Intracranial Germinoma: Atypical Presentation

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Abstract

Fourteen year old female patient referred in June 2013 to the Emergency Department due to seizures of recent onset. The patient had a six-month history of behavioral changes and impaired academic performance; also, days before the seizure episodes she developed vomiting. The physical examination documented bradypsychia and papilledema. The results of hormone testing showed panhypopituitarism, a condition of the hypothalamic-hypophysis axis. An MRI was performed and it showed a heterogeneous tumor that compromises the frontal periventricular white matter extending through the rostrum of the corpus callosum, infiltrates the ependyma, it is heterogeneous with cystic areas; after contrast, it presents heterogeneous enhancement. In univoxel MR spectroscopy, it was observed an increase of choline, lipid and lactate, and a decrease in N-acetyl aspartate. It associates with the existence of edema in the bifrontal white matter, there is mass effect given by the compression of the frontal recesses of the lateral ventricles and effacement of the frontal anterior sulci. There is a second lesion that compromises the tuber cinereum, pituitary stalk and optic chiasm, it enhances after contrast administration and presents cystic areas. For the morphological characteristics and changes in spectroscopy, differential diagnosis as primitive neuroectodermal tumor (PNET) and glioblastoma were planted. The frozen biopsy reports a small cell tumor: PNET vs. Lymphoma. Due to the latter, a complete macroscopic resection is performed via a bifrontal craniotomy with an interhemispheric approach. Diabetes insipidus is developed immediately during the postoperative period. The full section biopsy reported a germinoma. Managed through sequential chemotherapy and radiation therapy.

Keywords: Germinoma; Neurosurgery; Neuropathology; Neuroradiology

Introduction

In germ cell tumors, germinomas account for approximately a 65%, classified as class III of the WHO [1-3]. Furthermore, they represent a 0.4-3.4% of brain tumors and an 8-15% of the pediatric instances. Between 80-90% of the cases occur in people under 25 years of age, with a peak incidence rate between 10-14 year olds. They are not commonly diagnosed past the patient's third decade [3,4] and it is most common in male patients. In terms of location, suprasellar is most common in women and in the pineal region for men [2,3,5,6]. Most are located towards the midline and more than the 80% appear in structures above the third ventricle, the pineal gland is being the most common place of origin followed by the suprasellar compartment, for instance, the neurohypophyseal axis, periventricular, intraventricular, lymph nodes, basal ganglia, brain hemispheres, intramedullary, among others. They are most common in the suprasellar and thalamic regions as well as the basal ganglia [3,5,7].

Its etiology is unknown [3].

Pure germ cell tumors, as the one at hand, when related to the Central Nervous System, are called germinomas, seminomas when they originate in the testicles and dysgerminoma when related to the ovaries. All these share the same histopathological pattern, immunohistochemistry profile and serum markers [1].

Case Report

Fourteen year old female patient referred in June 2013 to the Emergency Department due to seizures of recent onset. The patient had a six-month history of behavioral changes and impaired academic performance; also, days before the seizure episodes she developed vomiting. The patient denies suffering from any chronic pathology. The physical examination documented bradypsychia and papilledema. The results of hormone testing showed panhypopituitarism, a condition of the hypothalamic-hypophysis axis. An MRI was performed and it showed a heterogeneous tumor that compromises the frontal periventricular white matter extending through the rostrum of the corpus callosum, infiltrates the ependyma, it is heterogeneous with cystic areas; after contrast, it presents heterogeneous enhancement. In univoxel MR spectroscopy, it was observed an increase of choline, lipid and lactate, and a decrease in N-acetyl aspartate. It associates with the existence of edema in the bifrontal white matter, there is mass effect given by the compression of the frontal recesses of the lateral ventricles and effacement of the frontal anterior sulci. There is a second lesion that compromises the tuber cinereum, pituitary stalk and optic chiasm, it enhances after contrast administration and presents cystic areas. For the morphological characteristics and changes in spectroscopy, differential diagnosis as primitive neuroectodermal tumor (PNET) and glioblastoma were planted. Anticonvulsant and steroid therapy was initiated. The results of hormone testing show a decrease in T4, T3, TSH, LH, FSH, GRH and cortisol, panhypopituitarism, the hypothalamic-hypophysis axis is compromised. During surgery, a frozen biopsy is performed, which indicates a small-cell tumor: PNET vs. lymphoma. Due to the latter, a complete macroscopic resection is performed via a bifrontal craniotomy with an interhemispheric approach. Diabetes insipidus is developed immediately during the postoperative period and treated with DDAVP. An iliac crest biopsy is performed as well as a bone marrow aspiration,
both reporting no neoplastic infiltration. Studies of the Cerebrospinal fluid (CSF) result negative for tumor markers, but positive for the presence of neoplastic cells (Figures 1-6).

A Suprasellar Germinoma is therefore diagnosed.

A postoperative CT scan showed no residual lesion, hence metastatic disease was ruled out in thorax and abdomen.

Based on these findings, the decision is to proceed with sequential chemotherapy in a four-cycle schedule of BEP (Bleomycin, Etoposide and Cisplatin) and radiation of the neural axis in a dose of 45 Gy in cranial and 30.6 Gy in the spinal fields.

As of January 2015, the patient is in excellent clinical condition with pharmacological treatment with Levothyroxine, DDAVP and hydrocortisone. The LCR cytology continues to result negative for malignancy and with no evidence or relapse upon imaging.

Discussion

Clinical discussion

By affecting the pineal region, a compression and obstruction of the cerebral aqueduct is produced, causing hydrocephalus as well as intracranial hypertension, Parnaud syndrome when the rostral pretectal area and the superior colliculus are compressed; also, deafness when compressing the inferior colliculus, delayed growth, sexual maturation, early puberty, behavioral changes, and impaired academic performance.
A classic triad is determined when the suprasellar region is affected, when there are visual field defects, diabetes insipidus and panhypopituitarism. Further metastases seedings through the CSF can result in radiculopathy and myelopathy [2,3,5-8]. Reports show that many patients state to suffer from memory loss; a retrospective study shows that a 42% incidence rate of significant amnesia was observed in older patients within the typical age group. No relation was found between hydrocephalus at the time of diagnosis, radiation exposure or involvement of the classic memory structures; which suggests that there is a significant risk of amnesia between these patients [9-11].

**Histogenesis**

They are accepted to represent the progeny of primordial germ cells that migrated aberrantly or with purpose to the embryonic CNS instead of developing in the genital ridges. They have been specifically defined as an enigmatic population of skeletal muscle cells native to the development of the pineal gland, proposed as possible descendants of primitive germ elements attracted to this organ during neuroembriogenesis [3].

Alternative to this hypothesis is the proposition of its origin in a variety of displaced embryonic tissue and incorporated into the developing neural tube, in which case, only the germinoma would derive from the lost primordial germ cells, hence qualifying as a true germ cell neoplasm [3].

Another theory involves toti- or pluri-potent stem cells [3].

The differences between these types of tumors may reflect different creation mechanisms instead of divergent cellular origins [3].

Investigations with regards to the molecular biology involved in the pathosis have been initiated. Mutations in KIT, KRAS/ NRAS as well as caspase B-lineage lymphoma (CBL) have been described [8].

**Prognosis**

The predictive factor of most value is the histological subtype. Pure germinomas are extremely radiosensitive [1,3,6,9,11,14]. The five-year survival rate is estimated to over 75% and the ten-year rate to 69% with radiation alone, adding chemotherapy can improve disease control by reducing the radiation dose. Germinomas with syncytiotrophoblast cells or that are associated with elevated B-hCG levels have reported a higher risk of local failure, and a modest decrease in survival [3,9,15].

The typical patterns of progression for this disease are local recurrence and dissemination through the CSF, abdominal contamination via ventriculoperitoneal shunts and hematogenous spread, mainly to lungs and bones [1-3].

**Management**

Performance of serum and CSF (B-hCG, AFP, PLAP) [2,8,16]. Tumor markers as well as CSF cytology [5,15] is recommended.

MRI of the neuraxis (cervical, thoracic, lumbar) for metastatic seeding [2,5,8,16].

Lesion biopsy [2,8,16].

Chemotherapy and radiation therapy [2,8]. In the final report of the SIOP CNS GCT 96 study, multinational, prospective, non-randomized, in which single craniospinal irradiation was compared with chemotherapy followed by focal irradiation to the primary site, it was concluded that localized germinomas can be treated with reduced craniospinal radiation alone or with chemotherapy and radiation in a reduced field. There was no difference in the overall five-year survival rate, but a difference was noted in terms of progression-free survival; also, the relapse pattern suggests that the ventricles must be included in the radiation field, and that a low site, it was concluded that localized germinomas can be treated with reduced craniospinal radiation alone or with chemotherapy and/or radiation [19].
Total resection of the lesion is usually not recommended because of the risk of surgical complications and the fact that germinomas are affectedly sensitive to radiation; the latter unless the patient’s clinical stability is compromised [5].

If there is a case of hydrocephalus, external ventricular drainage is recommended in order to prevent peritoneal seeding, this, despite the uncommonness of its presentation, and that after the treatment of their tumor, the patient will probably not need a permanent device [2,5,8].

Clinical monitoring is recommended for 10 years and imaging for at least 5 years. If there were positive tumor markers, the recommendation is to follow up with markers as well [8].

Conclusion
As with all patients, it is important to make use of all the resources available in order to make an accurate diagnosis considering that the prognosis and quality of life of the patients depend on it. This case was challenging in terms of diagnosis since it was atypical both clinically and radiologically.

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