range, 0–408).

We found that the LRFS rate was significantly lower in patients with tumor located in C1–C2 compared with other tumor sites ($P = .03$). Other factors that affected LRFS rate on univariate analysis included age, history of previous treatment, pathology (classical vs dedifferentiated type), resection margin, and the use of adjuvant radiotherapy and/or chemotherapy. Only pathology remained significant on multivariate Cox regression analysis. We found the same trend in adjuvant

Table 1. Univariate analysis of prognostic factors affecting LRFS and OS in 171 patients with positive margins

Factors	<i>n</i>	LRFS %	<i>P</i>	OS %	<i>P</i>
Age, y <60/≥60	112/49	28.6 vs 31.9	.673	60.7 vs 51.0	.252
Sex, M/F	103/57	27.5 vs 33.9	.394	59.2 vs 56.1	.705
Treatment history, no/yes	111/17	36.7 vs 5.9	.012	61.3 vs 47.1	.267
Location, C1–2/C3–L5/S1–5	11/38/64	0 vs 35.1 vs 39.7	.037	54.4 vs 65.8 vs 53.1	.447
Bladder and bowel function, no/yes ^a	21/17	–	–	61.9 vs 58.8	.847
Tumor size, ≤6 cm/>6 cm	18/40	55.6 vs 30.0	.063	61.1 vs 57.5	.796
Preoperative selective arterial embolism, no/yes	149/6	32.7 vs 0	.178	55.0 vs 83.3	.231
Surgical approach, anterior or posterior/combined	35/23	44.1 vs 27.3	.203	77.1 vs 52.2	.047
Chemotherapy, no/yes	103/9	29.7 vs 11.1	.441	58.3 vs 0	.001
Adjuvant radiotherapy, no/yes (positive margin)	33/113	12.5 vs 32.1	.023	39.4 vs 61.9	.021
Surgery after recurrence, no/yes	39/35	–	–	53.8 vs 51.4	.835
Adjuvant radiotherapy after recurrence, no/yes	12/159	–	–	33.3 vs 59.1	.082
Complication, no/yes	28/26	–	–	60.7 vs 57.7	.821
Postoperative recurrence, no/yes	118/51	–	–	44.9 vs 84.3	<.001
Postoperative distant metastasis, no/yes	110/48	–	–	64.5 vs 33.3	<.001

^aThere were not enough cases to perform analysis.

radiotherapy as had Meng et al—patients who were treated with postoperative radiotherapy had lower LRFS than those who were not (57.5% vs 39.7%, $P < .001$). This may be attributed to selection bias, as patients with incomplete resections were more likely to receive radiotherapy than those with complete excisions. Their lower survival rates may be secondary to incomplete resection margin rather than the effect of radiotherapy. In a subgroup analysis of 171 patients with positive margins (Table 1), we found that those who received radiotherapy had a higher LRFS than those who did not (32.1% vs 12.5%, $P = .023$). On the multivariate analysis of patients with positive margins, previous treatment history, location in C1–C2, and tumor size were significantly associated with decreased LRFS. Adjuvant radiotherapy and location in C3–C5 did not demonstrate significant association with LRFS. However, we acknowledge that this multivariate analysis has a limited sample size ($n = 29$) and may not have enough power to achieve statistical significance for some factors.

In conclusion, we provided a dataset on spinal chordomas complementary to the paper by Meng et al. Our large sample size enabled us to perform subgroup analysis, which showed that adjuvant radiotherapy may be beneficial in patients with positive surgical margins. Prospective studies in patients with spinal chordoma and positive surgical margins are needed to define the role of postoperative radiotherapy in the management of spinal chordomas.

Funding

This work was supported by the Natural Science Foundation of China (81301988 to L.Y.).

Conflict of interest statement. None declared.

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Received 4 June 2015; accepted 6 June 2015

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From histology to neurocognition: the influence of tumor grade in glioma of the left temporal lobe on neurocognitive function

The morphology of a tumor and the histologic grade assigned to it represent the behavioral nature of a neoplasm and, generally, the prognostic value that can be expected. Such a histologic criterion is applied to tumors throughout the body, and the brain is not exceptional in this regard. Where the brain is exceptional is in the fact that it functions in a neurocognitive context that can be encumbered by way of pathologic insult, including neoplastic transformations. Concertedly, it has been proposed in practice that the degree of tumor grade may influence the neurocognitive function (NCF) in the brain as established by the behavioral context of the tumor.

This supposition is explored by Noll et al¹ in a study to determine the relationship between histologic grade and NCF in patients with glioma of the left temporal lobe prior to surgical resection. By assessing the preoperative neuropsychological profile of each patient with a glioma histologically low-grade (II) or high-grade (III or IV), Noll et al found that patients with confirmed high-grade lesions experienced greater rates of neurocognitive impairment. The frequency of neurocognitive impairment was demonstrated with greater relative frequency in patients with confirmed high-grade tumors than those with low-grade tumors. Measures of verbal learning, processing speed, executive functioning, and language were evaluated and, as the report would indicate, patients with high-grade tumors fared more poorly than their lower-grade counterparts, although it is important to note that the majority of patients, irrespective of neoplastic grade, exhibited impaired NCF (74% of all patients on at least one neurocognitive measure).¹

Interestingly, deficit of NCF in high- and low-grade gliomas was observed independently of lesion size, supporting the