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INVITED PAPER

Advances in surgical techniques for resection of childhood cerebellopontine angle ependymomas are key to survival

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Abstract
Background Childhood cerebellopontine angle (CPA) ependymoma is an uncommon anatomical variant of posterior fossa ependymoma. In infants and young children, the tumor often goes undetected until it causes hydrocephalus. As CPA ependymomas grow, they distort the anatomy and encase cranial nerves and vessels, thereby making resection a formidable surgical challenge.
Purpose The purpose of this paper is to describe the surgical technique used to achieve gross total resection (GTR) of CPA ependymomas and demonstrate improved survival in these patients.
Materials and methods 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).
Results 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%.
Conclusion Our novel surgical techniques greatly improve central nervous system function and survival among pediatric patients with CPA ependymoma.

Keywords Pediatric ependymoma · Posterior fossa · Cerebellopontine angle

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Introduction

Cerebellopontine angle (CPA) ependymoma is a rare form of ependymoma that typically arises in infants and young children. CPA ependymoma originates from ependymal rests within the foramen of Luschka and grows both laterally into the CPA and medially into the fourth ventricle [1, 2]. CPA ependymomas pose a particular surgical challenge. They rarely invade the floor of the brain stem as do fourth ventricular ependymomas. CPA ependymomas appear to arise from the lateral aspect of the brain stem and have a propensity to encase the lower cranial nerves, the posterior inferior cerebellar artery (PICA), and the basilar artery. As CPA ependymomas grow, they displace surrounding tissue, i.e., they cause the brain stem to rotate, thereby altering the anatomy and distorting the posterior fossa landmarks.

CPA ependymomas are more common in infants and young children and are often quite large before they become clinically apparent; patients typically present with

symptoms and signs of increased intracranial pressure secondary to hydrocephalus. Cranial nerve deficit at presentation is uncommon. Cure is possible with surgical resection and subsequent radiotherapy; however, the combination of limited blood volume in young children, large tumor size, distorted anatomy, and encasement of cranial nerves and blood vessels make complete removal of this tumor a formidable surgical challenge.

The extent of surgical resection of ependymoma is a major determinant of outcome and long-term survival in pediatric patients [3–10]. However, national multicenter trials of pediatric ependymoma have reported that gross total resection (GTR; see the "Materials and methods" section for the definition) of these tumors is achieved in <50% of cases [8]. Historical 5-year overall survival (OS) estimates range from 50% to 64%, with the progression-free survival (PFS) estimates lower at 23% to 45% [7, 8, 11–13]. We have recently reported our overall ependymoma series of 153 pediatric cases treated from 1987 to 2007 at St. Jude with a median follow-up of 5.2 years (range, 0.3–10.5 years). The 5-year estimate of OS of standard ependymoma was 87.3±5% and that of the 7-year OS was 82.7±6% [14]. For malignant ependymoma, the 5-year OS was 62.1±0.7% and the 7-year OS was 62.1±0.1%. In this series, we achieved 81.7% GTR and 11.1% near-total resection (NTR) [14].

In this paper, we describe the advances made in the surgical technique utilized to achieve GTR of CPA ependymoma, to share lessons learned in dealing with surgery-related morbidity, and to demonstrate improved clinical outcome and survival in children with this disease that in the past was associated with very poor prognosis.

Materials and methods

Patient demographics

The Institutional Review Board at St. Jude Children's Research Hospital (St. Jude) approved this retrospective review of the records of all pediatric patients with ependymomas treated at our institution from 1995 to 2006. From this cohort, we selected 45 children and adolescents who had undergone a surgical procedure (performed by RAS and FAB) at St. Jude and who met the radiological criteria for CPA ependymoma. CPA ependymoma was defined as a tumor arising at or near the foramen of Luschka with the majority of the tumor bulk being extra-axial (i.e., in the CPA and along the lateral aspect of the brain stem). Fifteen children had undergone a previous surgical procedure before they were referred to St. Jude, and five had undergone a previous surgical procedure plus radiotherapy before referral.

RT1 protocol

From 1998 to 2004, St. Jude enrolled children into the institution's RT1 protocol in which the treatment regimen included maximal tumor resection and subsequent three-dimensional conformal radiotherapy to improve survival and reduce the amount of radiation administered to the normal central nervous system of pediatric patients with ependymoma. After their initial surgical resection and before they proceeded to radiotherapy, all patients underwent neuroimaging, including magnetic resonance imaging (MRI) of the spine, to examine the amount of residual tumor. If there was residual disease and no evidence of metastatic disease, then a second surgical resection was performed prior to initiation of radiation therapy.

From 1997 to 2008, we treated 153 children with ependymomas at St. Jude; of which 122 had infratentorial ependymoma [14] and 45 had CPA ependymoma [2]. Of those, 30 underwent a primary surgical procedure performed by the authors (RAS and FAB) and 15 had prior incomplete tumor resections done elsewhere, as mentioned above, before undergoing a definitive surgical procedure at St. Jude. The 40 children who had not previously received radiotherapy were entered into the RT1 protocol. The 45 children who underwent surgical resections by RAS and FAB are the focus of this report. The results of these procedures are compared with those of a previous report that included 11 children who underwent surgical resection for CPA ependymoma at St. Jude between 1985 and 1995 [15].

It is difficult to ascertain from the literature the frequency of the anatomical variant of posterior fossa ependymoma, CPA ependymoma, because most studies do not analyze these tumors separately. The large percentage (32.78%) of cases of CPA in our series of 122 cases of infratentorial ependymomas is difficult to explain; however, our institution's referral pattern reflects complex disease. In addition, we previously published a report demonstrating success with this difficult surgical entity [15] which may have biased referral.

Preoperative evaluation

Children with CPA ependymomas usually present with signs and symptoms of increased intracranial pressure, headache and early morning vomiting secondary to tumor mass, and obstructive hydrocephalus like other children with posterior fossa tumors. On examination, they may have papilledema and mild ataxia but only rarely do they have cranial nerve deficit in spite of the tumor completely encasing the lower cranial nerves (Fig. 1a). The tumors are usually extremely large at presentation probably because the tumor originates laterally and grows extra-axially as

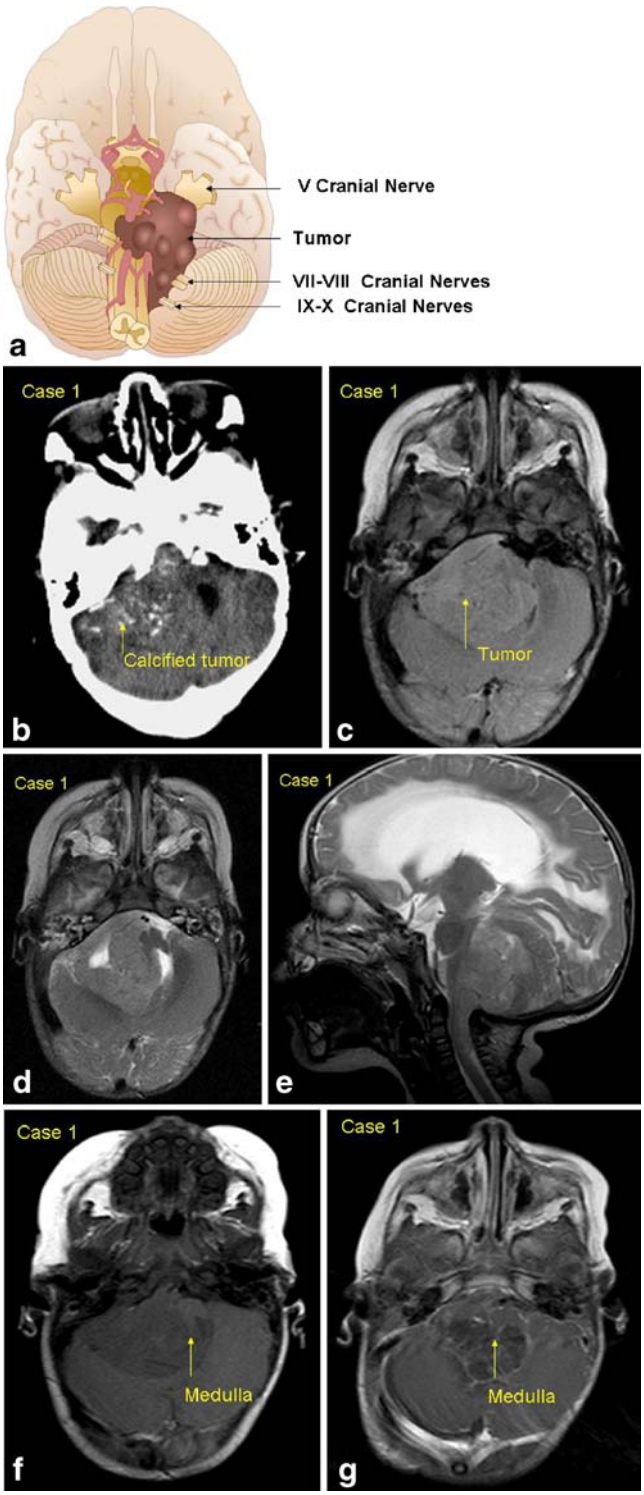

Fig. 1 **a** Anterior view of brain demonstrating rotation of brain stem produced by slow-growing CPA ependymoma and encasement of arteries and lower cranial nerves by tumor. **b** CT without contrast demonstrates large calcified tumor. **c** MR flair without Gd demonstrates large extra-axial tumor. **d** MR T2 axial view demonstrates brain stem displacement and rotation. Vertebral arteries are displaced. **e** T2 sagittal view extension of tumor inferiorly to C3 and hydrocephalus. **f** MR T1 without Gd axial view demonstrates brain stem displacement. **g** MR T1 with Gd axial view shows patchy enhancement

well as into the fourth ventricle with hydrocephalus being a relatively late development.

Computed tomography (CT) scan is often the first study the primary physician obtains and will demonstrate a large extra-axial mass in the posterior fossa with marked shift of the brain stem and IV ventricle. Calcification is often present confirming the slowly progressive growth pattern (Fig. 1b).

MRI demonstrates a hyperintense tumor on T1 sequence with variable patterns of enhancement from none to dense (Figs. 1, 2, and 3). The amount of enhancement is critical because, on the postoperative images, it is sometimes difficult to appreciate significant residual tumor in the cases that are nonenhancing or weakly enhancing. The T1 without Gd and T2 sequence usually best demonstrates the encasement of the vertebral, posterior inferior cerebellar, and basilar arteries (Fig. 2a, b, f). It is important to appreciate the rotation and the position of the brain stem for correct surgical planning (Fig. 1a, d, e). The differential diagnosis includes medulloblastoma and juvenile pilocytic astrocytoma; therefore, a spinal MRI is useful to rule out metastatic disease. None of our 45 children with CPA ependymoma had spinal metastasis.

Because of the young age of the child and the chance of significant blood loss, fresh blood should be requested because of the lower potassium level in fresh blood. In our early series, we had a cardiac arrest from hyperkalemia because of rapid transfusion with nonwashed blood. Blood banks usually provide the oldest blood to surgeons to use to prevent it from expiring without being used.

Surgical procedures

Patient positioning

After general endotracheal anesthesia is administered, the patient is placed in the prone position with the chin flexed to the chest and rotated toward the ipsilateral shoulder (Fig. 4). Children older than 2 years are placed in pin fixation; those younger than 2 years are placed on a horseshoe headrest with maximum flexion and the forehead is positioned in a well-padded headrest. This position protects the eyes from pressure but requires lifting the head every 30 min to prevent pressure necrosis of the skin. All patients are carefully strapped to the table to allow maximal side-to-side rotation, thereby alternating exposure of the CPA, lateral medulla, and floor of the brain stem as needed.

Incision and preparation of the surgical field

The skin incision is marked from the C2 vertebrae up the suboccipital midline and above the confluence of the sinuses. It is then curved into a “lazy S” that ends behind

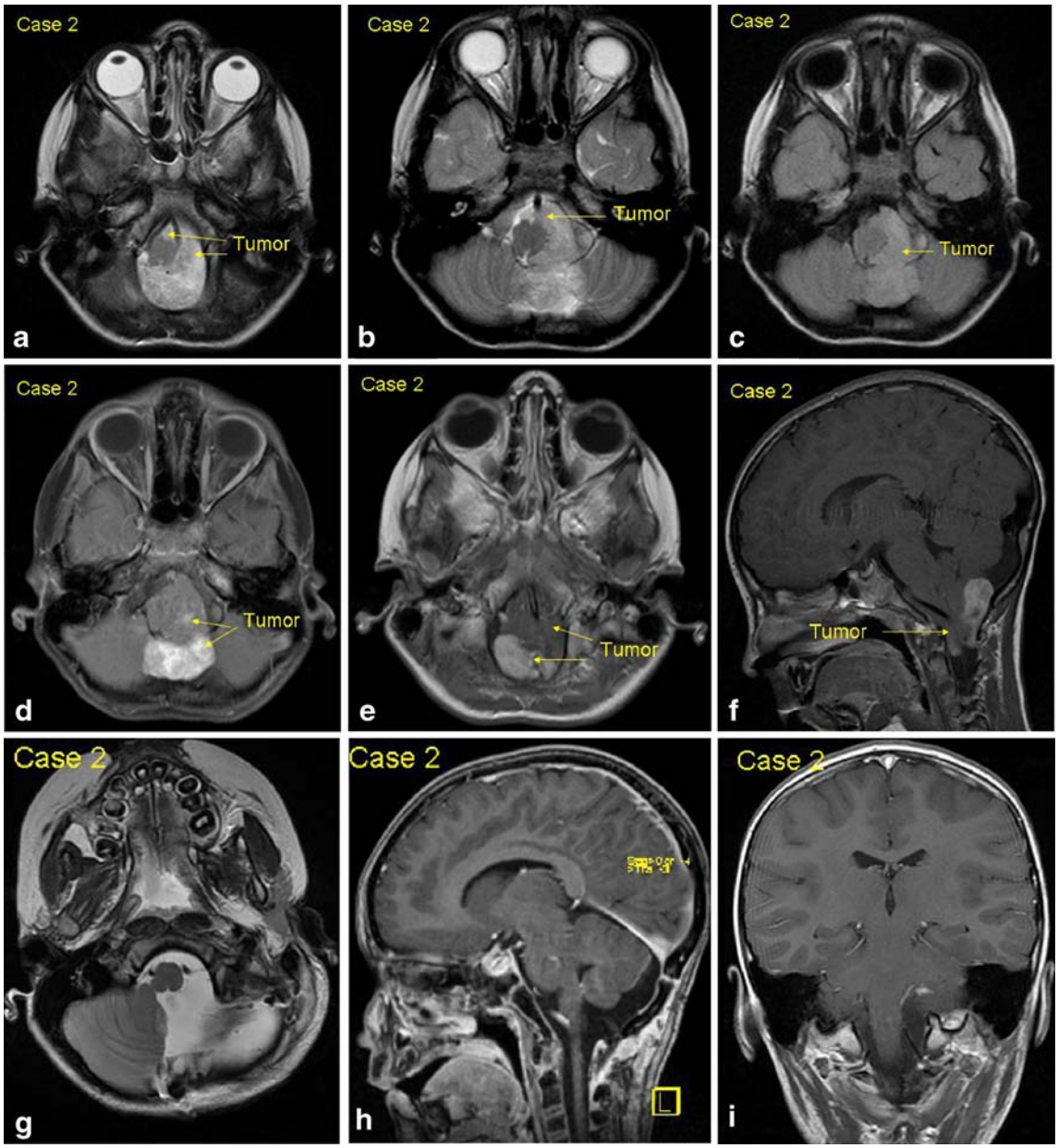

Fig. 2 **a** MR T2 axial view demonstrating tumor encasing left vertebral artery. **b** MR T2 axial view demonstrating tumor separating basilar artery 9 mm from medulla. **c** MR flair axial view demonstrates tumor. **d** MR flair axial view with Gd demonstrates minimal enhancement (*upper arrow*) and dense enhancement (*lower arrow*). **e** MR axial view with Gd demonstrates nonenhancing tumor (*upper arrow*) and enhancing tumor (*lower arrow*). **f** MR sagittal view with Gd demonstrates nonenhancing tumor anterior to basilar artery and enhancing tumor dorsally. **g** MR T2 axial view demonstrates no tumor postoperatively. **h** MR T1 axial view post-Gd demonstrates no tumor postoperatively. **i** MR T1 coronal view post-Gd demonstrates no tumor postoperatively

the ipsilateral ear (Fig. 5). If a surgeon has previously used a midline incision (a common error), then one may convert the skin incision to a "hockey stick" extending toward the ipsilateral ear. These skin incisions allow the bony suboccipital craniotomy to extend across the midline up to the transverse sinuses and laterally to the sigmoid sinus. In young children, it is important to leave bone covering the sigmoid sinus to prevent clotting of the sinus at that site. If the sinus is exposed, it is crucial to keep it covered with moist Gelfoam® and cottonoids. With this exposure, the medial condyle can also be partially (less than one third) resected. The arch of C1 is always removed with additional laminotomy, as needed to remove the cervical extension of the tumor. If hydrocephalus is present, placement of an external ventricular drain may be necessary prior to opening the dura. Mannitol is routinely given. As the dura is opened, it is important to isolate the surgical area by temporarily placing Gelfoam in the spinal subarachnoid space. The use

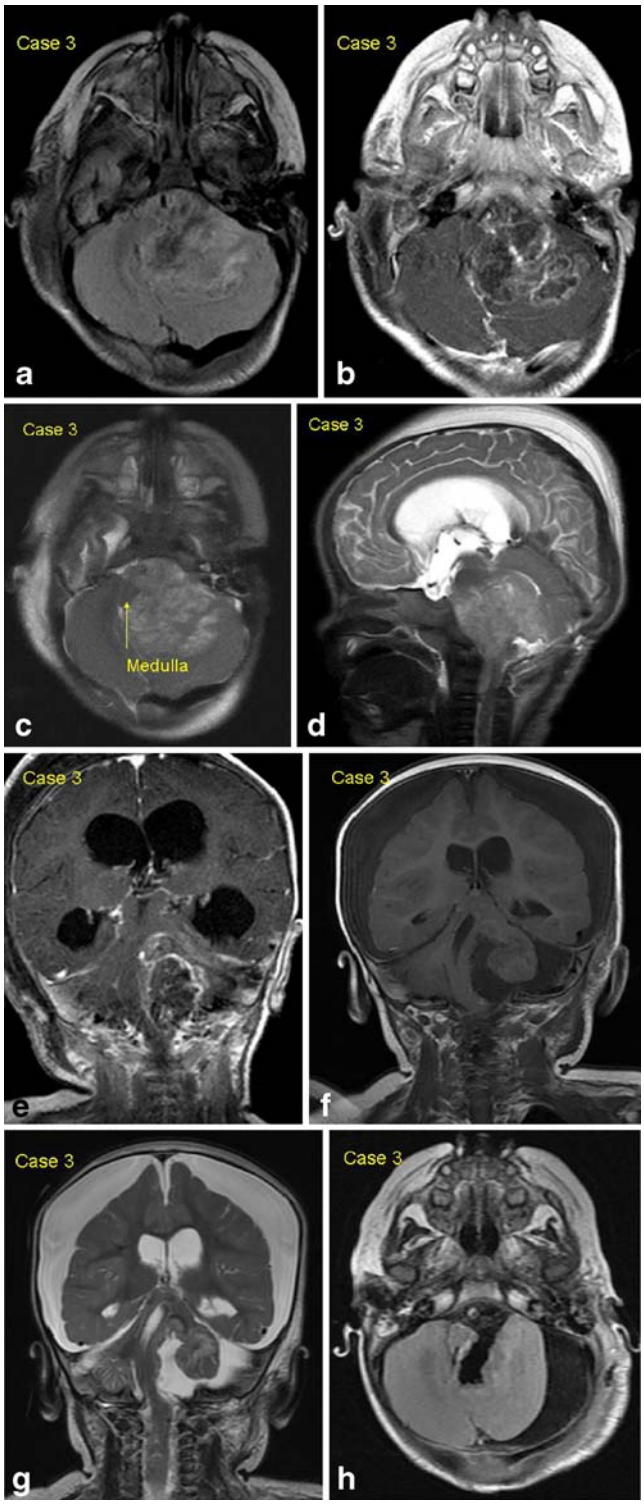

Fig. 3 **a** MR T1 without contrast shows separation of basilar artery from brain stem. **b** MR T1 with Gd demonstrates patchy enhancement pattern. **c** MR T2 axial view demonstrates displacement and rotation of brain stem by tumor. **d** MR T2 sagittal view with extension of tumor to second cervical vertebrae. **e** MR T1 with Gd coronal view demonstrating deformation of brain stem. **f** MR T1 postoperative scan with residual brain stem displacement and bilateral extra-axial fluid in the subdural space with improvement in hydrocephalus. **g** MR T2 coronal view of postoperative scan with residual brain stem displacement and bilateral extra-axial fluid in the subdural space with improvement in hydrocephalus. **h** MR flair axial view demonstrating brain stem deformation, rotation, and no residual tumor postoperatively

of Gelfoam is crucial to avoid subarachnoid spread of floating tumor cells during the lengthy surgical procedure.

Microsurgical tumor resection

The operating microscope is set up in the quadroscope mode with the surgeons standing across from each other, both having stereoscopic vision. The vast majority of the cases were performed by RAS and FAB operating together during the critical portion of the surgery. No self-retaining retractors are utilized. Retraction is maintained by one surgeon while the other dissects the tumor. Duties are then reversed on the opposite surgical field.

Microsurgical tumor resection generally begins with the removal of the spinal portion of the tumor. As the surgeon proceeds cephalad to the obex, the vertebral artery (Fig. 6b) and the PICA should be dissected free, thereby isolating and occluding the tumor-feeding vessels. In infants and small children, it is important that the surgeon occlude the major blood supply to the tumor, while preserving the parent vessel, before initiating major tumor debulking. Next, the surgeon removes the portion of the tumor located within the fourth ventricle. We favor using an ultrasonic aspirator to resect the tumor in the standard manner, proceeding cephalad until the aqueduct of Sylvius is opened, being careful to protect the floor of the fourth ventricle with Gelfoam.

At this point, the surgeon can distinguish a true CPA ependymoma from a fourth ventricular ependymoma because the latter arises from the floor of the brain stem or the cerebellum, whereas the CPA ependymoma originates from the lateral brain stem at the foramen of Luschka [2]. The surgeon must be cautious and appreciate how the laterally positioned tumor has distorted the anatomy of the fourth ventricle, i.e., the medulla and pons will be elevated and rotated. It is imperative that, on the preoperative MR image, the distortion of the brain stem be appreciated (Fig. 1c, d), so that the surgeon can decide the correct surgical approach. If this anatomical distortion is not appreciated, the surgeon may inadvertently traverse the tumor into the brain stem, especially if there is significant bleeding. After the portion of tumor within the fourth ventricle is removed, sufficient cerebellar relaxation will occur, thereby allowing the surgeon to proceed to the most challenging part of the dissection, i.e., removing the CPA ependymoma from the cranial nerves and vasculature.

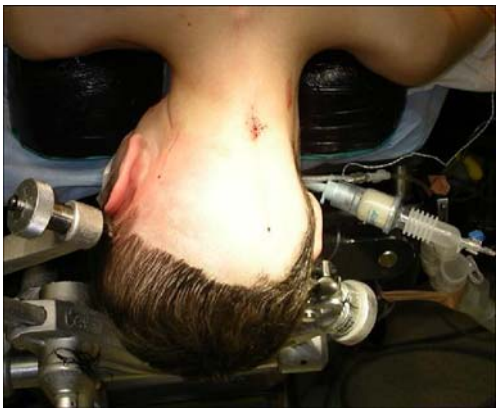

Fig. 4 Position of patient for right CPA with head turned to the right, allowing direct access to tumor and midline

Removal of tumor from the lower cranial nerves

We did not monitor cranial nerve function in this series because our primary goal was to remove the tumor, even if evoked potentials were lost. After the tumor has been removed from the fourth ventricle and hydrocephalus has been relieved, the surgeon can remove the tumor from the lower cranial nerves. It is crucial that the dissection of the tumor proceed from lateral where they exit to their origin medially (brain stem) (Fig. 6c). Because of the rotation of the brain stem and tumor arising from the lateral brain stem, the anatomy is completely distorted. Attempting to remove the tumor from medial to lateral will likely result in the loss of cranial nerves VII, VIII, IX, and X, which are almost always completely encased by the tumor. The ultrasonic aspirator is used to laterally remove the superficial portion of the tumor.

By following the sigmoid sinus inferiorly, the surgeon will find the jugular foramen and the hair-like cranial nerves IX and X. The tumor surrounding the lower cranial nerves is removed by using microdissection instruments and low-amplitude suction, not the ultrasonic aspirator. These nerves are very fragile and are often invaded by tumor. Maintenance

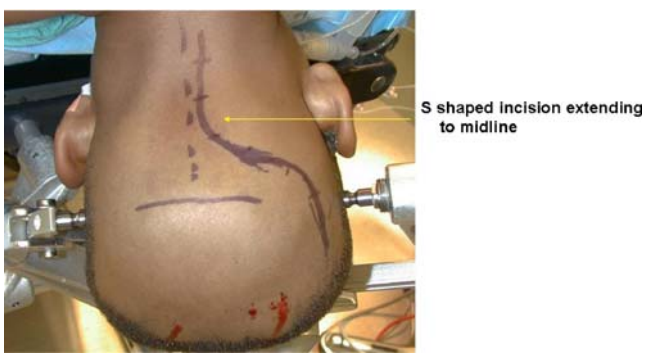

Fig. 5 Preferred incision which allows muscle splitting, lateral approach, and access to midline

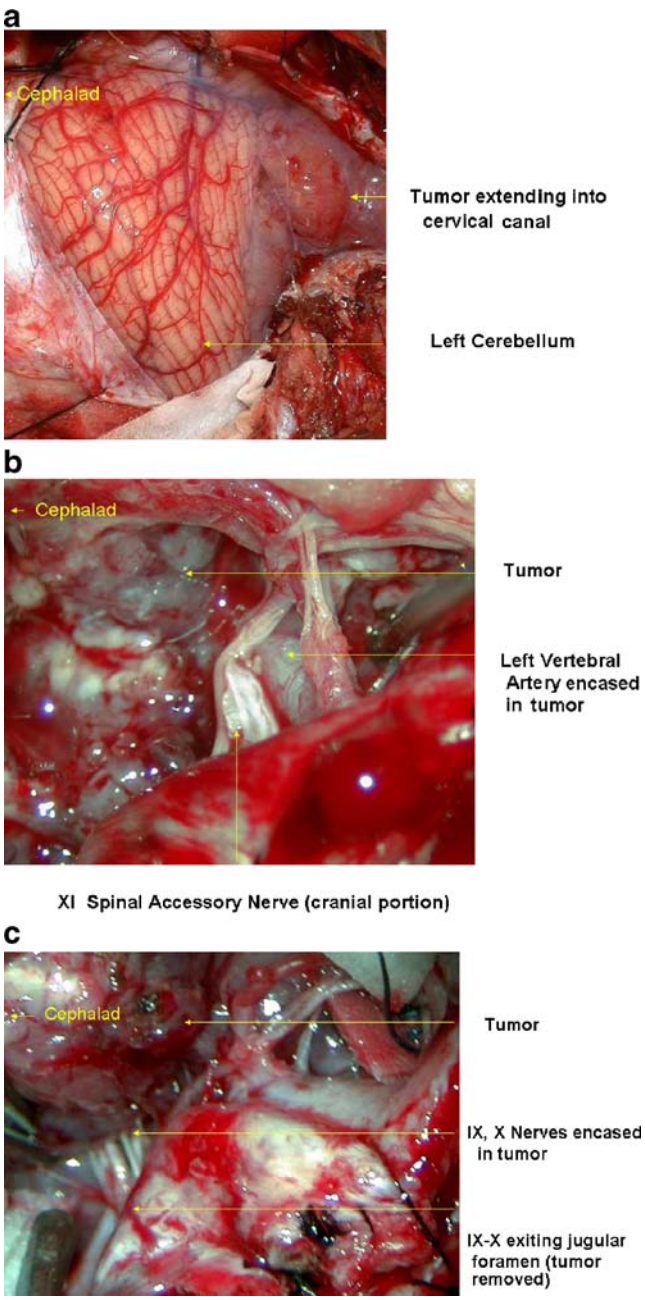

Fig. 6 **a**–**e** Microsurgical tumor resection, removal of tumor from the lower cranial nerves, and removal of tumor from the vasculature

of the integrity of the tumor capsule facilitates the dissection, as the tumors are quite vascular and tend to bleed each time the capsule is broached. This hinders visualization, impedes dissection, and requires bipolar coagulation in the proximity of the delicate cranial nerves.

As stated above, meticulous tumor dissection must proceed from lateral, where the nerves exit the skull, to medial, along cranial nerves IX and X. Often, indolent tumor growth elongates these nerves by 1 to 3 cm. Once cranial nerves IX and X are adequately exposed, the surgeon proceeds along the

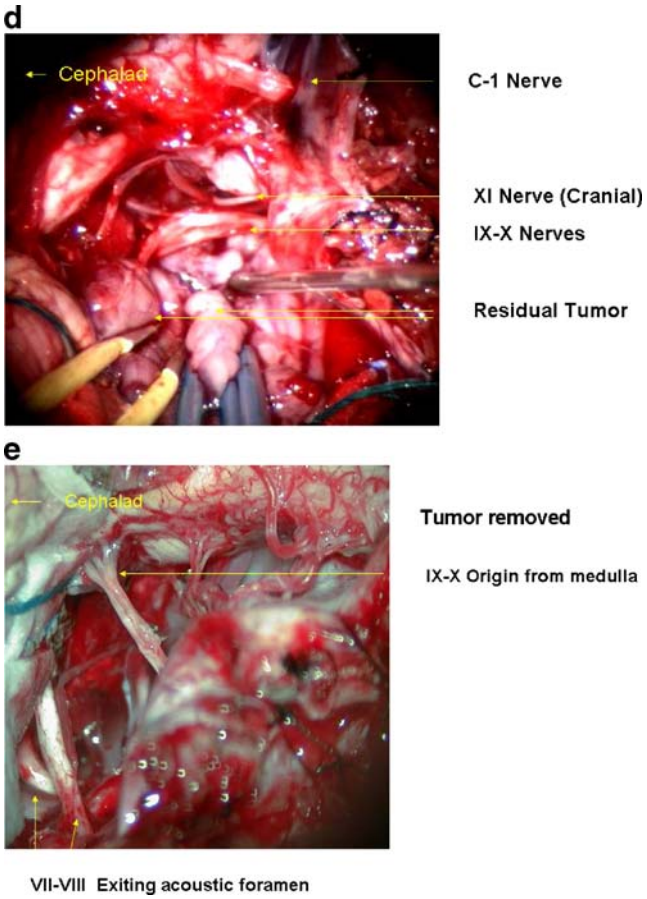

Fig. 6 (continued)

lateral skull base to identify the acoustic canal and cranial nerves VII and VIII, which traverse the acoustic foramen (Fig. 6e). The tumor must be retrieved from within the acoustic canal. This tissue can be gently teased away from the nerves. Only rarely does the bony canal require unroofing with a high-speed diamond drill. It is important to minimize the manipulation of the nerves. We have only rarely preserved function of cranial nerve VIII though the nerves remain intact. The anterior inferior cerebellar artery (AICA) must be identified and preserved. The acoustic vein, which drains blood from this area, can produce troublesome bleeding if inadvertently torn.

As the lateral brain stem decompresses, the telovelar space opens. This allows access to any residual tumor within the fourth ventricle or the foramen of Luschka. Because the lateral aspect of the pons is generally distorted and rotated away from the tumor, it can be difficult to distinguish the lateral brain stem from the floor of the fourth ventricle. The cerebellar tonsil, if not previously mobilized, must be elevated at this point so that the lateral margin of the fourth ventricle can be followed superiorly to clarify this confusing anatomy. The surgeon can identify and protect the entry zones of the cranial nerve roots by working within the tumor and debulking with the ultrasonic aspirator, while dissecting the tumor away from the pia mater along the side of the brain stem.

Removal of tumor from the vasculature

CPA ependymomas typically encase the AICA and the vertebral artery (Fig. 6b). These arteries must be carefully dissected with a microdissector and low-pressure suction and preserved. This dissection is usually relatively simple. The basilar artery is often displaced but rarely totally encased. Diligence is required to spare the medial perforating blood vessels that arise from the basilar artery and enter the brain stem. These vessels, which are normally 1 to 2 mm in length, may be elongated as much as 1 cm or more. Diligence is required to avoid injury to these hair-like vessels. If tumor removal from the fourth ventricle, lateral brain stem, and cranial nerves was performed correctly, then the final portion of the procedure is done in an avascular field that offers a direct view of the basilar artery, resulting from rotation of the brain stem by the growing tumor, correct preoperative positioning of the patient, and the use of the lateral surgical approach. We have never encountered medullary-perforating vessels arising from the vertebral artery below the basilar apex. Medullary-perforating vessels arise from the caudal loop of the PICA and are meticulously protected at the beginning of the surgical dissection.

Final surgical notes

Once the tumor resection is completed, it is important that all Gelfoam and Surgicel be removed from the field because foreign material enhances on later MR images and may be mistaken for residual or recurrent tumor. In none of our cases were intradural hemostatic agents left and no child experienced a postoperative hematoma requiring reoperation for removal. The dura is then patched to accommodate postoperative edema and promote CSF circulation, and the bone flap is replaced with microplates and screws. Meticulous detail to closure is important. We utilize dural tack-up sutures and suture the muscle to the bone flap, thereby eliminating dead space so that a postoperative psuedomeningocele be a harbinger of hydrocephalus rather than the result of poor surgical closure. This facilitates the decision regarding reoperation to repair the CSF leak versus permanent CSF diversion (shunt).

Classification of surgical complications

Surgical complications were classified as either “minor” or “major.” Minor complications included those events that resolved in a timely manner. These included mild hoarseness, temporary swallowing difficulty, temporary mild

facial asymmetry, shunt malfunction, new shunt placement, etc. Major complications were those that were potentially life-threatening and either required a long recovery period or were permanent. These events included hemiparesis, meningitis, cranial nerve palsy, and impaired vocal cord and swallowing functions.

Postoperative care

After surgery, the patient remains intubated overnight. When the child is fully awake, an experienced otolaryngologist (ENT) extubates the child and assesses vocal cord movement and gag reflex. It is possible to have adequate closure of the vocal cords but inadequate sensation, which can result in aspiration of saliva. If the ENT deems the vocal cord function inadequate, then a tracheotomy is performed. If vocal cord function is adequate, the patient remains extubated with continued monitoring for 24 h in the intensive care unit. Patients who tolerate extubation then undergo a swallowing test using fluoroscopic imaging. Some patients are able to avoid tracheotomy but require feeding gastrostomy (G-tube).

Postoperative imaging and surgical resection classification

Within 48 h of surgery, postoperative MRI is performed to determine the adequacy of surgical resection. It is critical to compare the preoperative images side by side with the postoperative ones, and appreciating residual tumor in the poorly enhancing tumor is often challenging. GTR is defined as no evidence of residual tumor on postoperative images; NTR is defined as <1.5 mL of residual tumor on postoperative images; and subtotal resection (STR) is defined as more than 1.5 mL of residual tumor on postoperative images. If postoperative images indicate that STR was achieved, we recommend that the patient undergo an additional surgical procedure before proceeding to radiation therapy.

Results

Patient demographics

Our cohort of 45 pediatric patients included 30 boys and 15 girls (Table 1). The mean age at diagnosis was 2.93 years (range, 0.54–18.44 years); 51% of the children were younger than 3 years and 76% were younger than 6 years. The majority (73%) were Caucasian. Thirty (66.7%) children presented with de novo disease and were treated primarily at our institution; ten (22.2%) had previously undergone surgery and were referred to St. Jude after initial incomplete surgical resections; and five (11.1%) had previously undergone surgery and received radiation therapy, after which the tumor recurred. These patients underwent a second surgical procedure at St. Jude before proceeding to repeat radiation therapy [16]. Among this latter group of 15 patients, three had three previous surgical procedures; five had two previous procedures; and seven had one failed procedure.

Table 1 Patient demographics in a series of 45 pediatric patients with CPA ependymoma

Characteristic	No. of patients (%)
Sex	
Male	30 (67)
Female	15(33)
Race	
White	33 (73)
Other	12 (27)
Age at diagnosis (years)	
<3	23 (51)
<6	34 (76)
≥6	11 (24)
Treatment prior to referral to St. Jude	
Surgical resection only	10 (22)
Surgical resection and radiotherapy	5 (11)

Surgical procedure metrics

In our series, we accomplished GTR in 43 (95.56%) cases and NTR in two (4.44%) cases. The average duration of surgical procedures was 5.7 h with a median time of 5 h and range of 2–13 h. The duration of the surgical procedure was longer for younger patients (<3 years) than older ones (>3 years). In fact, the duration and age at the time of surgery were negatively rank-correlated ($r_{\text{Spearman}}=-0.46$, $p=0.0016$). This relationship was more obvious in patients who experienced minor complications. Surgical duration appeared to be associated with complications, i.e., as the time required to remove a tumor increased, so did the rate of complications (Table 2), suggesting more difficult surgery. Surgical complications also related to prior surgical procedure and radiation (Table 3).

The median duration of surgery with no complications was 4.75 h, that of procedures with minor complications was 5.68 h, and that of procedures with major complications was 6 h. This finding reflects the degree of difficulty associated with tumor removal, the size of the patient, and most importantly, the size of the tumor.

Our surgical experience gained over the past 11 years is illustrated in Fig. 7. Although the duration of surgical procedures involving no complications or major complications has remained consistent, that of procedures involving

Table 2 Relations between surgical complications and duration of procedure and hospital stay

Surgical complication	*n*	Duration of surgical procedure (h)		Duration of hospital stay (days)	
		Median	Range	Median	Range
None	18	4.75	2.75–8	6	3–20
Minor	14	5.68	2–9.25	12.5	4–39
Major	13	6	4.4–13	19	9–33

minor complications showed a trend toward decreasing ($r_{Spearman}$=−0.52, p=0.058). The average blood loss during surgical procedures was 240 mL; during surgery, only ten of 45 (22.2%) patients required transfusions. The average hospital stay was 14 days (median, 11 days; range, 3–39 days), reflecting both improved surgical outcome and advances in postoperative care.

Surgical complications

Surgical complications were classified as minor or major, and in our series, 18 (40%) procedures involved no complications. Major complication occurred during 13 procedures; this classification included the following events: hemiparesis (n=1 patient), cranial nerve palsy VI, VII, VIII, IX, or X (n=11), tracheotomy (n=7), G-tube placement (n=9), and meningitis (n=1). Minor complications occurred during 14 surgical procedures; these included the following events: mild facial asymmetry that promptly cleared, minor hoarseness or swallowing difficulty that cleared (n=8 patients), shunt malfunction (n=3), new shunt placement (n=2), cerebral salt wasting (n=1), and psuedomeningocele (n=1). Unilateral hearing loss was permanently lost in virtually all of the patients in which there was bulky tumor. Only one child still requires a permanent tracheotomy for ventilatory assistance at night for central sleep apnea and G-tube. All the others were decannulated within 1 year of surgery. The function of cranial nerve VI always recovered to some degree, though strabismus surgery may be required. Recovery of cranial nerve VII function was variable in seven of nine cases; two children had permanent facial paralysis and underwent cranial nerve XII to VII anastomosis.

No surgical mortalities occurred in our series. One child, who had undergone three previous surgical procedures and radiation therapy before referral to St. Jude, experienced a brain stem infarction related to the loss of an arterial perforator at the time of surgery; this patient did not awaken. Two patients experienced hemiparesis after surgery, one of whom also had undergone two prior surgeries, radiation therapy, and chemotherapy. That patient experienced an incomplete recovery. The other patient has only minor residual weakness.

New complications did not appear to be associated with whether a child had had previous surgery. It is difficult to analyze the increased difficulty presented by previous surgery plus radiation because these children were picked up early and referred with small tumor burdens. As a surgeon, the problems encountered with the thickness of the scarring after surgery plus radiation is a definite technical problem that was not revealed by our analysis. The only bad result (child did not awaken) occurred in a

Table 3 Relations between surgical complications and treatment prior to referral to St. Jude

Prior treatment	Surgical complication (*n*)		
	None	Minor	Major
Surgical resection			
Yes	15	10	10
No	3	4	3
Radiotherapy			
Yes	5	4	3
No	13	10	10

See text for the definition of the classification of complications

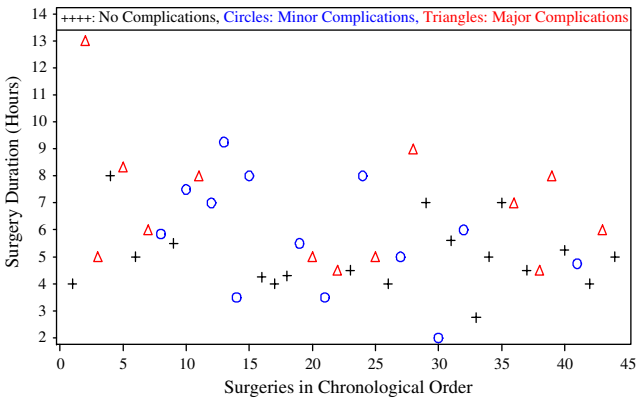

Fig. 7 Relationship between duration of surgery and surgical experience. While the surgery duration for the patients who had no surgical complications and major complications stayed about the same over the years, there seems to be a trend of decrease in the duration of surgery for patients who had minor complications. There is a suggestive negative rank-correlation for patients with minor complications ($r_{Spearman}$=−0.52, p=0.058), which suggests that surgeries of patients with minor complications got shorter over the years

child who had undergone multiple previous surgical procedures and radiotherapy. Complications appeared to be more common in younger patients, but we found no statistically significant associations between complications and age.

Because of the multiple variables imposed in our series of children having prior surgery and prior radiation, it makes analysis of PFS and OS in the 45 children difficult to interpret. As such, we analyzed only the 24 children who had definitive surgery at our institution within 3 months of diagnosis, followed by conformal radiation; this resulted in a PFS rate of 53.8% and OS rate of 64% (Fig. 8).

Discussion

The current standard of care for children with ependymoma is maximum surgical resection followed by local radiotherapy [6, 7, 9, 10, 17]. The single-most important determinant of outcome for patients with ependymoma is the extent of tumor resection [14]. This places a great deal of responsibility on the pediatric neurosurgeon to achieve a maximal safe resection. The 5-year probability reported in the literature of OS in children who receive a GTR is 67% to 80% and the 5-year PFS is 51% to 75% [5, 7, 9, 11, 13, 17, 21]. In striking comparison, the 5-year PFS of children who undergo STR is 22% to 47% and their 5-year PFS is 0% to 26%. This has led many authors to suggest that pediatric patients with residual ependymoma on postoperative MR images should undergo an additional resection [5, 12, 18–21]. Utilizing this approach, we have reoperated in order to achieve minimal disease before going on to radiation and reported our ependymoma series of 153 pediatric cases with a median follow-up of 5.2 years (range, 0.3–10.5 years). The 5-year estimate of OS of standard ependymoma was 87.3±5% and that of 7-year OS was 82.7±6% [14].

Studies have shown that infants and children younger than 3 years with ependymoma experience poorer survival than do older children with the disease [20]. We feel that this difference can best be explained by the fact that GTR is accomplished less frequently in posterior fossa surgery in young children. Resection of ependymoma in an infant is one of the more challenging tasks a neurosurgeon will ever undertake. The posterior fossa is smaller in these patients; vascular tumors in young children who have a decreased blood volume increase the difficulty because the child may quickly become unstable with moderate blood loss. Therefore, it is not surprising that, in the previous reports, the incidence of GTR was <50% [8, 21]. Also, children <3 years had radiation withheld, delayed, or reduced in dose intensity, further decreasing chance for long-term survival.

Unlike medulloblastomas that extend laterally and tend to displace (rather than encase) cranial nerves and maintain a normal arachnoid plane, CPA ependymomas grow laterally in the same anatomical location, but encase the cranial nerves and vasculature and distort the normal brain anatomy by elevating and rotating the lower brain stem (Fig. 1c, e). The difficulty of surgical resection of these tumors is increased because of the small size of the posterior fossa and the reduced blood volume in young children. Because of these unique variables, attention to detail regarding the surgical technique is essential.

Our experience with this unique tumor has led us to conclude that it arises from the lateral aspect of the medulla in the CPA, at the junction of the pons and medulla, where it is densely attached. True CPA ependymomas never arise from the floor of the pons or medulla. This is supported by the fact that, in five cases within our series, tumors reoccurred in the original location; they regrew laterally; and they were attached to the brain stem. Because of this lateral origin, the surgeon must be prepared to approach the tumor laterally.

The improvements in surgical technique described herein plus conformal radiation resulted in a PFS rate of 53.8% and an OS rate of 64% (Fig. 8) in 24 pediatric patients who underwent definitive surgery at our institution within

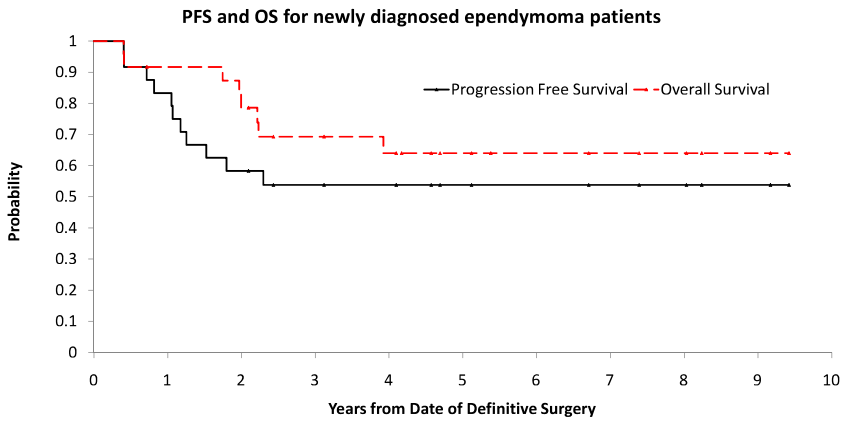

Fig. 8 Survival estimates for newly diagnosed ependymoma patients. Considering the complications that arise due to the fact that the surgeries were performed at different disease stages in this patient cohort, we took the approach that estimating any type of survival would be meaningful only in the group of newly diagnosed patients. Therefore, the following survival estimates are based on 24 patients whose definitive surgeries were done within 90 days of their diagnosis dates

3 months of diagnosis of CPA ependymoma. These improvements are also reflected by our ability to achieve GTR in 95.6% of these patients and NTR in 4.4%. These results also compare favorably with those from our overall series of 122 children with posterior fossa ependymoma.

In our early experience with 11 cases of CPA ependymoma (1984–1995), the complication rate was extremely high [15]. The group consisted of eight patients whose disease was diagnosed at St. Jude and three who were referred to our institution after incomplete tumor resection. One child presenting in extremis, underwent a surgical procedure but died within 24 h when the parents did not want to continue heroic measures and was not included in the analysis. The average duration of surgical procedures in our early cohort was more than 9 h with an average blood loss of 407 mL. In the current series, the operative time improved to 5.7 h with an average blood loss of 240 mL, with only ten of 45 children requiring transfusions.

In the earlier study, GTR was achieved in eight patients and NTR was achieved in two of the surviving children. Morbidity was high, i.e., nine of the ten patients required a postoperative tracheotomy and G-tube; all ten suffered significant cranial nerve deficits; and four experienced hemiparesis. Three patients are long-term survivors with good quality of life, moderate neurologic deficit, and mild developmental delay secondary to conventional posterior fossa irradiation. Five children died of progressive disease; one died of an acute subdural hematoma while undergoing chemotherapy; and one died of shunt malfunction. All the children eventually had their tracheotomy and G-tubes removed, except the child who died of shunt malfunction. In contrast, in the current series, 18 (40%) of the 40 children experienced no complication; 14 (31%) had only minor complication(s); and 13 (29%) experienced major complications (i.e., seven had a tracheotomy and nine had a G-tube all of which were removed within 1 year post surgery).

The improvements observed in the current cohort are the result of the evolving surgical technique and marked improvement in the quality of microsurgical instruments and operating microscopes. However, the major factor is the improvement gained through increased operative experience. In fact, we showed an improved learning curve for two senior neurosurgeons (FAB and RAS) over our 11-year experience with CPA ependymoma (Fig. 8).

Long-term survival of ependymomas requires the use of radiation therapy after surgical resection. Historically, low dosages of radiotherapy have been administered to infants in an effort to reduce the treatment's harmful effects on the developing brain. An additional source of improved survival of the current cohort is the use of conformal (reduced volume) radiation therapy. All 45 children in the current series received conformal radiation, which allows the administration of higher doses of radiation (54–59.5 Gy) to the tumor, while sparing the surrounding tissues (i.e., temporal lobes and auditory structures).

Conclusions

CPA ependymoma is an anatomical variant of ependymoma in which young age at diagnosis and anatomical inaccessibility are key negative prognostic factors. Historically, the anatomical inaccessibility of these tumors has limited the degree of surgical resection. Using the surgical techniques described herein, we have now achieved >95% GTR and approximately 4% NTR with moderate morbidity. Complete surgical resection is followed by conformal radiation therapy. This treatment regimen translates to a 53.4% probability of PFS and a 64% probability of OS. We conclude that optimal treatment of pediatric patients with CPA ependymoma requires aggressive surgical resection by an experienced neurosurgical team and focused irradiation.

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