



Cervical Primitive Neuroectodermal Tumor in an Adult: Case Report and Literature Review*

Tumor neuroectodérmico primitivo cervical em adulto: Relato de caso e revisão da literatura

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Abstract

Introduction Primitive neuroectodermal tumors are rare neoplasms of the central nervous system that occur in children, with few reports in adults. These tumors are found most often in the cerebral hemispheres, with spinal cord disorders being rare.

Case Report A 71-year-old man with motor and sensory deficits in the upper limbs, cervical pain, and urinary incontinence presented to the Neurosurgery Service. The physical examination revealed grade-III motor strength on the right side, grade IV- on the left upper limb, and grade IV+ on the left lower limb. A magnetic resonance imaging scan showed an expansive intramedullary lesion with a C3-C4 epicenter. Spinal decompression, lesional biopsy, and adjuvant radiotherapy were performed. The anatomopathological report showed a primitive neuroectodermal tumor. After a new treatment with adjuvant radiotherapy (20 × 1.8 Gy in the skull and neuroaxis and 5 × 1.8 Gy in tumor boost), the patient progressed without recurrence.

Conclusion Since the characteristics of the tumor are similar to those of medulloblastoma, it is necessary to expand the studies on these lesions, to better understand their pathophysiology and list better diagnostic and therapeutic methods, in addition to those already available.

Keywords

- ▶ primitive neuroectodermal tumors
- ▶ adult
- ▶ medulloblastoma

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Resumo

Introdução Os tumores neuroectodérmicos primitivos são neoplasias raras do sistema nervoso central que ocorrem em crianças, com escassos relatos em adultos. Esses tumores são encontrados mais frequentemente nos hemisférios cerebrais, sendo raros os acometimentos medulares.

Relato de Caso Um homem de 71 anos com déficits motor e sensitivo em membros superiores, algia cervical e incontinência urinária apresentou-se ao Serviço de Neurocirurgia. O exame físico revelou força de grau III à direita, de grau IV- no membro superior esquerdo, e de grau IV+ no membro inferior esquerdo. Um exame de ressonância magnética denotou lesão expansiva intramedular com epicentro em C3-C4. Foram realizadas descompressão medular, biópsia lesional e radioterapia adjuvante. O laudo anatomopatológico evidenciou tumor neuroectodérmico primitivo. Após novo tratamento com radioterapia adjuvante (20 × 1,8 Gy no crânio e neuroeixo e 5 × 1,8 Gy em *boost* tumoral), o paciente seguiu sem recidiva.

Conclusões Uma vez que as características do tumor se assemelham às do meduloblastoma, torna-se necessário ampliar os estudos acerca dessas lesões, a fim de compreender melhor sua fisiopatologia e elencar melhores métodos diagnósticos e terapêuticos, além dos já disponíveis.

Palavras-chave

- ▶ tumor neuroectodérmico primitivo
- ▶ adulto
- ▶ meduloblastoma

Introduction

Primitive neuroectodermal tumors (PNETs) represent ~ 2.5% of neoplasms that affect the pediatric population, whereas, among adults, cases are scarce, with 57 cases reported in the literature.¹⁻⁴

They affect the brain hemispheres more frequently, and may spread to the cerebrospinal fluid throughout the neuroaxis.^{2,4,5} According to their location, extension and presentation, they can be clinically subdivided into “pineal tumors” and “non-pineal tumors,” with the former being associated with a better prognosis.⁴ Imaging methods, such as computed tomography (CT) and magnetic resonance imaging (MRI), denote a lesion that resembles medulloblastoma; thus, it is necessary to perform a histological analysis of the lesion for diagnostic confirmation.²⁻⁸

Radical resection, followed by radiation on the entire neuroaxis, are the mainstays of the treatment, with better results when adding adjuvant chemotherapy to the treatment.^{4,5,9-11} The models proposed to elucidate the long-term prognosis demonstrate that adults with PNETs have a survival rate that ranges from ~ 50% to 60% in 5 years, and from 40% to 50% in 10 years.⁵

In the present article, we report a case of PNET in an adult individual, whose infrequent presentation differs from the main data found in the literature. Although such a lesion can affect other regions of the neuroaxis, spinal disorders are rare, and even less frequent in individuals with advanced age.

Case Report

Male patient, 71 years old, referred to the Oncology Neurosurgery Service due to suspected primary neoplasia. He presented with altered sensitivity in the upper limbs, progressive loss of strength in the right dimidium, progression to

reduced strength in the left dimidium, cervical pain, and urinary incontinence with 15 days of evolution. The physical examination revealed grade-III motor strength on the right side, grade IV- on the left upper limb, and grade IV+ on the left lower limb. An MRI scan showed an expansive intramedullary lesion with an epicenter in C3-C4. The hypotheses of astrocytoma, ependymoma, or metastatic process were raised. He was urgently admitted to undergo a cervical spine decompression procedure.

The patient underwent resection of an intramedullary tumor without complications. Upon postoperative examination, he was alert and communicative, with tetraparesis more pronounced on the right side. He was discharged from hospital three days after surgery.

The report of the surgical specimen revealed poorly-differentiated neoplasia. The immunohistochemical panel (▶ **Table 1**) yielded unspecific results, showing probable medulloblastoma.

After discharge, he presented symptoms of COVID-19 and evolved with clinical improvement. A Chest CT scan showed signs of pulmonary thromboembolism, requiring anticoagulation. He was followed up in an outpatient and physiotherapeutic basis. About two months after the surgery, he had relative strength recovery in the left dimidium, persisting with plegia in the right dimidium. In a discussion with a specialized team, craniospinal radiotherapy (36 Gy in the neuroaxis and 45 Gy boost) was indicated. A skull MRI scan did not reveal evidence of metastasis or expansive lesions.

Three months after the initial intervention, without having started the proposed adjuvant radiotherapy, he sought care for worsening of the left dimidial paresis and urinary retention lasting for four days.

A new MRI scan (▶ **Fig. 1**) showed an intramedullary image with intermediate signal on T1 and T2, with slight

Table 1 Immunohistochemical panel of the tumor specimen

Biomarker	Result
CD99	Positive
Vimentin	Positive
CD20	Negative
CK7	Negative
CKAE/AE3	Negative
EMA	Negative
CD45	Negative
p63	Negative
S100	Negative
Myogenin	Negative
Melan-A	Negative
Desmin	Negative

Note: The report stated that the set of morphological and immunohistochemical aspects with positivity for CD99 is suggestive of medulloblastoma. Negativity for cytokeratins and EMA does not favor primary neoplasms of epithelial origin. CD45 negativity does not favor lymphoproliferative neoplasms. Negativity for S100 does not favor the diagnosis of melanoma or undifferentiated malignancy. Abbreviations: CKAE/A3, cytokeratin AE3; EMA, epithelial membrane antigen.



Fig. 1 Sequence of magnetic resonance imaging scans in sagittal section (A, B) showing intramedullary lesion with intermediate signal on T2, measuring ~33 mm in the craniocaudal axis at the height of C3-C4.

contrast enhancement, measuring ~ 33 mm in the longest axis (craniocaudal) at the height of C3-C4, nonspecific, which raised the suspicion of residual/recurrent injury. There was

Table 2 Immunohistochemical panel of the specimen removed in the second surgical procedure

Biomarker	Result
CD99	Positive
GFAP	Positive
Vimentin	Positive
Ki67	Positive in 70% of the nuclei
CKAE1/AE3	Negative
Cromogranin-A	Negative
S100	Negative
Synaptophysin	Negative

Abbreviations: CKAE1/A3, cytokeratin AE1/AE3; GFAP, glial fibrillary acidic protein.

an extensive signal change in the adjacent spinal cord extending from C1 to T1, characterized by a high signal on T2. A new surgical approach was chosen, which was performed without complications. The patient did not present any infection in the postoperative period. He was discharged from hospital three days after the intervention, with hemiplegia on the right side and grade-II muscle strength on the left side. The anatomopathological analysis of the specimen revealed poorly-differentiated small-round-blue-cell neoplasm. The immunohistochemical panel (►Table 2) was compatible with a PNET, and the images can be seen in ►Fig. 2.

Adjuvant radiotherapy was started 1 month after surgery, with a dose of 20×1.8 Gy in the skull and neuraxis and 5×1.8 Gy in tumor boost, for 1 month. During the follow-up, the patient asked for the interruption of the physiotherapy.

A new MRI (►Fig. 3) revealed no tumor recurrence, with an area of evident thinning between C2 and C3 and posterior spinal cord retraction. In addition, control abdominal CT showed a renal nodule measuring $3.5 \times 3.2 \times 4.2$ cm, compatible with a probable neoplastic lesion, which was not present in the control CT that had been performed 4 months ago.

The case herein reported has been under follow-up for 9 months, and, since the last surgery ~ 6 months ago – the patient has not presented a new tumor recurrence, despite the fact that the origin of the renal nodule of origin is yet to be clarified.

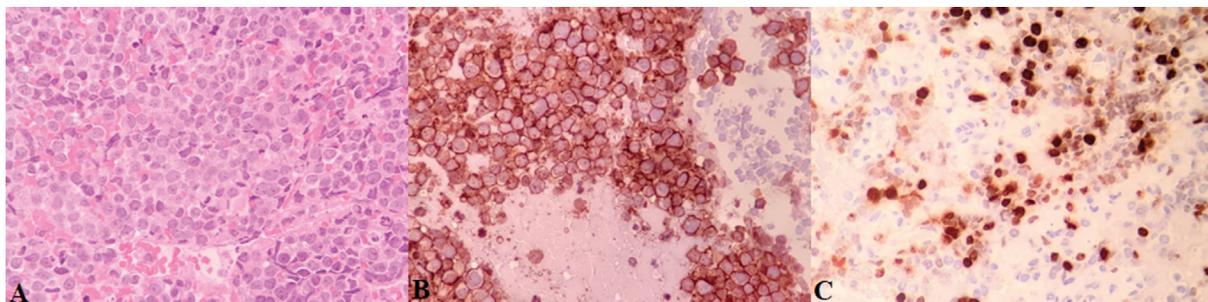


Fig. 2 (A) Histopathology of the tumor in hematoxylin and eosin staining showing small, round cells. (B) CD99 positive expression. (C) Reaction with Ki-67 antibody showing nuclear staining with ~ 70% of the neoplasia nuclei.

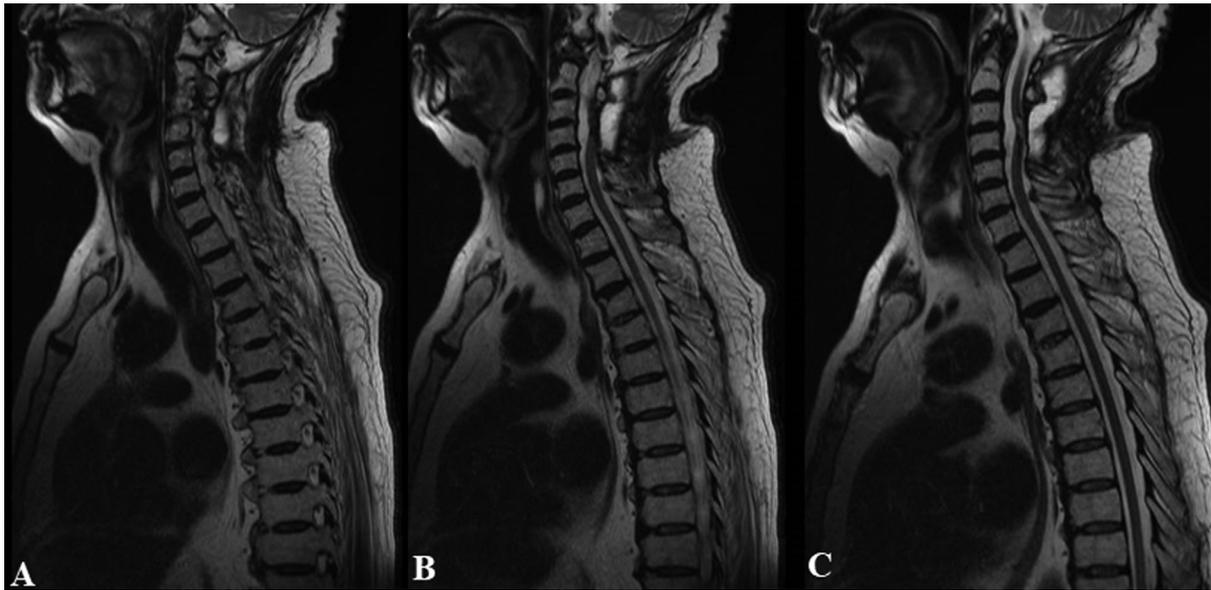


Fig. 3 Sequence of magnetic resonance imaging scans (A-C) in axial section, T2-weighted, showing thinning between C2 and C3 and subsequent retraction of the spinal cord, without tumor in this topography.

Discussion

Primitive neuroectodermal tumors are rare neoplasms of the central nervous system (CNS) that can affect children and adults.¹⁻⁹ When compared with other tumors in the pediatric population, PNETs represent ~ 2.5% of neoplasms, and, after medulloblastoma and astrocytoma, they are the most common embryonic tumor of childhood (the average age at diagnosis is 9 years old).¹⁻⁵ The incidence ratio among male and female individuals is of 1.1 and 0.8 per million inhabitants respectively.^{2,3}

The pathophysiological mechanisms of PNETs are still not well understood; however, there is a small association with the mechanisms responsible for the development of medulloblastomas, in addition to a record of origin in the germ cell matrix of the primitive neural tube.¹⁻⁶ In addition, the location of these tumors is not specific, so they may be found in any portion of the CNS, such as the posterior fossa, the brainstem, and the spinal cord.^{2,5} However, they are found more frequently in the cerebral hemispheres, and may spread to the CSF throughout the neuroaxis.^{2,4,5} They can present malignant behavior, which is observed mainly in the most undifferentiated PNETs.^{2,4,5}

In the present report, on spinal topography, the lesion showed signs and symptoms of involvement of the ascending and descending tracts. The clinical manifestations of these tumors vary according to their location.²⁻⁵ Thus, signs and symptoms of intracranial hypertension, such as headache, nausea, vomiting, focal motor changes or even seizures can be observed.²⁻⁵ The complementary evaluation with imaging methods and analysis of the CSF should be used to assist the diagnosis, identify possible spread throughout the neuroaxis, rule out other possible diagnoses, and establish a therapeutic plan.¹⁻⁶

On CT and MRI scans, the lesions resemble a medulloblastoma; thus, it is necessary to perform a histological analysis of the lesion for diagnostic confirmation.²⁻⁸

In 2007, the WHO¹² defined four histological subtypes of PNETs according to the histological analysis: CNS neuroblastoma; CNS ganglioneuroblastoma; medulloepithelioma; and ependymoblastoma. Subsequently, another subtype was included in the classification, the so-called embryonal tumor with abundant neuropile and true rosettes (ETANTR). However, such subgroups are not uniform variants.²

Therefore, molecular studies²⁻⁶ were conducted to more accurately determine the cell origin of PNETs. Based on the transcriptional signature of these lesions, it was possible to determine the occurrence of three molecular subgroups: group 1 consists of genes from neural stem cells; group 2 is associated with oligoneural genes; and group 3 is composed of genes involved in mesenchymal differentiation.²

Advances in immunohistochemistry techniques have enabled an even better differentiation between these groups, which can contribute to the diagnostic evaluation.⁵⁻⁷ However, studies^{2,4-7} demonstrate that these factors, when evaluated in isolation, can result in failures, given the presence of some of these signatures in other CNS tumors.

The following markers of histological analysis and immunohistochemical markers of these tumors are described in the literature: positivity for LIN28 and oligodendrocyte transcription factor 2 (OLIG2) in the tumors in groups 1 and 2 respectively. However, there is no specific correlation for tumors in group 3, which are classified as negative markers for LIN28/OLIG2, showing positivity for insulin-like growth factor 2 (IGF-2).²

Surgical resection, radiotherapy, and chemotherapy are the treatments that can be used in these tumors.^{2,3,5,7,9} The therapeutic approach should be studied on a case-by-case basis, considering the different locations of these lesions.²⁻¹¹ However, studies^{4,5,9-11} suggest that radical resection followed by radiation in the entire neuroaxis is the mainstay of treatment, with better results when adding adjuvant chemotherapy. When used, the chemotherapeutic agents that

have yielded the best therapeutic responses were CCNU (lomustina), vincristine, cisplatin, procarbazine, etoposide, temozolamide, cyclophosphamide, and carboplatin.^{5,8}

Prognostic assessment and risk of recurrence can be estimated from the analysis of Ki-67 markers and nuclear proliferation antigen (NPA), while p53 protein positivity is associated with lower survival rates disease free.^{5,6,8} This explains why most of the studies^{1-3,5-9} found are case reports and molecular studies, considering that new therapeutic tests are being developed, which made it difficult to correlate postoperative outcomes and long-term prognoses with those of our patient.

The models proposed to elucidate the long-term prognosis show that survival in adults ranges from ~ 50% to 60% in 5 years, and from 40% to 50% in 10 years.⁵ Furthermore, when the prognosis is compared among molecular subgroups, subgroup-1 tumors present a survival rate of 0.8 years, and subgroups 2 and 3, 1.8 and 4.3 years respectively.² Thus, the molecular assessment provided us with an overview of the prognosis, which was possible to observe during the follow-up of our patient.

Thus, the need for further studies on the molecular characteristics of PNETs is evident, as the different forms can have different outcomes, which directs the conduct toward more radical or palliative therapies.¹⁻⁹

Conclusion

We report here a rare type of CNS tumor in an adult. Such a tumor is even less frequent in spinal topography. Given its uniqueness and reduced finding of similar cases in the literature, we suggest that further studies on PNETs be carried out. Thus, it will be possible to distinguish among other neoplasms that affect the CNS, and to predict better parameters for the diagnosis, treatment and long-term follow-up.

Ethics Statement

The present study complied with all institutional guidelines for studies on human beings. Informed consent was obtained from the person responsible for the patient.

Conflict of Interests

The authors have no conflict of interests to declare.

References

- Jain A, Sharma MC, Suri V, et al. Spectrum of pediatric brain tumors in India: a multi-institutional study. *Neurol India* 2011;59(02):208–211. Doi: 10.4103/0028-3886.79142
- Adamski J, Ramaswamy V, Huang A, Bouffet E. Advances in managing medulloblastoma and intracranial primitive neuroectodermal tumors. *F1000Prime Rep* 2014;6:56–67. Doi: 10.12703/p6-56
- Zheng YC, Jung SM, Lee ST, et al. Adult supratentorial extra-pineal primitive neuro-ectodermal tumors. *J Clin Neurosci* 2014;21(05):803–809. Doi: 10.1016/j.jocn.2013.07.025
- Biswas S, Burke A, Cherian S, et al. Non-pineal supratentorial primitive neuro-ectodermal tumors (sPNET) in teenagers and young adults: Time to reconsider cisplatin based chemotherapy after cranio-spinal irradiation? *Pediatr Blood Cancer* 2009;52(07):796–803. Doi: 10.1002/pbc.21899
- Terheggen F, Troost D, Majoie CB, Leenstra S, Richel DJ. Local recurrence and distant metastasis of supratentorial primitive neuro-ectodermal tumor in an adult patient successfully treated with intensive induction chemotherapy and maintenance temozolomide. *J Neurooncol* 2007;82(01):113–116. Doi: 10.1007/s11060-006-9249-3
- Zhang Q, Su X, Liang S. [A clinicopathological analysis of primitive neuroectodermal tumors of the CNS]. *Zhonghua Bing Li Xue Za Zhi* 1998;27(04):282–285
- Vassal G, Terrier-Lacombe MJ, Lellouch-Tubiana A, et al. Tumorigenicity of cerebellar primitive neuro-ectodermal tumors in athymic mice correlates with poor prognosis in children. *Int J Cancer* 1996;69(02):146–151. Doi: 10.1002/(sici)1097-0215(19960422)69:2%3C146:aid-ijc14%3E3.0.co;2-7
- Halliday GC, Junckerstorff RC, Bentel JM, et al. The case for DNA methylation based molecular profiling to improve diagnostic accuracy for central nervous system embryonal tumors (not otherwise specified) in adults. *J Clin Neurosci* 2018;47:163–167. Doi: 10.1016/j.jocn.2017.09.013
- Maaz AUR, Yousif T, Saleh A, et al. Presenting symptoms and time to diagnosis for Pediatric Central Nervous System Tumors in Qatar: a report from Pediatric Neuro-Oncology Service in Qatar. *Childs Nerv Syst* 2021;37(02):465–474. Doi: 10.1007/s00381-020-04815-z
- Rombi B, Vennarini S, Vinante L, Ravanelli D, Amichetti M. Proton radiotherapy for pediatric tumors: review of first clinical results. *Ital J Pediatr* 2014;40:74–82. Doi: 10.1186/s13052-014-0074-6
- Miralbell R, Lomax A, Russo M. Potential role of proton therapy in the treatment of pediatric medulloblastoma/primitive neuroectodermal tumors: spinal theca irradiation. *Int J Radiat Oncol Biol Phys* 1997;38(04):805–811. Doi: 10.1016/s0360-3016(97)00005-9
- Louis D, Ohgaki H, Wiestler O, Cavenee W. WHO classification of tumours of the central nervous system. Lyon: IARC Press; 2007