Cerebellopontine angle ependymoma

Cerebellopontine angle ependymoma are uncommon variants of infratentorial ependymomas originating from ependymal cell rests which are present in the foramen of Luschka and appear to arise from the lateral surface of brain stem. They have a propensity to encase the lower cranial nerves and adjacent blood vessels namely posterior Inferior cerebellar artery. They grow laterally, further into cerebellopontine angle (CPA) and medially into the fourth ventricle. As they grow they displace the surrounding tissues bringing about rotation of the brainstem and unlike relatively commoner fourth ventricle ependymomas, brain stem involvement does not occur at an early stage. This alters the anatomy and distorts the posterior fossa landmarks affecting the surgical approach and increases the operative difficulty.

Diagnosis

They assume a large size before becoming symptomatic. Initial presentation is with features of raised ICP because of hydrocephalous. Involvement of cranial nerves and brain stem occurs at a later stage.

CPA ependymomas on the plain CT scan appear as large extra axial masses in posterior fossa pushing the brain stem and fourth ventricle to the opposite side. Although no magnetic resonance imaging features are pathognomonic of ependymoma, these generally appear as lobulated tumors, which are hypointense on T1W images and hyperintense on T2W images, demonstrate irregular enhancement and are markedly heterogeneous due to calcification, hemorrhage, cystic components, or necrosis. T1 and T2 sequences are required to exactly delineate the encasement of vessels and to appreciate the rotation and positioning of brain stem for correct surgical planning.

Ependymomas in general have a propensity for neuraxis metastasis. However, no cases of neuraxis metastasis from CP angle ependymomas have been reported.

Differential diagnosis

Differential diagnosis include, meningioma, schwannoma of the vestibular nerve, or lower cranial nerves, and choroid plexus papilloma, vascular ectasia, and aneurysms. Less common lesions are epidermoid and other schwannomas as well as metastases, paragangliomas, and arachnoidal cysts.

Intra-axial tumors in the area of the cerebellopontine angle include the medulloblastoma, astrocytoma, and the ependymoma.

The occurrence of a primary myxopapillary ependymoma and subependymoma at CPA has also been reported.

Mridha et al. have reported the occurrence of a metastatic lesion at CPA from lumbo-sacral myxopapillary ependymoma.

Histologically, a variety of types, including cellular, clear cell, papillary, tanycytic, and myxopapillary have been described. Various forms of differentiation, including lipomatous, cartilaginous and osseous melanotic, neuronal and, most recently, sarcomatous have been described in ependymomas.

Treatment

Gross or near total excision (GTR) offers the patient maximal chances of prolonged overall survival (OS) as well as progression-free survival (PFS). Surgical resection in a young child remains a formidable task because of small size of posterior fossa, lower amount of blood, and significant difficulty in appreciating the local anatomy because of displacement of normal structures. Use of technological advances such as Cavitron Ultrasonic Aspirator (CUSA) and neurophysiologic monitoring would allow for total or near total resection of tumors. Post-operative MRI must be performed within 48 h of surgery to evaluate the extent of surgery. Second look surgery has been recommended to maximize the extent in the case of unexpected residual tumor or when the decision for a staged operation is made.

Adjuvant therapy of CPA ependymomas in age <3 years in the form of post-op radiotherapy although the standard line of treatment today based on results from the St. Jude RT-1 trial, is a new endeavor.

The group of patients with gross total or near total excision is recommended conformal radiotherapy. Focal irradiation for patients with localized ependymoma has also evolved. It administers higher doses of radiation (54-59.5Gy) to the tumor while sparing the surrounding tissues using a 10 mm clinical target volume and therefore beneficial in children below 3 years.

Proton radiotherapy although dosimetrically superior to photon radiotherapy is likely to become available after its clinical significance and population subset likely to benefit by its use is clearly defined. The role of neuraxis irradiation is limited to cases, which have proven metastasis at presentation.

The best response rates to combination chemotherapy in primary ependymoma have been demonstrated in younger children who received pre-irradiation chemotherapy in an attempt to delay RT. In the POG 8633 infant study for patients less than 3 years of age, Duffner et al. reported a 48% response rate following two cycles of combination chemotherapy that consisted of vincristine, cyclophosphamide, cisplatin, and etoposide in 25 children with residual tumor after initial surgery, demonstrating that the use of post-operative chemotherapy may allow the delay of RT for a clinically relevant period of time in younger children with ependymoma.

Similarly, in a recent study by the French Society of Pediatric Oncology (SFOP), children with ependymoma under the age of 5 were treated with seven cycles of alternating courses of procarbazine and carboplatin, etoposide and cisplatin, vincristine and cyclophosphamide over 1.5 years.

Despite the lack of any partial (PR) or complete responses (CR) in patients with residual disease post-initial surgery, 23% of patients remained alive at 4 years without the use of RT, suggesting that there exists a small subset of patients for whom cure may be possible with surgery and post-operative chemotherapy alone.

Presently, chemotherapy is reserved for those with subtotal resection (STR) before they are taken up for second look surgery.

Approaches

Transpetrosal approach and/or suboccipital approach.

Sanford et al. discuss the surgical approach used for and outcome in 11 infants (< or =3 years) who were treated at the institution for ependymomas arising in the cerebellar-pontine (C-P) angle. The median age of the group was 19 months (range: 6-26 months). Of these 11 patients, the initial surgery for 8 was performed at our center and achieved a gross total resection (GTR) in 4 patients and a subtotal resection (STR) in the remaining 4. The 3 patients who had tumor debulking performed elsewhere were subsequently referred to our institution and had definitive surgery after receiving 3-4 courses of chemotherapy; one of these children had a GTR, whereas the remaining 2 had an STR. During the immediate postoperative period, 9 patients had cranial nerve deficits that necessitated placement of a tracheostomy and a gastrostomy feeding tube; these were discontinued in 6 of the 9 patients as the deficits resolved. The majority of the permanent cranial nerve deficits involved the sixth and seventh cranial nerves. Of the 11 patients, 4 have died (progressive disease, n = 1; accidental death, n = 2; withdrawal of life support, n = 1); the remaining 7 patients are alive, with a median follow-up of 37 months (range: 20-73 months). Aggressive surgical resection for tumors arising in the C-P region is associated with postoperative deficits, which resolve over time with appropriate supportive care. This approach may increase the number of children in whom GTR is achieved, thereby potentially increasing the cure rate for these patients [1)]

Outcome

Extent of tumor resection remains the single most important prognostic factor for childhood CPA ependymoma. The 5 year probability of OS in patients with GTR is 67-80% and 5 year PFS as 51-75%.

As compared to this, 5 year PFS of patients with STR is 22-47%. This strongly signifies the role of additional resection for residual tumor, if any. Children under 3 years of age experience poor survival.

This has been explained previously by the fact that gross total resection (GTR) is accomplished less frequently in CPA surgery in young children. In addition, radiotherapy at age <3 years is generally withheld, delayed, or reduced in intensity, further reducing chances of long-term survival. Significance of histological grade continues to be debated and remains controversial.

Ependymomas in pediatric age are usually classified in WHO grade II (Low grade or differentiated ependymomas) or grade III (high grade or anaplastic ependymomas). Foci of hypercellularity, nuclear pleomorphism and anaplasia, necrosis, mitoses > 10 per 10 high power field and vascular proliferation qualify for grade III. The histological grade predicts the event free survival but not the overall survival.

Proliferating indices have a role on patients' survival rates. Definition of cut-off between benign and aggressive forms also remains controversial, although the cutoff for Ki-67 has been fixed at 20.5%. These limits are used to define low (<20.5%) and high (>20.5%) Ki-67 indices and predict favorable (>5 years survival) or unfavorable (<5 years) patients outcome.

Cytogenetic studies in one third of cases show deletions or rearrangements of 6q, 17, and 22 and gain of 1q chromosomes are detected, Gain of 1q25 indicates a poor prognosis.

In conclusion, CPA ependymomas in children <3 years are rare and its successful management remains elusive. The mainstay of treatment in CP angle ependymoma in children <3 years is gross total resection followed by conformal radiotherapy which enables higher doses to be given with least side effects. Prophylactic radiotherapy to neuroaxis has role only to those who have proven metastasis. The role of chemotherapy either neo-adjuvant or following the surgery in these cases is still not defined [2)].

Case series

Surgical techniques used for GTR in 45 patients with CPA ependymoma treated from 1997 to 2008 are described. Results of those procedures are compared with data from 11 patients who previously underwent surgical resection (1985-1995).

We achieved GTR in 43 (95.6%) patients and near-total resection in two (4.4%); the probability of progression-free survival was 53.8%, and that of overall survival was 64%.

Our novel surgical techniques greatly improve central nervous system function and survival among pediatric patients with CPA ependymoma [3].

Case reports

2012

A 2-year-old child. Gross total excision was achieved followed by administration of radiotherapy. In this article, a review of literature for this rare entity and the difficulties faced in the surgery and adjuvant treatment has been discussed [4].

A case of a 57-year-old man with a large cerebellopontine angle (CPA) tumor which expanded into the jugular foramen. Complete surgical excision of the tumor was achieved through a retrosigmoid approach and the histopathological diagnosis was subependymoma. Subependymomas located exclusively in the CPA without extension into the fourth ventricle are extremely rare. The mainly pathological features and the difficulty in correctly diagnosing these cases preoperatively, even with MRI, are discussed [5]

2011

Myxopapillary ependymoma of the cerebellopontine angle [6]

1997

A 38-year-old male presented with a posterior fossa ependymoma with unusual extension from the cerebellopontine angle to the pineal region. Magnetic resonance imaging clearly demonstrated that these two components were continuous through the right ambient cistern. Computed tomography using a bone algorithm revealed enlargement of the right internal auditory canal. This case suggests that ependymoma can extend anywhere within the subarachnoid space along the path of least resistance [7].

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