Supratentorial neuroectodermal tumor in a 4 years old child presented with intratumoral hemorrhage – Case presentation and review of the literature

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Abstract

Brain tumors represent the most frequent solid malignancy in children and the first cause of cancer-related deaths in pediatric population. Supratentorial neuroectodermal tumor (PNET) represents one of the most aggressive brain tumors at this age. Incidence of S-PNET is 2-3% of all brain tumors in children, but reaches up to 20% of brain tumors in 0 - 3 years old children. Although in the last years the outcome has improved, the prognosis remains dismal. We choose to present the case of a 4 years old child who was at presentation in a comatose state (GCS 4 points) with anisocoria (right pupil was mydriatic). The performed head CT-scan showed a right fronto-parietal tumor with intratumoral hemorrhage, maximal dimensions of 52/75/70 mm and a midline shift of 15 mm. The surgery was performed in emergency and we made a gross total resection. Immediate postoperative CT-scan confirmed the total resection. The histopathological diagnosis was S-PNET, this result being confirmed by immunochemistry. After neuromotor rehabilitation, at the 4 month follow-up visit the GOS was MD. The patient was also referred to the oncologist and was made chemotherapy and radiotherapy of the entire craniospinal axis. The tumor showed no signs of recurrence during 12 months of follow-up.

Keywords: S-PNET, Child, Prognostic

Introduction

Supratentorial PNET is one of the most aggressive brain tumors in the pediatric population. It represents 2-3% of all brain tumors in children, this percent rising up to 20% in the 0 - 3 years old population. Due to the small incidence, the relative recent description of this entity (S-PNET was firstly described in 1973, while the first description of medulloblastomas dates from 1925) and the fact that in the WHO classification those tumors were discordant, there are few data in the literature concerning this subject when comparing with medulloblastomas. The highest incidence of S-PNET is at young age. Signs and symptoms at presentation are seizures, signs of intracranial hypertension, focal neurologic deficits. Although in the last years the management of these cases has improved, the outcome is very poor.

Case presentation

History and presentation: A four years child was admitted in the clinic in coma, GCS 4 points, with anisocoria (right pupil was mydriatic). The patient had headaches, debuted 5 months before, and nausea vomiting for 3 days before admission in the hospital, those being diagnosed as gastrointestinal disorders. In the day of admission the child went to bed and did not wake up. Before these 5 months, she had no history of medical problems.

Clinical and neurological examination: The patient was in coma, GCS 4 points, with anisocoria (right pupil was mydriatic), Babinsky positive on the right side, hemodynamically stable, intubated oro-tracheal and mechanically ventilated (CPAP).

Neuroimaging investigations: A brain CT-scan was performed, which revealed a fronto-parietal mass, heterogeneous, with areas of hemorrhage, without contrast enhancement and minimal surrounding edema, maximal dimensions of 52/75/70 mm and a midline shift of 15 mm (Figure 1, 2). Due to the neurological and clinical state we did not performed a preoperative brain MRI.

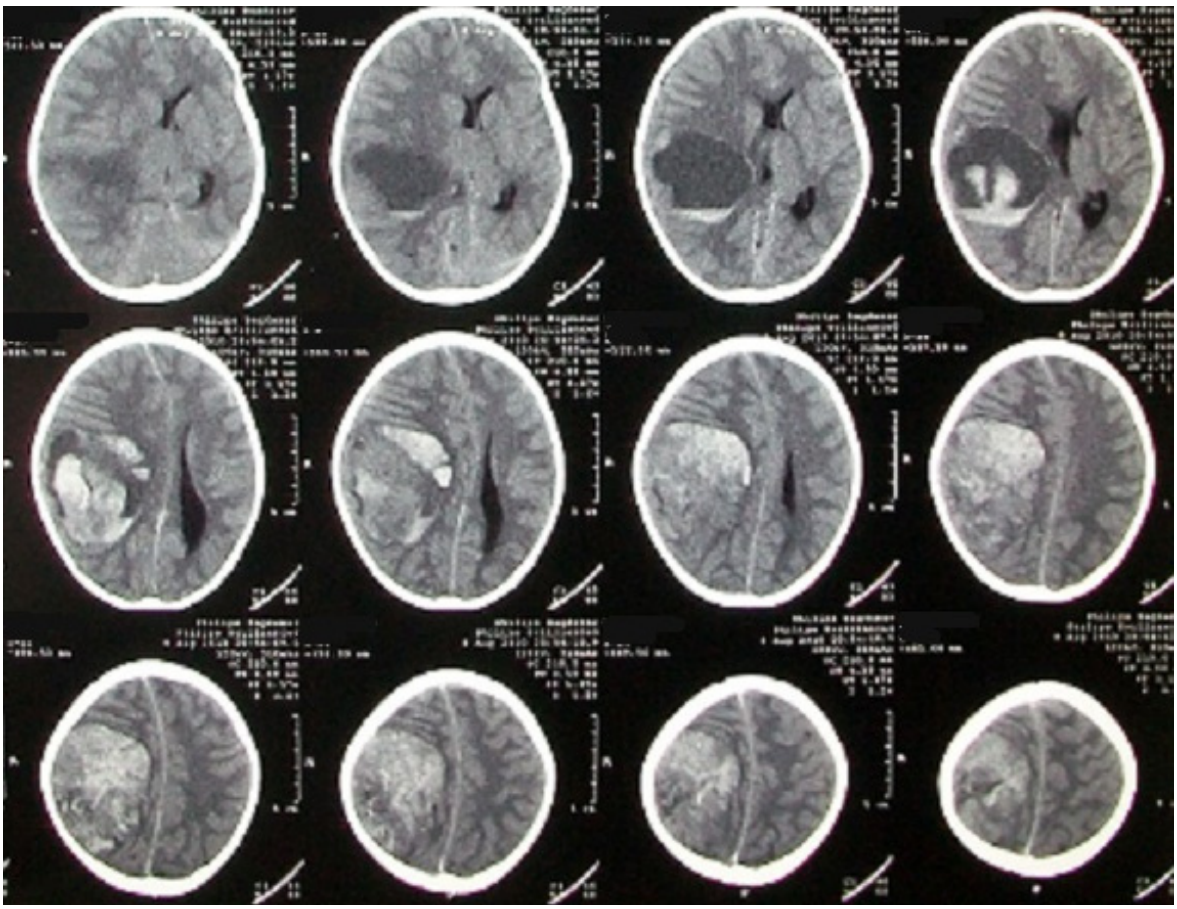

Figure 1 Preoperative native CT-scan

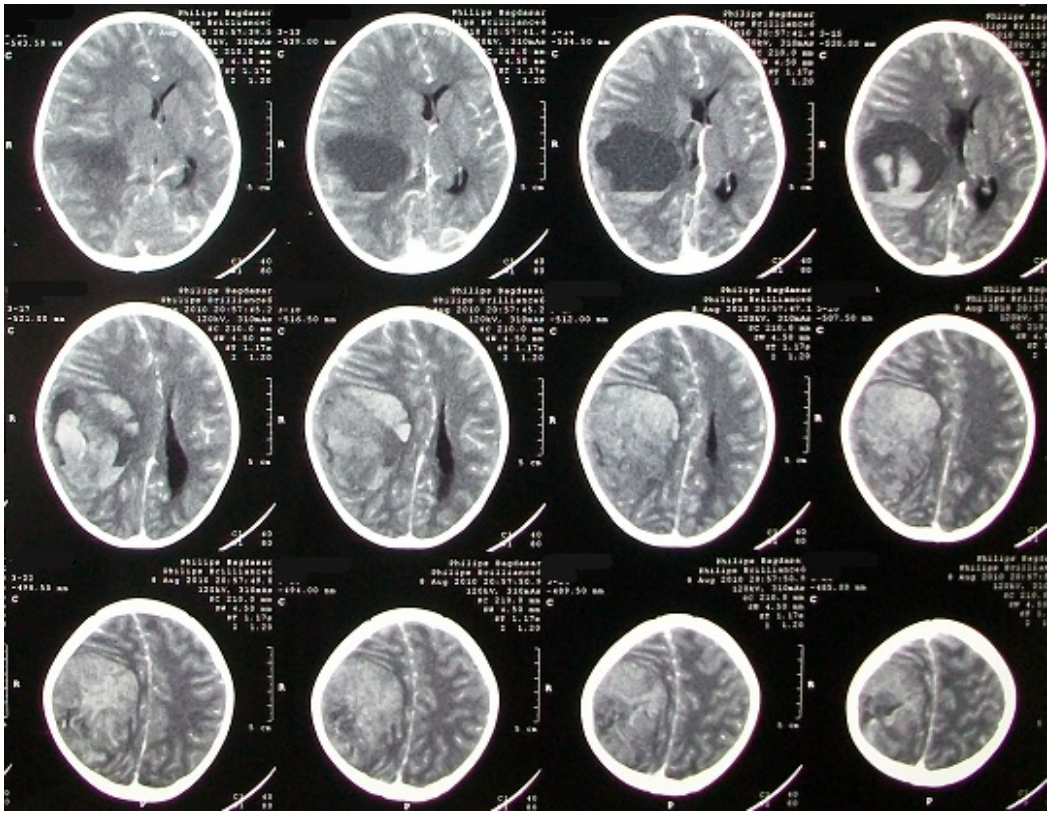

Figure 2 Preoperative CT-scan with contrast enhancement

Operation: We operated the child in emergency. A fronto-parietal bone flap was made, dura mater, in tension, was incised semicircular with medial pedicle. We found a fronto-parietal tumor heterogenous, friable, with intratumoral hemorrhage, with a diameter of approximately 7 cm. We made gross total excision. At the end of the operation the brain was collapsed, pulsatile. Dura mater was sutured in "water-tight" fashion, and the bone flap was fixated. The surgical intervention lasts 3 hours and 45 minutes and the blood loss was 300 ml.

Postoperative course: Postoperative the child was transferred in the ICU, intubated oro-tracheal and mechanically ventilated. Postoperative brain CT-scan confirmed the gross-total resection, and showed no signs of postoperative hemorrhage (Figure 3). The spinal MRI showed no signs of dissemination. After 3 weeks she was transferred in a neuromotor rehabilitation centre (GOS= SD).

The histopatological diagnosis was PNET, which was confirmed by the immunohistochemical tests. The patient was referred to the oncologist. The oncologic treatment was chemotherapy and radiotherapy of the entire craniospinal axis.

Follow-up: At the one month follow-up visit the child's neurological state had improved and brain MRI showed no signs of tumor recurrence (Figure 4). At the 4 months postoperative visit,GOS was MD – the child was conscious, with left hemiparesis (ASIA 4), with partial right third nerve palsy. Brain MRI (Figure 5) showed no signs of tumor recurrence.

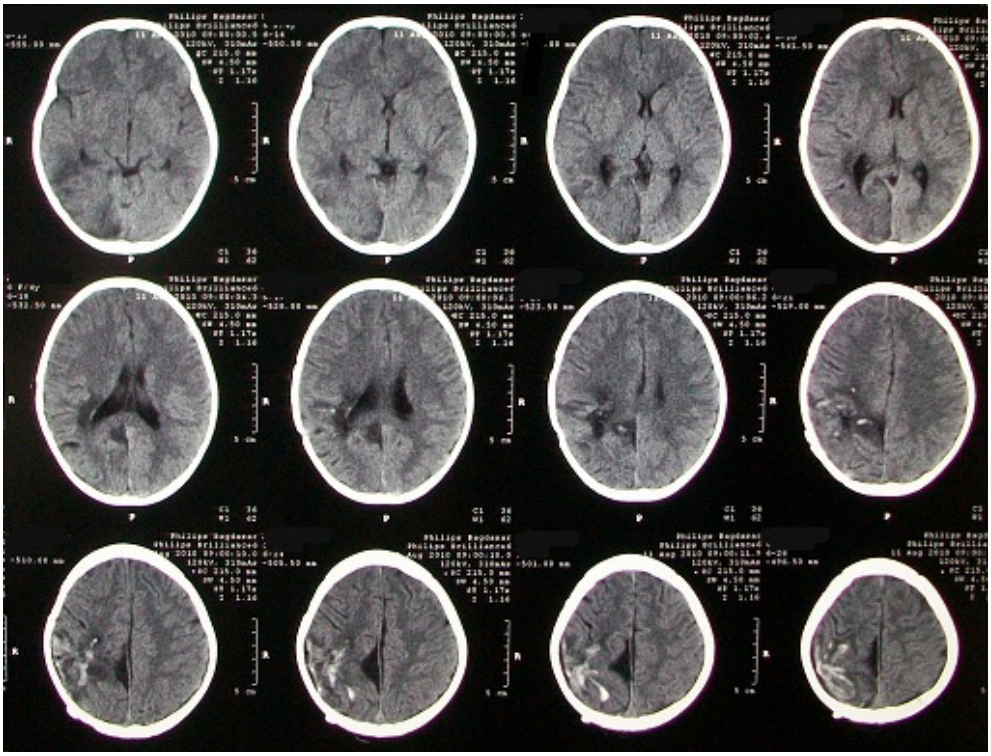

Figure 3 Postoperative CT-scan

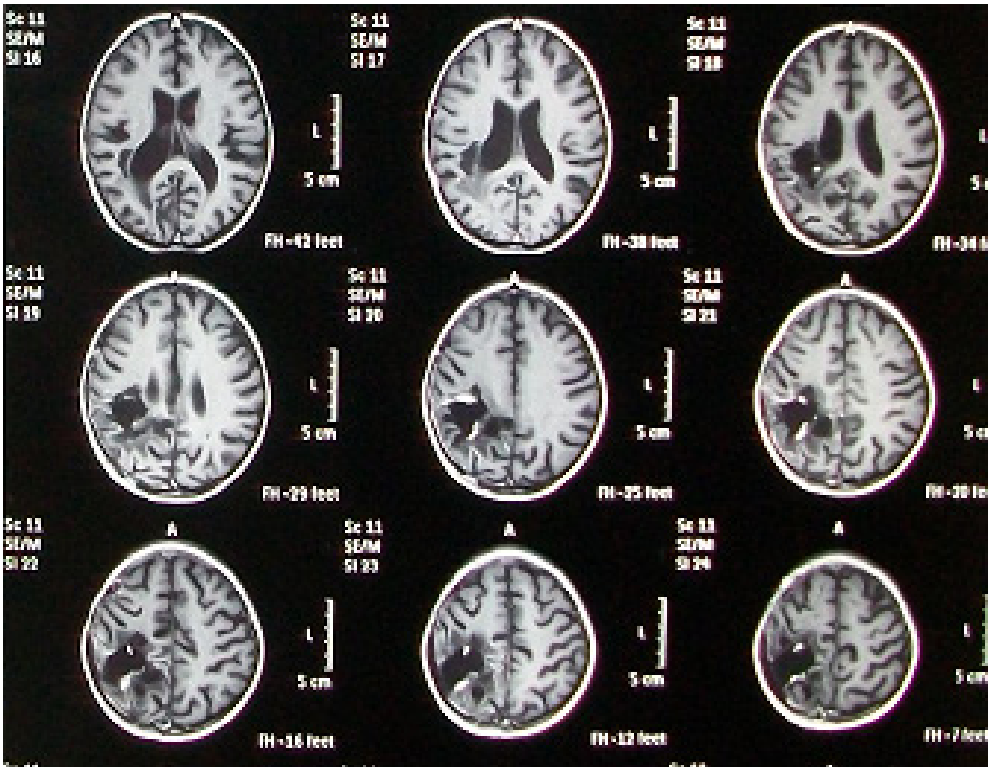

Figure 4 One month postoperative MRI

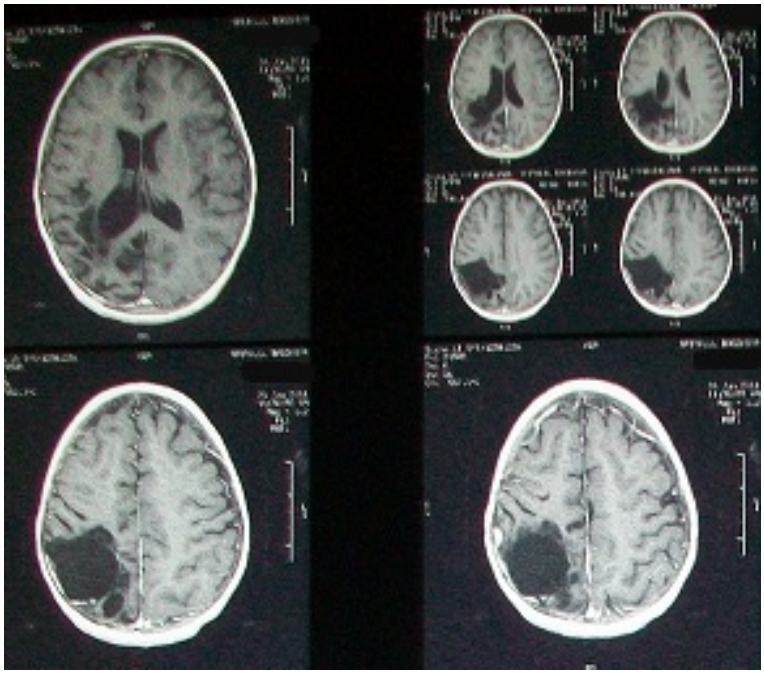

Figure 5 Four months postoperative MRI

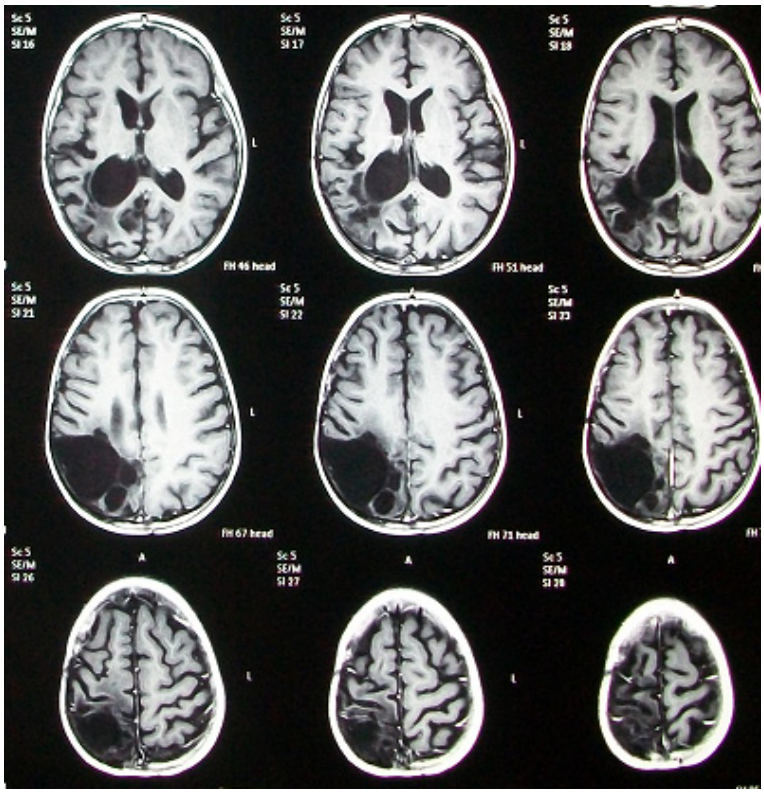

Figure 6 One year postoperative MRI

The next follow-up visits were made at one year postoperative and, also, the brain MRI (Figure 6) showed no signs of tumor recurrence and the neurologic status had improved. In the future for follow-up will be made a brain MRI every 6 months, or faster if the neurological status impose so.

Discussions

The entity of S-PNET was described for the first time in 1973 by Hart and Earl. Over the time there had been divergences in classifying those tumors. For example in the WHO classification published in 1993, S-PNET and medulloblastomas were classified as embryonal tumors with multipotent differentiation. Until the 2000 publication of the WHO classification, medulloblastomas were considered infratentorial PNET and until then, those two types of tumors were studied together. In the 2000 published WHO classification those entities were separated in two distinct subtypes of embryonal tumors. In the most recent WHO classification (2007) the tumors categorized as S-PNET were CNS neuroblastomas, CNS Ganglioneuroblastomas, Medulloblastomas and Ependymoblastomas. Due to those divergences there are relatively few studies focalized on S-PNET in the literature.

S-PNETs are malignant embryonal tumors which can be phenotypically poorly differentiated or can show different degrees of differentiation along neuronal, astrocytic and ependymal lines. Tumors with neuronal differentiation are termed CNS neuroblastomas, if also neuroplastic ganglion cells are present, the term is CNS ganglioneuroblastoma. Tumors presenting features of the embryonal neural tube formation are named medulloepitheliomas and those with ependymoblastic rosettes are termed ependymoblastomas. All those types of tumors (which in the previous classifications were different entities) are variants of CNS PNETs. In this classification is described an unusual PNET called “embryonal tumor with abundant neuropil and true rosettes” and can occur in the cerebrum, brain stem and cerebellum of young children.

Despite the progress made in the management of S-PNETs the prognostic remains poor. The majority of studies included patients with tumors categorized as PNET before the last WHO classification.Biswas and co. found a 5 years survival rate of 9% (study of 11 patients with S-PNET published in 2009).In the CCG 921 trial were included 44 patients with S-PNETs and the PFS at 3 years was 33%, the factors of negative prognosis being metastatic disease (all patients with metastatic disease died) and young age. In German HIT 88/89 and HIT 91 trials were enrolled 63 patients with S-PNET and the 3 years PFS was 39,1%.

S-PNETs can disseminate via CSF (Cerebrospinal fluid) or can generate extraneural metastases. Rubens and co. reported a case of a small child (23 months old) with lung metastases but with long survival. Extraneural metastases are very rare, more frequent in medulloblastomas than in S-PNETs. Craniospinal metastases occur in approximately 17-27% of S-PNETs and the presence of dissemination at the moment of diagnosis is a poor prognostic factor. This dissemination can be detected using CSF cytology (lumbar or intracranial) or by using neuroimaging techniques (MRI of full neuraxis). There is a percent of divergences between those methods of detecting craniospinal dissemination. However, most treatment

protocols recommend the use of CSF cytology obtained by lumbar tap.

The positive cytology without MRI findings of metastases can suggest an early stage of dissemination. Terterov and co. found that MRI findings are correlated with survival, whereas perioperative CSF cytology does not. Some studies try to evaluate with accuracy the best method for the diagnosis of craniospinal dissemination and the opportunity to avoid the irradiation of the entire neuraxis in cases of localized disease to avoid the post irradiation complications.

In the case we presented that the child had no craniospinal dissemination, but the oncologist decided, in accordance with current protocols, to do irradiation of the entire craniospinal axis after chemotherapy.

Another factor that has impact on the survival is the grade of resection. Usually those tumors are located in eloquent areas ant gross total resection cannot be accomplished. In the CCG 921 study authors found that the dimensions of the residual tumor is an important prognostic factor, but only in patients with localized disease. In the case which we presented the postoperative CT-scan confirmed the gross total resection and the 1, 4 and 12 months postoperative brain MRI showed no signs of tumor recurrence. The good postoperative course is in accordance with the current literature (GTR and no signs of disseminated disease), but there may be other factors that contribute to that evolution. There is necessarily to continue the study of this entity in order to identify other prognostic factors and new treatment strategies to improve the survival period and the quality of life of pediatric patients with S-PNET. In CCG 921 and in the German HIT trials GTR could be accomplished in just 40% of the cases of S-PNETs. In those two studies the amount of residual tumor was not a prognostic factor, probably due to the small number of cases, but there was a tendency for a better survival in children with less residual tumor.

Another prognostic factor is the age. Small children have a worse prognostic, although it is difficult to establish if age itself is a prognostic factor due to the fact that children younger than 3 years cannot undergo radiotherapy. In children younger than 3 years old, radiotherapy can cause significant late effects such as endocrine abnormalities, impaired axial growth, hearing impairment, neuropsychological dysfunction and secondary tumors. In the French Society of Pediatric Oncology infant study, the median survival period in patients with S-PNET was 12 months and the 2 years PFS was 4%.

The MRI appearance of S-PNETs is very heterogeneous. Usually there are big lesions, without or with minimal surrounding edema, and can show cystic degeneration, necrosis, and intratumoral hemorrhage.

In present the majority of studies referring to the S-PNETs focus on the different strategies of chemotherapy and the identification of target molecules for adjuvant therapies.

Also new methods of treatment are developed. Pinakin and co published a case of treatment of S-PNET located in right thalamus extended into the right midbrain, using magnetic-resonance-guided laser-induced thermal therapy, with good results at 6 months of follow-up. This method may be promising for tumors located in high-eloquent areas.

Conclusion

We presented a case of a small child with S-PNET admitted in the hospital with intratumoral hemorrhage and poor neurological status, without signs of disseminated disease, but with good postoperative evolution after gross total resection, chemotherapy and irradiation of the entire neuraxis. Although in the last years the survival period of those children has improved, is necessary to develop new strategies to improve the quality of life and survival in pediatric patients with S-PNETs.

Abbreviations

S-PNET = supratentorial neuroectodermal tumor; GCS = Glasgow Coma Scale; CT = computed tomography; WHO = World Health Organization; CNS = Central Nervous System; GOS = Glasgow Outcome Scale; MD = Moderate Disability; ICU = Intensive Care Unit; PFS = Progression Free Survival; CSF = Cerebrospinal Fluid; GTR = Gross Total Resection; MRI = Magnetic Resonance Imaging.

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