Primary intramedullary neurocytoma: Case report and literature analysis

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INTRODUCTION

Primary intramedullary neurocytoma, first described by Coca et al.,[3] is extremely rare. It has been hypothesized that intramedullary neurocytoma can originate from the primitive neuroectodermal cells surrounding the central canal region in fetal life. Due to the rarity of this pathology, only a few cases have been reported in the literature.[1−3,5−9] Moreover, it is difficult to collect a wide series in a single institution to perform a survival analysis and give indications about prognosis and treatment.
a wide series in a single institution in order to perform a survival analysis and give indications about prognosis and treatment. Thus, the aim of this study was to report a case of primary intramedullary neurocytoma and to perform a systematic statistical analysis of cases reported in the literature in order to identify potentially prognostic factors on neurological outcome and recurrence risk.

**CASE REPORT**

A 37-year-old woman was admitted because of a 9 months history of diffuse axial and low back pain. The neurological examination showed a hypesthesia in the left lower limb and bilateral hyperactive deep tendon reflexes. Spinal magnetic resonance imaging (MRI) with gadolinium showed an intramedullary lesion at T8–T9 level, with solid and cystic components, hypo- and hyper-intense on T2-weighted images and with dishomogeneous contrast enhancement after gadolinium administration associated to the cranial syrinx [Figure 1]. Under neurophysiological intraoperative monitoring, the patient was submitted to T8–T9 laminotomy and total lesion removal. On histology, the lesion was composed of round to the oval cells with finely dispersed chromatin and small nucleoli; ganglion cell differentiation was commonly present among the neurocytic cells. Hyalinized vessels were also observed [Figure 2a]. “Atypical” histological features (mitotic activity, microvascular proliferation, and necrosis) were not present. Immunohistochemically, the neoplastic cells were positive for synaptophysin [Figure 2b]. The MIB-1 labeling index was 1%. The histological diagnosis of extraventricular neurocytoma with ganglion cell differentiation was made.

**DISCUSSION**

A literature search was made in the PubMed database including the following terms: Neurocytoma, spinal neurocytoma, neurocytoma of the spinal cord, intramedullary neurocytoma, and extraventricular neurocytoma. Twenty-one articles were found. We excluded from the analysis articles with a follow-up fewer than 6 months or with no information about the follow-up. Fifteen articles [1‑3,5‑9,19] and the present case (22 patients, 15/male, 7/female) were eligible for the analysis. The clinical and outcome data are reported in Table 1. We studied the impact of age, sex, number of involved levels (≤2 vs. >2), entity of resection (subtotal vs. gross total), postoperative radiotherapy (RT), and proliferation index (Ki67) on the neurological outcome of the patients and on the recurrence of the tumor. Comparison of categorical variables was performed by the χ² statistic. The Kaplan–Meier curves were plotted to calculate the progression-free survival (PFS) of these patients. \( P < 0.05 \) was considered as statistically significant. The mean age of the selected patients was 36.45 ± 17.77 years with a mean follow-up of 38.18 ± 58.46 months. A subtotal resection (STR) was achieved in 14 (64%) [1,2,5,11,12,16,17,19] while a gross total resection (GTR) was feasible only in 7 cases [3,9,10,13‑15,18] and in the present case (36%). Adjuvant RT was performed only in 7 patients (31.81%) [1,12,16,17]. The clinical outcome at follow-up was reported stable in 4 cases [1,11,12] and improved in the present case and in 11 [2,3,5,10,11,14‑17] from the literature, with an overall good functional outcome in 72.72% of patients. The mean PFS was 22.65 ± 1.11 months [Figure 3] with a 1-year PFS of 95.45% and a 2-year PFS of 86.36%.

Among the considered potentially prognostic factors, we found a statistically significant better neurological outcome in the patients who underwent adjuvant RT \( (P = 0.04) \). All the patients with a number of involved levels ≤2 [Table 1] reported a stable or improved
Moreover, it can show cystic contrast enhancement. Moreover, the extremely variable features on MRI make the differential diagnosis very hard. Likewise astrocytoma, its signal can range from iso- to hypointensity on T1-weighted images and iso- to hyperintensity on T2-weighted images, with homo- or heterogenous contrast enhancement. Moreover, it can show cystic components or intratumoral hemorrhage similarly to ependymomas and hemangioblastomas and can display the exophytic growth mimicking a meningioma. From a surgical point of view, from our literature analysis, it appears evident how it usually involves more spinal segments (70% of reported cases, Table 1) and that a GTR is very difficult to achieve (only 36% of cases). Thus, the preservation of a good functional outcome with a STR instead of a GTR should be kept in mind approaching an intramedullary neurocytoma. In fact, from our analysis, we found a worsening of the neurological function in 3 out of 5 patients (60%) submitted to GTR and only in 3 out of 14 cases (21.42%) who underwent a STR. Moreover, a GTR did not significantly decrease the risk of the recurrence being a lower Ki67 (MIB-1) the factor more strongly related to a lower tumor recurrence. Thus, the histopathological examination is crucial both to make the diagnosis (based on some peculiarities, such as the presence of ganglion cell differentiation, lower cell density and immunoreactivity for glial fibrillary acidic protein, Ki-67 [%]) but also to determine the recurrence risk. Considering the recurrence risk, a Ki67 (MIB-1) lower than 2% was associated with a statistically significant lower risk of recurrence ($P = 0.0157$).

The primary intramedullary neurocytoma represents a challenge for a neurosurgeon. Preoperative radiological diagnosis can be difficult due to the rarity of this pathology. From a surgical point of view, from our literature analysis, it appears evident how it usually involves more spinal segments (70% of reported cases, Table 1) and that a GTR is very difficult to achieve (only 36% of cases). Thus, the preservation of a good functional outcome with a STR instead of a GTR should be kept in mind approaching an intramedullary neurocytoma. In fact, from our analysis, we found a worsening of the neurological function in 3 out of 5 patients (60%) submitted to GTR and only in 3 out of 14 cases (21.42%) who underwent a STR. Moreover, a GTR did not significantly decrease the risk of the recurrence being a lower Ki67 (MIB-1) the factor more strongly related to a lower tumor recurrence. Thus, the histopathological examination is crucial both to make the diagnosis (based on some peculiarities, such as the presence of ganglion cell differentiation, lower cell density and immunoreactivity for glial fibrillary acidic protein, Ki-67 [%]).

### Table 1: Clinical and outcome findings of primary intramedullary neurocytoma studies included in the analysis

| Author, year | Age | Sex | Location | Resection | RT | Ki-67 (%) | PFS (months) | Follow-up (months) | Recurrence | Neurological function at follow-up |
|-------------|-----|-----|----------|-----------|----|-----------|--------------|--------------------|------------|----------------------------------|
| Tatter et al., 1994[17] | 65  | Male | C2-C6    | STR       | Yes | NA        | 120          | 120                | Not        | Improved                         |
|             | 49  | Male | C3-C4    | STR       | Yes | NA        | 24           | 60                 | Yes        | Improved                         |
| Coca et al., 1994[18] | 67  | Male | T11-T12  | GTR       | Not | NA        | 30           | 30                 | Not        | Improved                         |
| Stapleton et al., 1997[19] | 12  | Male | C4-T1    | GTR       | Not | NA        | 24           | 24                 | Not        | Improved                         |
| Stephan et al., 1999[20] | 46  | Female | T12-L1  | GTR       | Not | 1         | 12           | 12                 | Not        | Improved                         |
| Ashkan et al., 2000[21] | 12  | Male | C2-T1    | STR       | Not | NA        | 33           | 33                 | Not        | Improved                         |
| Martin et al., 2002[22] | 50  | Male | T2-T5    | GTR       | Not | 2         | 24           | 24                 | Not        | Worsened                         |
| Sharma et al., 2005[23] | 24  | Male | C5-T1    | GTR       | Not | 9         | 10           | 24                 | Yes        | Worsened; dead for intracranial metastasis |
| Gokhan et al., 2008[24] | 49  | Female | C3-C6   | STR       | Not | 1         | 7            | 7                  | Not        | Improved                         |
| Marucci et al., 2009[25] | 51  | Male | T10-T11  | GTR       | Not | 1         | 12           | 12                 | Not        | Improved                         |
| Polli et al., 2009[26] | 6   | Male | C1-C7    | STR       | Not | 1         | 276          | 276                | Not        | Worsened                         |
|             | 15  | Male | C1-T11   | STR       | Not | 1         | 24           | 24                 | Not        | Worsened                         |
|             | 37  | Female | T12-L1  | STR       | Yes | 5         | 15           | 27                 | Yes        | Stable                           |
| Tsoi et al., 2011[27] | 54  | Female | T3-T5   | GTR       | Not | 1         | 6            | 6                  | Not        | Worsened                         |
| Agarwal et al., 2011[28] | 16  | Male | NA       | STR       | Yes | NA        | 6            | 6                  | Not        | Stable                           |
|             | 25  | Male | NA       | STR       | Yes | NA        | 6            | 6                  | Not        | Stable                           |
| Wu et al., 2014[29] | 48  | Female | Medulla-T1 | STR   | Not | NA        | 18           | 18                 | Not        | Worsened                         |
| Patil et al., 2014[30] | 26  | Male | Medulla-T4 | STR   | Not | NA        | 24           | 24                 | Not        | Improved                         |
|             | 39  | Male | T9-L1    | STR       | Not | NA        | 44           | 44                 | Not        | Stable                           |
| Sun et al., 2015[31] | 26  | Male | Medulla-T4 | STR   | Not | NA        | 24           | 24                 | Not        | Improved                         |
| Present case | 37  | Female | Medulla-T2 | STR   | Not | NA        | 24           | 24                 | Not        | Improved                         |

RT: Radiotherapy, PFS: Progression free survival, STR: Subtotal resection, GTR: Gross total resection, NA: Not available

Figure 3: The Kaplan–Meier analysis of progression-free survival of cases included in this review
protein, synaptophysin, and NeuN, markers for glial and neuronal differentiation (6-8) and to get the proliferative index (MIB-1). Due to its importance for the prognosis, this data should be routinely investigated (in our analysis it was available only in 10 out of 22 cases [45.45%]). However, the future research should clarify if a higher proliferative index should be considered as an indication for RT. In our analysis, RT seems to play a role in improving the neurological outcome at follow-up but not in preventing the tumor recurrence.

We tried to obtain some indications about the management of the primary intramedullary neurocytoma making an analysis of available cases in the literature. Although our study has some limitations, due to the heterogeneous nature of data, we think that the goal of the surgery should be to preserve a good neurological function even if a residual tumor has to be left. In fact, a GTR did not seem affect the tumor recurrence but is associated to a worsening of the neurological function in most of the cases. Moreover, the Ki67 (MIB-1) should be always evaluated because it seems strongly associated with the tumor recurrence. Further studies should clarify the role of adjuvant RT.

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Conflicts of interest
There are no conflicts of interest.

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