

Central neurocytoma – case report

Neurocitoma central – relato de caso

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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.

Keywords: Central neurocytoma; CNS tumors; pediatrics

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

Palavras chave: Neurocitoma central; Tumores do SNC; Pediatria

1. INTRODUCTION

Central neurocytoma was first described in 1982 by Hassoum et al. that reported a rare tumor composed by mature neuronal cells¹. The clinical features of these tumors are headache, seizures and symptoms of raised cranial pressure², due to its usual location in the third and fourth ventricle³ causing liquor obstruction. The diagnosis may be established with CT and MRI, electron microscopy and immunohistochemical methods³, to differentiate central neurocytoma from other CNS tumors, such as ependimomas, astrocytomas or oligodendromas (once their clinical and radiological aspects are nonspecific⁴, the differential diagnosis with other intraventricular tumors is difficult to establish⁵, and the histopathology appearance of the central neurocytoma and the oligodendroglioma can be similar⁶, distinguished by immunoreactivity⁶).

The first line of treatment is total surgical resection⁷. Radiation therapy is indicated when complete resection is not obtained or in cases of disease recurrence or progression. The use of chemotherapy isn't well established, indicated after a failure of surgical or radiation treatment⁷.

2. CASE REPORT

Patient of 16 years old, female, admitted at the Hospital Erasto Gaertner, with chronic headache since one year ago, worsening within the last 6 months. The patient also presented with paresthesia in right arm and neck pain, which one month earlier presented with reduced strength in right arm and difficult on speaking. Physical examination did not evidence any abnormalities. Neurological examination showed no deficits of sensibility or strength, neither cranial nerves disturbance. The laboratorial exams were normal.

The patient was submitted to CT scan (Fig. 1) that showed an expansive solid lesion, contrast enhanced, localized inside the third ventricle and lateral ventricles, around Monro foramen, measuring 78x48 mm in the diameters AP and transverse, showing a hipodense area in between, compatible with central neurocytoma. Lateral ventricles were enlarged. The patient was evaluated by a neurosurgeon and a biopsy of the lesion was indicated. The first attempt to remove a fragment for pathological study failed due intense bleeding during surgery – the bleeding obstructed the peritoneal shunt. One month later, a new procedure was performed and the stereotactic biopsy was obtained. The patient has evolved with no neurological disturbances, neither strength or sensibility disorders, referring complete regression of headaches.

Macroscopically, the tumor masses were irregular and friable, with haemorrhagic areas. Microscopically, the tumor was composed of monotonous sheets of small-to-medium-sized neoplastic cells with clear cytoplasm. The nuclei are uniform round-to-oval with a speckled chromatin and inconspicuous nucleoli. The capillary network was arborescent and well developed. Extensive hemorrhagic areas were present (Fig. 2).

The results of immunohistochemistry shows diffuse strong synaptophysin positivity, focal immunopositivity for GFAP limited to entrapped or reactive astrocytes. The Ki-67 proliferation index was 2% – histological and immunohistochemical profile compatible with central neurocytoma.

Due to its location deep into the third ventricle, and the great risk of bleeding during the procedure, the tumor was inoperable.

She was submitted to radiation therapy, 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 was begun, chemotherapy was associated to the treatment (ifosfamide plus etoposide and vincristine plus carboplatine). The granulocyte colons stimulating factor was used for 7 days after cycles of chemotherapy, in order to reduce hematological toxicities treatment related – such as febrile neutropenia.

The patient had a good evolution, with reduction of the tumor volume in control CT scans (49 x 26 mm), showed no neurological deficits, but presented with occasional headache – solved with common analgesics. At the moment, the patient has ended the treatment, and once the tumor is unresectable, there is no indication of a new surgical intervention. The patient will be maintained in clinical evaluation, with imaging exams to measure tumor size.

3. DISCUSSION

Central neurocytoma is a benign tumor, which corresponds to 0.25 to 0.5% of brain tumors⁷. It usually affects young adults and is located in the lateral and third ventricles, causing obstruction to the liquor drainage – headaches and other symptoms of raised intracranial pressure².

When evaluated by light microscopy, the tumor was first described as composed by small regular clear cells with numerous calcifications¹, also found synapses – tumor with neuronal differentiation¹. At electron microscopy tumor cells with synapse formation were seen², and immunohistochemical studies showed positivity for neuron-specific-enolase (NSE) and synaptophysin (SYN), an evidence of neuronal differentiation⁸. This immunocytochemical markers – NSE is found in early stages of neurogenesis and SYN is present only in mature neoplastic ganglion cells⁵, demonstrating neuronal origin of the tumor.

The imaging methods such as CT and MRI are used to evaluate location and assist on the diagnosis of the tumor, but the definite diagnosis is established by pathology analysis (electron microscopy and immunohistochemical studies)³. CT shows tumors located inside the ventricles, with punctuate and scattered pattern calcifications, small cysts and moderate enhancement to contrast³, and on MRI the tumor was isodense to cortical gray matter², with heterogeneous areas corresponding to the cysts and calcifications seen on CT². The attachment of the tumor to surrounding structures, the mass restriction to the ventricle area, and its great amount of blood vessels makes the tumor better seen on MRI². Although CT is superior on showing calcifications and to characterize the lesion: an intraventricular well circumscribed mass, with calcifications, located inside the lateral ventricles, which may present moderate contrast enhancement².

Differential diagnosis must be established with other CNS tumors such as intraventricular oligodendroma (it usually occurs inside the body of the lateral ventricle, and has large and irregular calcifications), astrocytoma and ependymoma (absence of cysts and calcifications)³. The WHO classification of tumors of the central nervous system, published in 2007, classifies central neurocytoma as tumor of neuroepithelial tissue (neuronal and mixed neuronal-glioma tumors), grade II⁹.

The treatment of choice for central neurocytoma is mainly surgery, with tumor total resection as the only treatment – benign tumor of slow growth – with cure or long term control¹⁰⁻¹¹⁻¹². Radiotherapy is used as adjuvant treatment when resection is subtotal¹⁰⁻¹¹⁻¹², once central neurocytoma is a hypervascular tumor (contrast enhanced), with good local control rates⁷. 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 disease⁷. In most studies is unclear if the treatment response was due to RT or chemotherapy, once they were administrated in close periods of time⁷.

In this case report, the patient was first submitted to surgery, with a biopsy. Then she was conducted to RT, and when this treatment had already started, chemotherapy was initiated. Radiation therapy is associated to good local control rates in patients with incomplete tumor resection¹⁰. Chemotherapy has shown response in recent studies¹⁰(see table 1), notably in patients with recurrent or progressive central neurocytoma¹², but there are few reports on this subject. As a benign tumor of slow growth, central neurocytoma still has surgery with complete resection as it's gold standard treatment, with radiation and chemotherapy playing a secondary role¹⁰⁻¹¹⁻¹².

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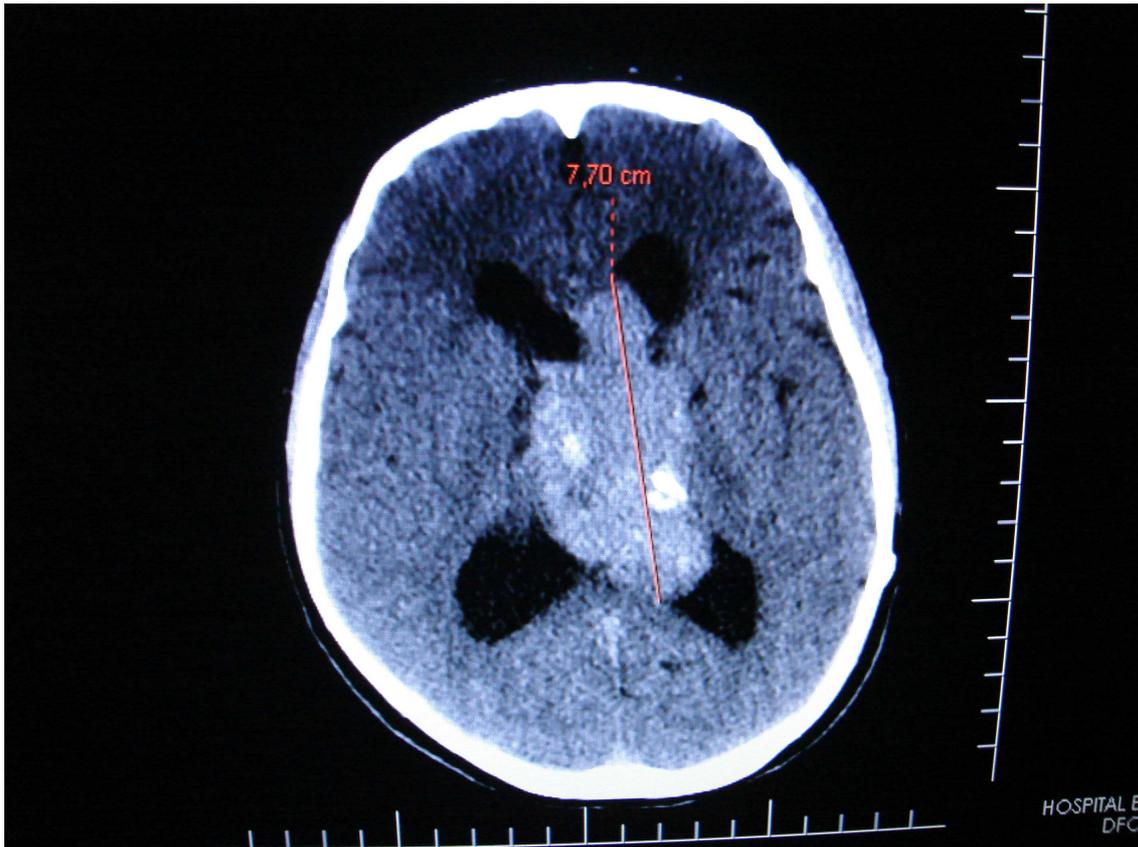


FIGURE 1: Central Neurocytoma - CT shows a large mass, with moderate contrast enhance, in the third ventricle and lateral ventricles, measuring about 78x48 mm. There is a hipodense area in between. Hydrocephalus is attenuated by a ventricular derivation.

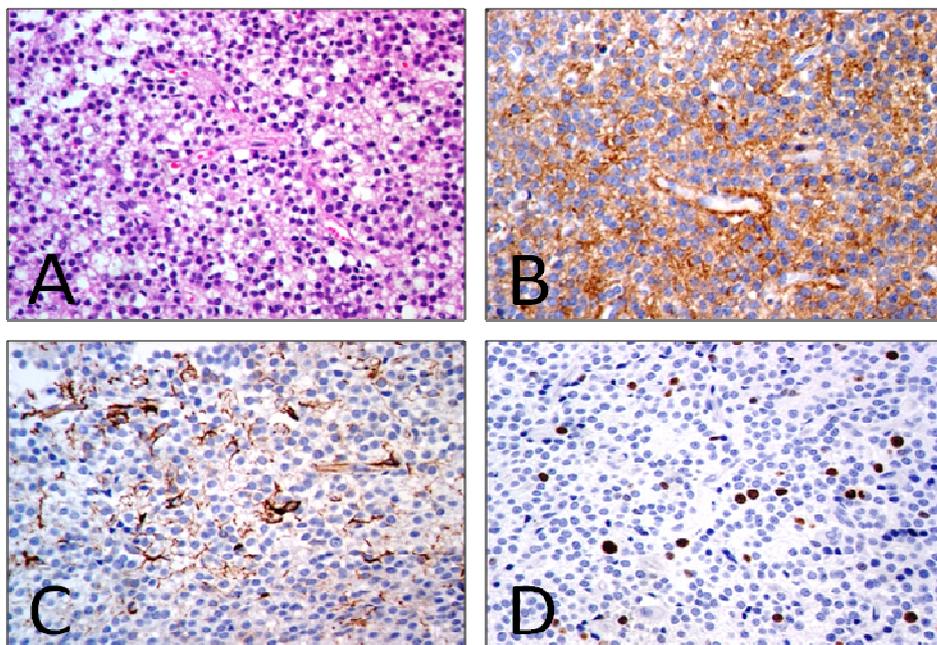


Figure 2: Central neurocytoma: A. Typical histological appearance of monotonous sheets of round cells with clear cytoplasm (HE, 40x); B. Strong and diffuse synaptophysin immunopositivity (40x); C. Immunopositivity for GFAP highlighted the entrapped or reactive astrocytes (40x); D. Ki-67 immunopositivity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

Table 1: retrospective analysis of clinical features and treatment options on central neurocytoma. (CTR: complete tumor resection; ITR: incomplete tumor resection, ICH: intracranial hypertension).

Author	n.of cases	Sex	Age (years)	Duration of symptoms	n. of patients with ICH
Hassoun J, Gambarelli D, Grisoli F (1982) ¹	2	M	32 – 39	1 to 3 years	2
Conrad, Marcelo, et al (2000) ¹⁰	3	1M:2F	17 - 35	6 months	3
Brandes Alba A. et al (2000) ⁹	3	1M:2F	22 - 61	2 months	3
Hanel, Ricardo A. et al (2001) ¹¹	1	F	35	Sudden intense headache	1
Von Koch, Cornelia S. et al (2003) ⁴	1	F	15	2 years	1
Chun-Lin-Chen,MD et al (2008) ¹²	9	2M:7F	17 – 45 (28,2)	1 month to 1 year (4.7 months)	9

n. of patients with EPILEPSY	n. of patients treated 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)