RESIDÊNCIA PEDIÁTRICA

RELATO DE CASO

Neurocitoma central

Central neurocytoma

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Palavras-chave:
neoplasias do sistema nervoso central, neurocitoma, oncologia, pediatria.

Resumo

O Neurocitoma central se apresenta como um tumor localizado no terceiro ventrículo, destruindo a parte anterior do fórnix, o septo pelúcido, invadindo o ventrículo lateral. Os pacientes podem apresentar sintomas como amnésia e distúrbios de comportamento; dores de cabeça e evidência clínica de aumento da pressão intracraniana. O diagnóstico diferencial deve ser estabelecido com ependimomas, astrocitomas, oligodendromas intraventriculares ou neuroblastomas cerebrais primários - o diagnóstico é feito por tomografia computadorizada ou ressonância nuclear magnética, microscopia eletrônica e métodos de imunohistoquímica. Este relato de descreve um caso de neurocitoma central em uma paciente de 16 anos de idade, os sinais e sintomas, exames de imagem (tomografia computadorizada e ressonância nuclear magnética), análise histopatológica e imunohistoquímica e o tratamento aplicado.

Keywords:
central nervous system neoplasms, medical oncology, neurocytoma, pediatrics.

Abstract

Central neurocytoma presents as a tumor located in the third ventricle, destroying the anterior part of the fornix, the septum pelucidum, invading lateral ventricle. The patients may have symptoms of amnesic and behavior disturbances; headache and clinical evidence of raised intracranial pressure. Differential diagnosis must be established with ependimomas, astrocytomas, intraventricular oligodendromas or primary cerebral neuroblastomas - diagnosis is made by CT or MRI, electron microscopy and immunohistochemical methods. This case report describes a central neurocytoma in a 16 year old patient, the signs and symptoms, imaging (Computed Tomography and Magnetic Nuclear Resonance), histopathological and immunohistochemistry analysis and the treatment applied.

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INTRODUCTION

Central neurocytoma was first described in 1982 by Hassoum et al.[1] who reported a rare tumor composed by mature neuronal cells. The clinical features of these tumors are headache, seizures and symptoms of raised cranial pressure[2], due to its usual location in the third and forth ventricle[3] causing liquor obstruction. The diagnosis may be established with CT and MRI, electron microscopy and immunohistochemical methods[3], to differentiate central neurocytoma from other Central Nervous System (CNS) tumors, such as ependimomas, astrocytomas or oligodendromas.

The first-line treatment is complete surgical resection of the tumor[4]. Radiation therapy is indicated when complete resection is not obtained or in cases of disease recurrence or progression. The use of chemotherapy is not well established. However, it is indicated when surgical and radiation treatment (RT) failure[4].

CASE REPORT

A 16 year old patient was admitted at the Hospital Erasto Gaertner, with chronic headache over the last year, which had worsened in the last six months. She also complained of right arm paresthesia and neck pain. One month earlier she had shown reduced right arm strength and difficulty speaking. The physical and laboratorial exams were normal.

The patient was submitted to a CT scan (Figure 1) which showed an expansive solid lesion, with enhanced contrast. The lesion was located in the third and lateral ventricles, around Monro foramen, measuring 78 x 48 mm in the Anterior-posterior (AP) and transverse diameter, showing a hipodense area in the middle, suggesting a central neurocytoma. Lateral ventricles were enlarged. The patient was evaluated by a neurosurgeon and a biopsy of the lesion was ordered. The first attempt to remove a fragment for pathological study failed due to an intense bleeding during the surgery. One month later, a new procedure was performed and the stereotactic biopsy was obtained. The patient has evolved with no further neurological symptoms.

Macroscopically, the tumor masses were irregular and friable, with haemorrhagic areas. Microscopically, the tumor was composed of monotonous sheets of smalltomediumsized neoplastic cells with clear cytoplasm. The nuclei were uniform roundtooval with a speckled chromatin and inconspicuous nucleoli. The capillary network was arborescent and well developed. Extensive hemorrhagic areas were present (Figure 2).

The immunohistochemical analysis showed a diffuse strong synaptophysin positivity, focal immunopositivity for GFAP limited to entrapped or reactive astrocytes. The Ki67 proliferation index was 2% - histological and immunohistochemical profile compatible with central neurocytoma. The tumor was inoperable due to its location, deep in the third ventricle, and the high risk of bleeding during the intervention.

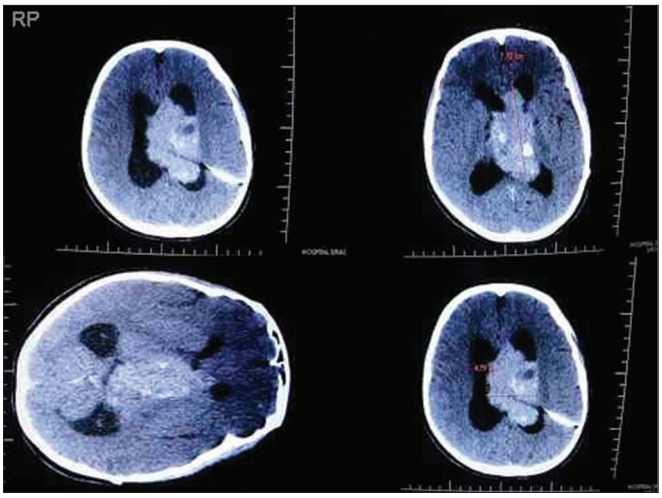

Figure 1. Central Neurocytoma: CT shows a large mass, with moderate contrast enhance, in the third ventricle and lateral ventricles, measuring about 78 x 48 mm. There is a hipodense area in between. Hydrocephalus is attenuated by a ventricular derivation.

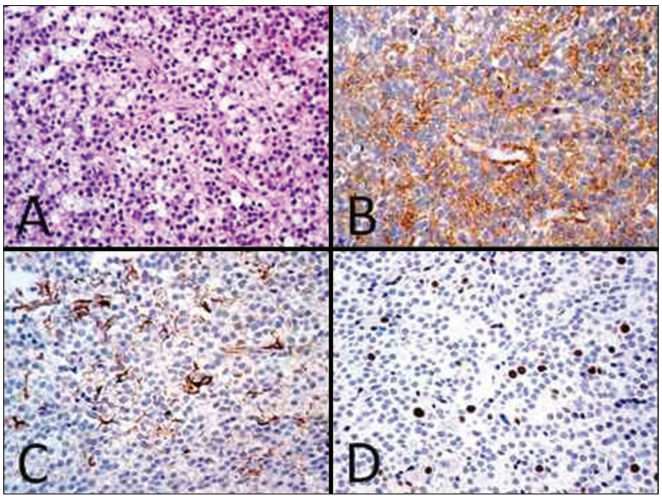

Figure 2. Central neurocytoma. A: Typical histological appearance of monotonous sheets of round cells with clear cytoplasm (HE, 40x); B: Strong and diffuse synaptophysin immunopositivity (40x); C: Immunopositivity for GFAP highlighted the entrapped or reactive astrocytes (40x); D: Ki-67 immunopositivity (40x).

She was submitted to RT, using a single phase localized 3D irradiation in the tumor area (Clinac 2100 c), in a dose of 54 Gy, divided in 30 fractions of 180 cGy. After the RT had begun, chemotherapy with (ifosfamide plus etoposide and vincristine plus carboplatin was added. The granulocyte colons stimulating factor was used for 7 days after cycles of chemotherapy, in order to reduce

hematological toxicities related to the treatment, such as febrile neutropenia.

After the treatment, an adequate response was observed, with a reduction in the tumor's volume (49 x 26 mm). Furthermore the patient presented with no neurological symptoms. Occasionally she complained of headaches which could be solved with common analgesics. At the moment, she has ended the treatment, and as the tumor is unresectable, there is no indication of further surgical intervention. She will be maintained in clinical evaluation, with imaging exams to measure tumor size.

DISCUSSION

Central neurocytoma is a benign tumor, accounting for 0.25% to 0.5% of CNS tumors[4]. It usually affects young adults and is located in the lateral and third ventricles. Headaches and other symptoms of raised intracranial pressure may occur due to the obstruction to the liquor drainage[2] (Table 1).

When evaluated by light microscopy, the tumor was first described as composed by small regular clear cells with numerous calcifications[1]. Synapses could also be seen - tumor with neuronal differentiation.

At electron microscopy tumor cells with synapse formation are seen, and immunohistochemical studies shows positivity for neuronspecificenolase (NSE) and synaptophysin (SYN), an evidence of neuronal differentiation[5]. These immunocytochemical markers - NSE can be found in early stages of neurogenesis. SYN is present only in mature neoplastic ganglion cells[5], demonstrating neuronal origin of the tumor.

The imaging methods such as CT scan and MRI are used to evaluate the location and to assist in the diagnosis of the tumor. Nevertheless, the final diagnosis is established by pathological analysis (electron microscopy and immunohistochemical studies)[3]. The CT scans show tumors located inside the ventricles, with scattered calcifications, small cysts and moderate enhancement to contrast[3]. On the MRI the tumor is isodense to cortical gray matter[2], with heterogeneous areas corresponding to the cysts and calcifications seen on CT scans[2].The attachment of the tumor to surrounding structures, the mass restriction to the ventricle area, and the large amount of blood vessels makes the tumor better seen on MRI2. However, the tumor is better observed on the CT scan. It is a better method to characterize an intraventricular well circumscribed mass, with calcifications, located inside the lateral ventricles, which may present moderate contrast enhancement[2].

A differential diagnosis must be established among other CNS tumors such as intraventricular oligodendroma (it usually occurs in the lateral ventricle, and has large and irregular calcifications), astrocytoma and ependymoma (absence of cysts and calcifications)[3].

The World Health Organization's (WHO) classification of tumors of the CNS, published in 2007, classifies central neurocytoma as a grade II neuroepithelial tissue tumor (neuronal and mixed neuronalglial tumors)[6].

Surgery, with total tumor resection is considered as the only treatment - benign tumor of slow growth - with cure or long term follow up[7-9].

Radiotherapy is used as adjuvant treatment when resection is subtotal[7-9], as central neurocytoma is a hipervascular tumor (contrast enhanced), with good local control rates[4]. Another option is chemotherapy. Although the role of this treatment is not well established for patients with central neurocytoma. It has been used as an adjuvant treatment when the tumor resection is incomplete and RT has failed or given after RT in patients with recurrent or progressive disease[4].

In this case report, the patient was first submitted to surgery, with a biopsy. Then, she received was conducted to RT, and when after this treatment had already started, chemotherapy was initiated. Radiation therapy is associated to good local control rates in patients with incomplete tumor ressection[7]. Chemotherapy has shown response in recent studies[7] (Table 2), notably in patients with recurrent or progressive central neurocytoma[9], but there are few

Table 1. Retrospective analysis of clinical features and treatment options on central neurocytoma.

n. of patients with EPILEPSY	n. of patients reated with SURGERY	n. of patients treated with RT	n. of patients treated with Chemo therapy	Outcome
NO	2 (Both CTR)	1	NO	1 (Died) 1 (survived with sequels)
NO	3 (2CTR; 1ITR)	NO	NO	3 (survived: no sequels)
NO	3 (1CTR; 2ITR)	2 (all after surgery)	3 (all months after tumor recurrence)	3 (survived; 1 with complete remission after CTR + RT + Chemotherapy
NO	1 (CTR)	NO	NO	1 (survived: mild mental confusion)
NO	1 (ITR)	NO	Patient election 6 cicles procarbazine, CCNU, VCR	1 (survived: stable lesion - 16 months follow up)
9	9 (7-CTR 2 ITR)	3 (postoperative)	NO	5 survived (1 with sequels) 2 died (1 sepsis; 1 tumor progression)

CTR: Complete tumor resection; ITR: Incomplete tumor resection; ICH: Intracranial hypertension.

reports on this subject. As a benign tumor of slow growth, central neurocytoma, surgery with complete resection is its gold standard treatment, with radiation and chemotherapy playing a secondary role[7-9].

Table 2. Retrospective analysis of clinical features and treatment options on central neurocytoma.

Author	n. of cases	Sex	Age (years)	Duration of symptoms	n. of patients with ICH
Hassoun J et al. (1982)[1]	2	M	32-39	1 to 3 years	2
Conrad M et al. (2000)[10]	3	1M:2F	17-35	6 months	3
Brandes AA et al. (2000)[9]	3	1M:2F	22-61	2 months	3
Hanel RA et al. (2001)[11]	1	F	35	Sudden intense headache	1
Von Koch C S et al. (2003)[4]	1	F	15	2 years	1
Chen CL et al. (2008)[12]	9	2M:7F	17-45 (28.2)	1 month to 1 year (4.7 months)	9

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