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ORIGINAL ARTICLE

Treatment of Choroid Plexus Tumours

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Abstract

Introduction: Choroid plexus tumors (CPT) develop from the neuroepithelial lining which is well fused with ependymal cells in the 6th week of pregnancy. There is a broad spectrum of histological and biological characteristics. These tumors 70% are seen in children. The most important symptom is findings of increased intracranial pressure. Computed tomography and magnetic resonance imaging are essential in diagnosis. The aim of this study was to evaluate the surgical results of patients with a diagnosis of choroid plexus papilloma who were operated in our clinic.

Methods: In this article, demographic characteristics, surgical approach, and results of 11 pediatric and three adult patients who underwent tumor excision between 2000 and 2020 were evaluated retrospectively.

Results: We evaluated the findings, the treatment approaches, and surgical outcomes of 11 pediatric and three adult cases who underwent grosstotal excision between 2000 and 2020.The pediatric cases comprised of eight choroid plexus papilloma, two atypical choroid plexus papilloma, and one diffuse villous hyperplasia filling supratentorial ventricles (left, right lateral ventricles, and third ventricle). In one of our adult cases (12th case), choroid plexus papilloma was located at the right lateral ventricle and we suspected of parenchymal infiltration but pathologic diagnosis was pilocytic astrocytoma. These two tumors together constructed collesion tumor. The other tumor located in the right pontocerebellar angle (Case 13) had undergone stereotactic radiosurgery 10 years previously as it had been considered to be meningioma, and as there had been no follow-up, growth had continued.

Discussion and Conclusion: CPTs show anaplastic transformation, may have an effect of irritation on the parenchyma, and may cause secondary tumors with the effect of parenchyma infiltration. Gamma knife treatment is not highly effective and the basic treatment should be considered to be grosstotal resection.

Keywords: Atypical choroid plexus papilloma; choroid plexus papilloma; diffuse villous hyperplasia.

Choroid plexus tumors (CPT), including the neuroepithelial (neuroectodermal) group, develop from the neuroepithelial lining which has fused well with ependymal cells while forming the choroid plexus in the 6th week of pregnancy. CPT is uncommon intracranial tumors, 70% of which are seen in childhood, and 50% of these are in in-

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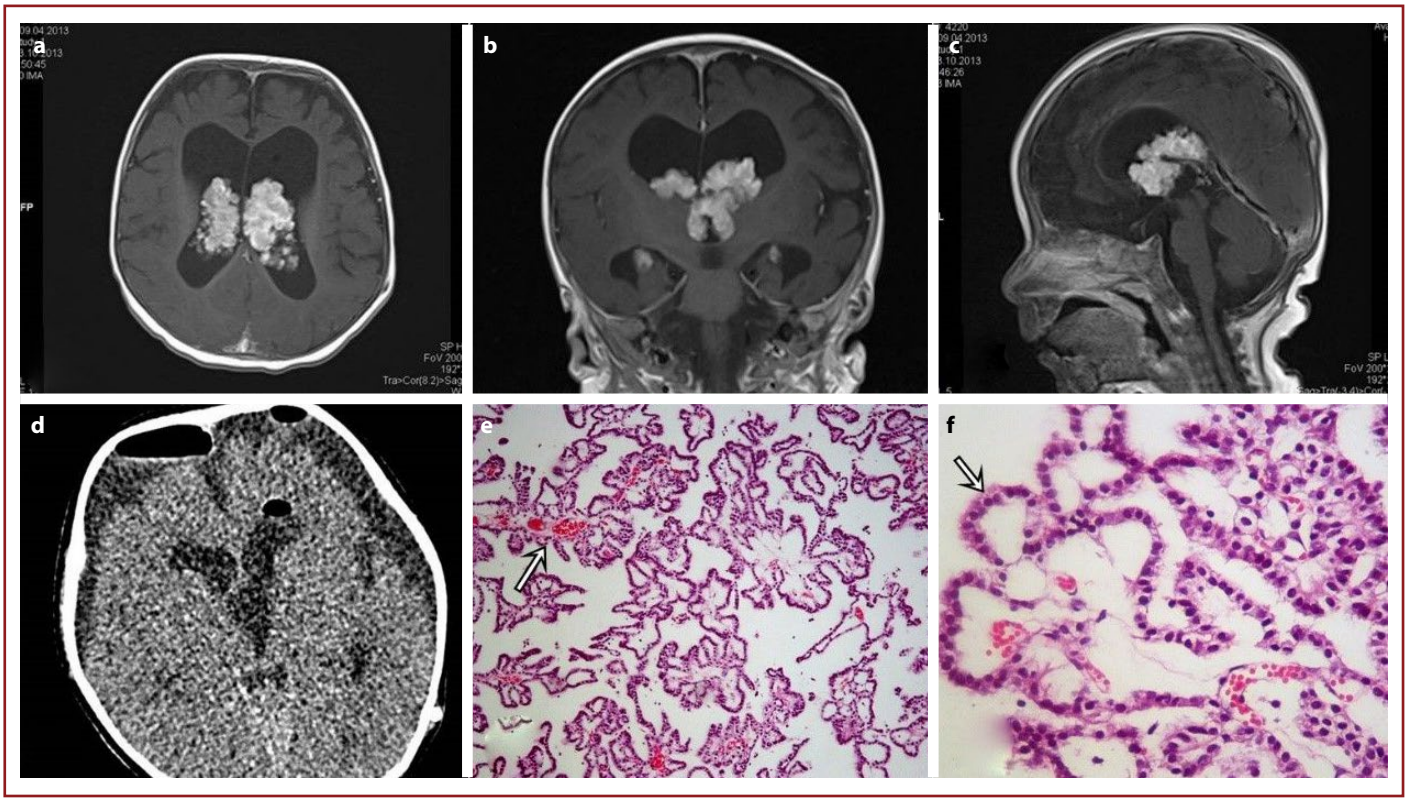

Figure 1. DVH: **(a-c)** pre-operative MRI, **(d)** post-operative CT, **(e)** Villous structure including vascular core (H and E; ×100), **(f)** Increased cuboid epithelial cells in normal size with eozinophilic cytoplasm (H and E; ×400).

fants aged <2 years. At the mean rate of 0.2–0.6%, CPT constitutes 4%–12% of the tumors seen in childhood. In adults, the majority of CPT are in the <40 years age group, and at equal rates in males and females[1-4]. CPT has a tendency for localization as lateral at the rate of 50%, fourth ventricle at 40% and third ventricle at 5%. In pediatric cases, CPT is usually located in the lateral ventricle atrium, the trigone, the temporal horn, and close to the foramen Monroe. Occasionally, it spreads to the third ventricle, extraventricular parenchyma, cerebellopontine angle, cerebellar medullar cistern, supracellar cistern, foramen magnum, or the spinal subarachnoid space, and very occasionally, there may be bilateral ventricular localization[1,5].

CPT are classified in four groups, according to histological and biological characteristics, ranging from well-demarcated benign hyperplasia and papilloma, to highly anaplastic, infiltrative carcinoma.

1. Diffuse villous hyperplasia (DVH) of the choroid plexus (WHO Grade I) which does not comprise a tumoral structure filling the lateral ventricles and third ventricle. Differentiation of this lesion as areal tumor or a simple hypertrophic choroid plexus is difficult (Fig. 1)
2. Choroid plexus papilloma (WHO Grade I) (Fig. 2)
3. Atypical choroid plexus papilloma (WHO Grade II) (Fig. 3)
4. Choroid plexus carcinoma (WHO Grade III).

In CPT, there may be findings of increased intracranial pressure (ICP), focal neurological symptoms, and in childhood, additional macrocephaly, fontanelle swelling, lethargy, and irritability[1,6,7]. Diagnosis is made from computed tomography (CT) and magnetic resonance imaging (MRI). On CT, the image ranges from isointensity to hyperintensity. A mass may be seen as non-specific spherical, multilobular,

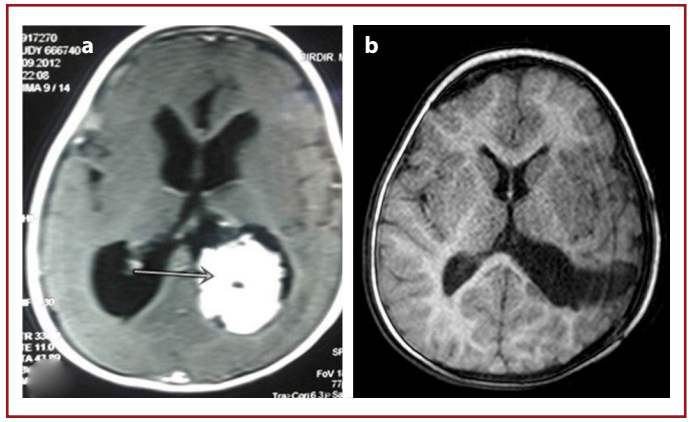

Figure 2. CPP **(a)** pre-operative MRI, **(b)** post-operative MRI at the 7th year.

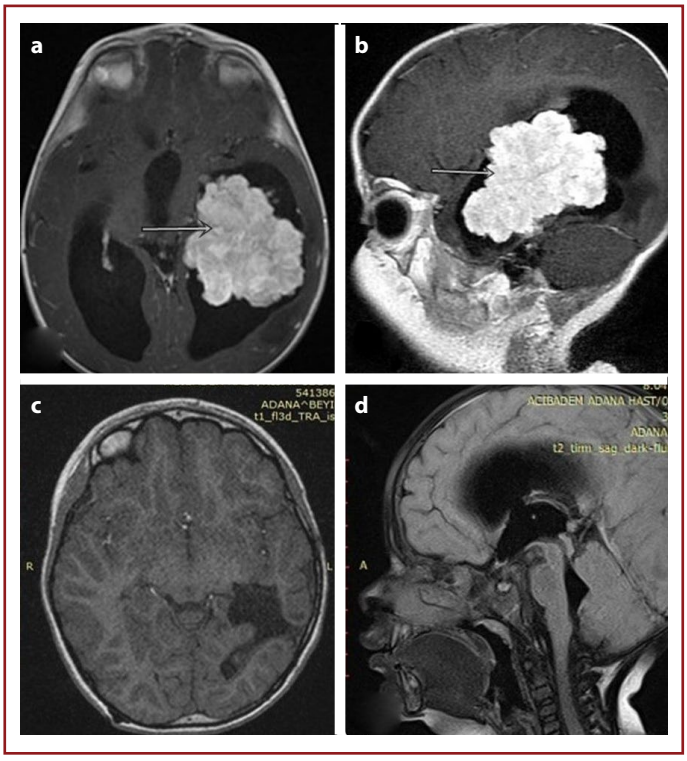

Figure 3. aCPP **(a, b)** pre-operative MRI, (c and d) post-operative MRI at the 3th year.

or cystic, the majority are calcified, and occasionally, there may be spread to other ventricles and cisterns. On MRI, on T1-weighted images, the mass has an image which is isointense or slightly hypointense, and on T2-weighted images, hyperintense lobulated homogenous various patterns are observed. With gadolinum administration, intense nodular and peripheral enhancement is seen. Detailed anatomy, detailed vascular supply with a serpentine signal, and enlarged blood vessel supply can be seen on MRI[8,9]. To reduce vascularity before the treatment of gross total resection (GTR) operation, chemotherapy, radiotherapy, endovascular feeding occlusion, and ventriculoperitoneal shunt can be applied to provide shrinkage[5,9]. The aim of this paper was to present and discuss the surgical treatments, clinical and neurological findings, pathology reports, and complications of a total of 14 patients operated on between 2000 and 2020. The patients comprised 11 children and third adults. In one of the pediatric cases (Case 11), DVH was localized in the right and left lateral and the third ventricle. In one of the adult patients (Case 12), there was a collision tumor of CPP localized in the right lateral ventricle and a pilocytic astrocytoma in the surrounding parenchyma.

Materials and Methods

A total of 14 patients who underwent surgery between 2000 and 2020 were included in the study. We conducted this study by retrospectively scanning patient data. These 11 pediatric cases and three adults, with 10 CCP, 2aCCP, 1 DVH, and one collision tumor of CPP and pilocytic astrocytoma, were evaluated in respect of diagnosis, symptoms, treatments, and histopathology. The mean age of the pediatric patients was 8.6 months (range, 2–12 months) and the mean age of the adults was 38.3 years (21–58 years). In the pediatric cases, supratentorial localization of the tumor was on the left in seven cases and on the right in three. In the pediatric case with DVH (Case 11), localization was left and right lateral and in the third ventricle. In the adult cases, localization was in the fourth ventricle in one case (Case 14), in the posterior fossa of the right PCA in one case (Case 13), and supratentorial localization in the right lateral ventricle in one case (Table 1).

Table 1. Demographic data of the patients and their distribution according to the cases

Diagnosis	n	F	M	Children		Age		Operation				
				n	Month	n	Adult	n	Semptoms		n	Postop
CPP	10	3	7	9	8- 6	1 (14. Case)	43	10 4 2 2	-ICP -POA -Papliedema -Seizures	-Transcortical -Superior temporal sulcus - Posterior Fossa	2	V.P Shunt
aCPP	2	1	1	1	10	1 (13. Case)	58	2 1 2	-ICP -Seizures -Papiledema	-Transcortical - PCA Posterior fossa medio lateral		-V.P. Shunt -Hematoma at the operation lodge V.P shunt
DVH	1		1	1 (11 Case)	4					- V.P Shunt - Transcallozal		V.P Shunt Kontrolu
Collsion Tumor	1		1			1 (12. Case)	21		- Seizures	- Transcortical		- SRS

All the cases were followed up with CT preoperatively and in the early post-operative period, and with MRI in the late post-operative period. GTR with a superior temporal sulcus approach was applied to all the tumors located in the lateral ventricle. In one adult case (Case 12), after GTR of the CPP in the right lateral ventricle, with the thought that there was cerebral parenchyma infiltration, subtotal resection was applied. The pathological diagnosis of the infiltrated section was reported as pilocytic astrocytoma, and the patient was evaluated as collision tumor. On the post-operative MRI, the mass was determined to have infiltrated the corpus callosum. Follow-up was applied with stereotactic radiosurgery (SRS) (Fig. 4).

In the case with DVH, first a VP shunt was applied and the findings of increased ICP continued so, with a trans-callosal approach, first the right then the left septum pellucidum were opened and the hyperplastic plexus was removed by bipolar coagulation. Plexectomy was then performed by entering the third ventricle from the right Monro foramen. The shunt end in the right lateral ventricle was cleaned and left in place, and ventricular drainage was performed for 1 day from the right lateral ventricle. In the case with CPP located in the fourth ventricle (Case 14), GTR was performed by opening the vermis with a median incision, and in the case with aCPP with the right PCA, localization (Case 13) access was gained with a mediolateral incision.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS vn. 17.0 software (SPSS Inc., Chicago, IL, USA).

Results

In the histopathological evaluation, 11 CPP, 2 aCPP, and 1 DVH were determined. Findings of increased ICP were predominant in the pediatric cases, which had a mean age of 8.3 months, and mean head circumference of 45 cm. Epilepsy was present preoperatively in three cases; in two of these cases epilepsy recovered postoperatively and in one case, epilepsy continued for 3 days in the post-operative period. At the 1-month post-operative follow-up examination, a VP shunt was applied to two cases as ventricular dilatation continued. Papillary stasis was determined in one case and primary optic atrophy in four cases. Ocular findings other than optic atrophy recovered after 1-month postoperatively. In case 12 with a collision tumor, epilepsy was present preoperatively but was not seen postoperatively. SRS was applied to the residual pilocytic astrocytoma infiltrating the corpus callosum. In case 13 with PCA local-

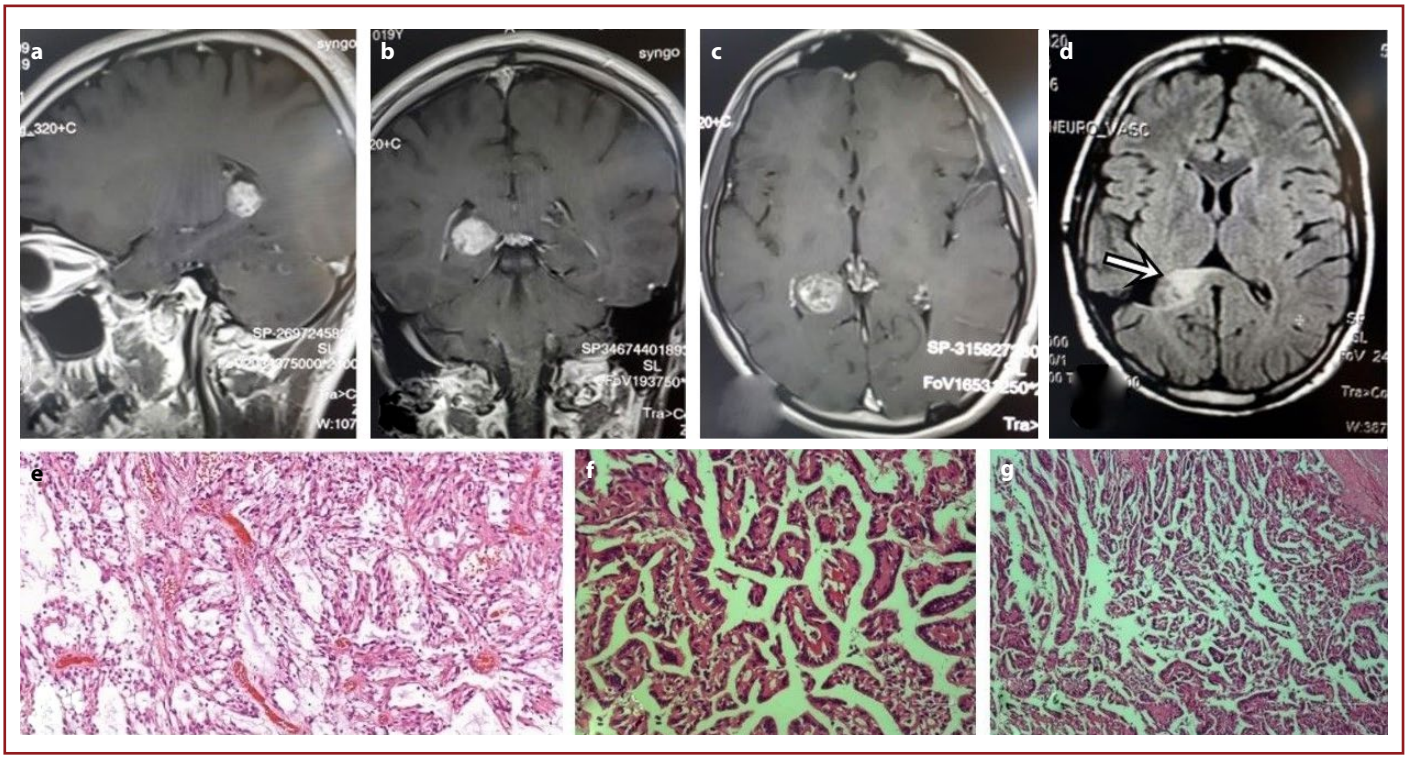

Figure 4. CPP and pilocytic astrocytoma **(a-c)** pre-operative MRI, **(d)** grosstotal CPP resection and residive pilocytic astrocytoma infiltrating corpus callosum, **(e)** the tumor is composed of piloid astrocytic cells. The cellularity is moderate, mitotic activity is low (×16, H and E), **(f)** CCP: H and E stain: papillary epithelial structures with bland cytology, **(g)** CCP IHC: S100 positivity.

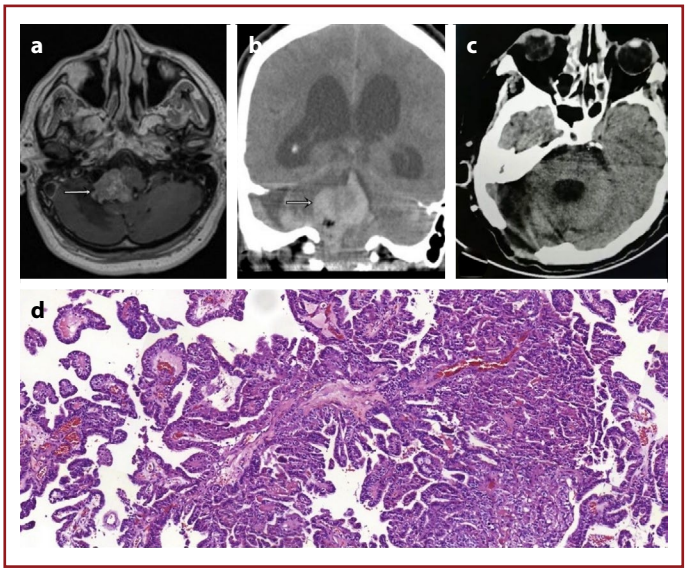

Figure 5. (a) Pre-operative aCPP MRI, **(b)** extensive hematoma at the operation area filling cisterna magna and growing into the spinal canal through foramen magnum, **(c)** post-operative CT at the 6th month, **(d)** the papillary configuration of the choroid plexus neoplasm is mostly retained, although there is small foci of solid component. Three mitotic figures were encountered in 10 high power field (×8, H and E).

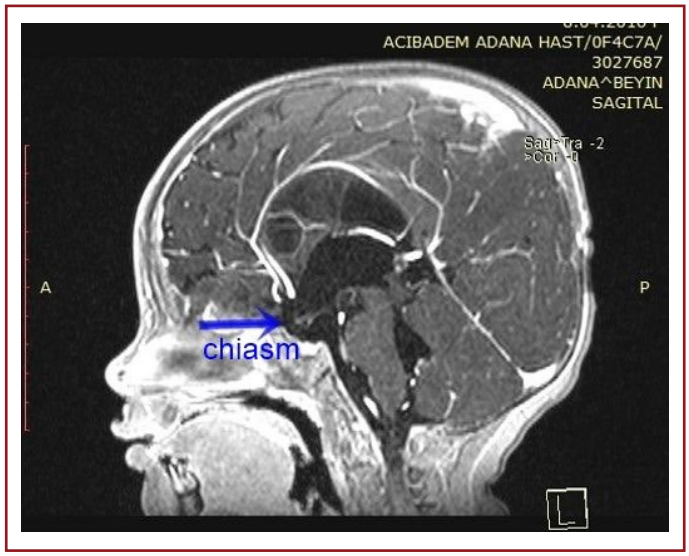

Figure 6. View of the chiasm on MRI, sagittal sections.

ization, SRS had been applied 10 years previously as it was assumed to be meningioma, but it was not effective and tumor growth continued with the emergence of papillary stasis, imbalance to the right, dysmetria, dysdiadochokinesia, and hearing loss. On post-operative day 3, right hemiparesis and respiratory difficulty developed, and surgery was performed again on the hematoma determined in the right upper cervical and PCA region. The hematoma was cleared by removing the lateral third of the cerebellum. At the follow-up examination 1 month later, VP shunt was applied as hydrocephalus was determined (Fig. 5).

In an adult patient with fourth ventricle localization (Case 14), with the exception of headache and papillary stasis, there were no other findings. This patient was discharged on the post-operative 4th day and the 1-month follow-up examination results were normal.

Discussion

In the literature, cases with CPT diagnosed on ultrasound in the prenatal period are accepted as congenital in origin. Signs of increased ICP, delayed mental development, hyrocephalus resistant to shunt, diencephalic findings, bobble head doll syndrome, seizures, vomiting, dehydration, and subarachnoid hemorrhage (SAH) are often in infancy and childhood. In adults, the predominant findings are seizures, focal neurological deficit, increased ICP, ataxia, and vomiting[3,10-12]. With the exception of case 12, findings of increased ICP were present in all the present study cases. In all the pediatric cases, there was ventricular dilatation associated with communicating type hydrocephalus, suggesting that it could be associated with over-production of CSF, limited outflow, decreased absorption, increased protein concentration in CSF, SAH, and tumor internal bleeding. In the adult cases 13 and 14, there was hydrocephalus associated with fourth ventricle obstruction. Although the ventricle became smaller postoperatively, in the 1st month ventricular expansion continued in two pediatric cases and adult case 13, so VP shunt was applied[5,7,11,13]. In case 11 with DVH, VP shunt was applied preoperatively, and was continued postoperatively. Papillary edema is observed much more frequently in children than in adults. However, in the current series, papillary stasis was present in two of the three adult cases and in one of the 11 pediatric cases. POA was present in four pediatric cases. Papillary edema is rarely seen in infants because of the soft skull. All the pediatric cases in this series were aged <1 year. As the head grows in an infant, cerebral spinal fluid (CSF) is pushed to the spinal subarachnoid space with swelling of the fontanelle, and ICP may be compensated by compression of the veins and orbita. The mechanism of the remote effect of distant tumors on the chiasm usually consists of the formation of hydrocephalus of the third ventricle with the dilated anterior wall causing damage to the chiasm through pressure from above. Thus, POA may develop (Fig. 6)[14,15].

Case 12 presented with the complaint of epilepsy and epilepsy was present in a total of three pediatric patients. In the patient with aCPP, epilepsy continued for 3 days postop-

eratively, and recovered at the end of 1 month with the administration of anti-epileptic drugs. In case 12 with collision tumor, the administration of anti-epileptic drugs was continued as the pilocytic astrocytoma was partially removed. In the diagnosis of CPT, ultrasound, CT, and especially MRI are currently preferred. Calcification is more evident on CT but MRI is considered superior because of the three-dimensional images showing anatomy and vascularization in detail. Proton magnetic resonance spectroscopy and MRI spectroscopy are important for the differential diagnosis of CPP and CPC. In CPC, choline and lactate are extremely high. CPC is invasive in character. Diagnosis of CPP and CPC must be differentiated from ependymoma, meningioma, neuroepithelial tumor astrocytoma, germinoma, teratoma, xanthogranuloma, pseudo tumor, and metastasis[2,8]. Case 13 had undergone brain MRI 10 years previously because of reduced hearing level in the right ear, and as the right PCA meningioma 0.5×1×1 cm in size was reported, SRS was applied without a biopsy being taken, and there was no follow-up. When the mass reached dimensions of 4×5×4 cm, papillary stasis developed in the head and with cerebellar findings, it was again thought to be meningioma. Surgery was performed and the histopathology examination was reported as aCPP. GTR is the most important prognostic factor in CPT. In tumor recurrence, in addition to histological grading, subtotal resection is of great importance in respect of invasion or infiltration of the tumor to the brain[16]. Hosmann[17] observed parenchymal infiltration in 32.2% of CPP cases. Recurrence is seen at rates of up to 25% especially if there is an infiltration zone around the tumor. GTR was performed in all the present cases and parenchymal infiltration was not observed in any case. There was an appearance similar to parenchymal infiltration around the CPP in case 12. This surrounding tissue was removed subtotally and the pathology diagnosis was reported as pilocytic astrocytoma. The operations were performed with a transcallosal or transcortical approach according to the tumor localization, vascular supply and the preference and experience of the surgeon. The localization in the majority of cases was reached by opening the superior temporal sulcus to the lateral ventricle, while protecting the supramarginal and angular gyruses[16-19]. In case 11 with DVH, the left ventricle was reached by opening first the right then the septum pellucidum with an anterior transcallosal approach, then GTR of the tumor was performed by entering the third ventricle from the right Monro foramen. In case 14, the tumor was reached with a posterior fossa median incision and in case 13 with a mediolateral incision and craniectomy. These tumors are highly vascularized and embolization can be applied after 3 years of age to prevent bleeding, and chemotherapy can be applied to shrink the tumor. In this way, the tumor can be shrunk by 30%. However, this method was not used in the current series as the vast majority of the cases were younger than 3 years[2,11,12,18]. The gross appearance of the tumor is a soft, pink, and globular mass with irregular projections. As the tumors are large, fragile, and could easily bleed, vigorous manipulation seems unwise. During mobilization, the arterial supply may be disrupted before visualization, so in this series, some parts of the tumor were coagulated to be able to easily remove it piecemeal (Fig. 7)[5,9].

As ultrasounic suction increases bleeding, debulking was not applied to any patient in this series. Bleeding was easily prevented by compressing bleeding areas with cotton swabs. The patients were monitored together with neuroanesthesiologists, neuroradiologists, and pediatric neurologists. Blood loss was replaced and hemodynamic stability was ensured. To prevent coagulation problems, fresh blood and red blood cells were used for replacement therapy as solutions without blood products such as dextran, and crystalloid could not be used[4,11,20]. DVH is known to be quite rare, and to the best of our knowledge, although there are 19 cases in the literature, there is no reported case of DVH originating from the third ventricle, but only of CPP in the lateral ventricles expanding to third ventricle and subarachnoid space. These cases may still be misdiagnosed as the more frequently seen bilateral CPP. On MRI, bilateral CPP is seen as asymmetrical widening, a lobular cystic appearance, finger-like invagination of the parenchyma, and significant contrast enhancement (Fig. 1). In histopathology, CPP has the characteristic features of papillary fronds lined by bland columnar epithelium. The absence of mitotic activity, nuclear pleomorphism, and necrosis distinguishes it clearlyfrom aCPP and CPC. DVH is differentiated from CPP not by the histopathological features, but by dense and homogenously enhanced lesion and exces-

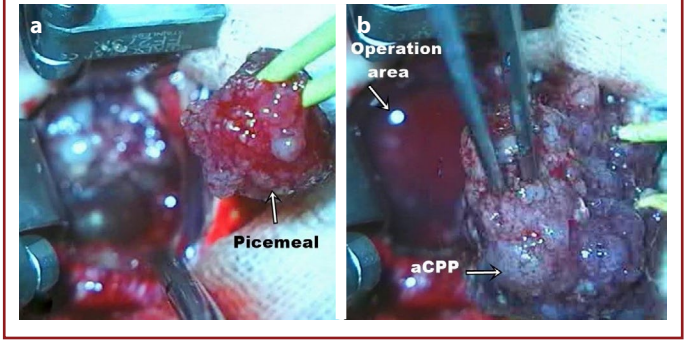

Figure 7. (a) Removal of the picemeal, **(b)** operation area and aCPP.

sive hydrocephalus on CT, and this usually resolves after GTR[1,16,20,21]. Definitive diagnosis is made with pathology examination. The presence of basal lamina, cyto keratin, S 100, and vimentin transthyretin positivity indicates CPP. Epithelial membrane antigen and glial fibrillary acid protein are generally negative[18]. The MIB labeling index is 0% in normal choroid plexus, 0.2% in CPP, 0.5 % in DVH, 3% in aCPP, and 4.14% in CPC. Ki 67and P53, are high in CPC, low in aCPP, and very low in CPP[17]. The DNA structures of DVH, CPP, aCPP, and CPC are similar and resemble the SV 40 virus, which is considered to contribute to the formation of this tumor through anaplastic transformation to CPC. In DVH, CSF drainage of 1800 cc/day is necessary for VP shunt as it surpasses the absorption capacity of the peritoneum. When these procedures are inadequate, ventriculoatrial shunt results in cardiac failure. In cases with DVH, endoscopic coagulation is applied to the hypertrophic choroid plexus, as enlarged feeding vessels are derived from the anterior and posterior choroidal artery, but when this is insufficient, an additional VP shunt is essential[1,6,7,11]. DVH was first reported by David[20] in 1924; plexectomy was recommended and high morbidity and mortality rates due to bleeding were reported. In 2008, Cappabianca[22] demonstrated dramatic shrinkage in DVH following endoscopic coagulation of feeder vessels and reported that the choroid plexus could be easily removed[10,12]. Halaert[11] performed plexectomyand observed hemiparesis and visual field defect. Tambuarini[23] coagulated the choroid plexus but as no improvement was observed, plexectomy was performed. In a study by Çataltepe[13] unilateral choroid plexus coagulation and VP shunt were applied, but this was seen to be inadequate, so plexectomy was performed. In the current series, plexotomy was performed with a transcallosal approach considering that choroid plexus coagulation could be inadequate in respect of the surgical aim of GTR without neurological deficit. When operating on infants, maximum attention is essential to prevent hypothermia, hypovolemia, and anemia and preserve mental and physical development[1,5,21]. Coagulation can be easily performed with light compression using cotton swabs rather than allowing the blood to leak from the tissue. As the tissue was highly fragile and was easily separated from the tumor following coagulation, there was no requirement for coagulation of the feeder vessels (Fig. 7). With the exception of the exit point of the feeder vessels, the anterior and posterior choroidal arteries were healthy and no complications developed postoperatively, and the signs of increased ICP were resolved. Plexotomy can be considered an essential therapeutic procedure in DVH and is also advantageous for a histological definitive diagnosis[7,16,20]. The three adult cases in this series were all male. Case 14, who was 43 years old, with fourth ventricle localization, had no findings other than papillary edema. The tumor was thought to be ependymoma and GTR was performed. The patient was discharged on postoperative day 4, the pathology examination was reported as CPP, and no complications developed. Case 13, who was 58 years old, with the right PCA localization, had been applied with SRS 10 years previously, had not been followed up and tumor growth had continued. With the complaints of decreased hearing, loss of balance, and headache, MRI was performed and a meningioma, 4 × 5 × 4 cm was reported. There was papillary edema and GTR was applied to the tumor. On post-operative day 3, hemiparesis developed in the right arm (cervical sign)[15]. On CT examination, there was seen to be extensive hematoma in the operative area, filling the cisterna magna and extending to the spinal canal through the foramen magnum. The hematoma was drained by removing the outer third of the cerebellum. The patient was admitted to the Intensive Care Unit and respiration was monitored for 10 days, then the patient was discharged with no deficit. At the 1-month follow-up examination, the ventricles were observed to have widened so VP shunt was applied. The pathology examination reported a diagnosis of aCPP. The application of SRS 10 years previously had not prevented tumor growth and bleeding. In the highly vascularized stroma aCPP operation, although the widespread bleeding in the form of oozing leakage was completely stopped, hematoma developed postoperatively (Fig. 5).

Kim[24] reported that recurrence occurred in 11 patients resistant to treatment, and with the application of SRS, the tumor became stable in four cases, and there was observed to be progression in seven. In case 12 of the current series, on MRI examination following an epileptic seizure, a mass was determined in the right lateral ventricle, infiltrat-

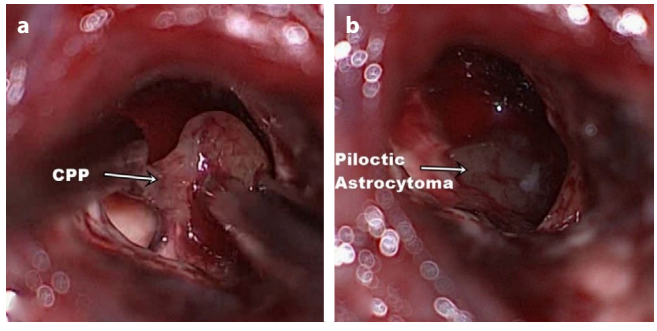

Figure 8. (a) CPP, **(b)** Pilocytic astrocytoma at the paranchym following CPP removal.

ing the surrounding parenchyma. GTR was applied to the CPP mass, and the parenchyma infiltration was removed subtotally. The histological diagnosis of the infiltration in the parenchyma was of pilocytic astrocytoma. It is extremely rare for more than one primary intracranial tumor of different histology to coexist in the same patient (Fig. 8) [22,25-27]. Of these coexisting intracranial masses, collision tumors are defined as two separate growths which have developed simultaneously either in close proximity or even within the same lesion. The majority of those cases have been seen after radiotherapy or are associated with familial tumor syndrome[22,28]. Collision tumors may be seen in cases of trauma, immunodeficiency syndrome, onco-viral infection, and metaplastic or hormone-induced proliferation. However, none of these conditions were present in case 12 (Figs. 4 and 8)[26]. In rare cases, brain tumors might increase the frequency of cell transformation through an irritant effect on the surrounding tissue and this might give rise to the development of a new tumor[28]. In the postoperative follow-up examinations of case 12, residual pilocytic astrocytoma was determined to have infiltrated the corpus callosum, so SRS was performed and close monitoring was started.

GTR is the optimal treatment for CPT, SRS is not highly effective, and if there is no infiltration to the parenchyma, the likelihood of residue is low. Secondary tumors may develop with the irritant effect on the surrounding parenchyma. Papillary stasis is seen more often in childhood than in adulthood, but is uncommon in infancy. POA may be caused by chiasm pressure of the anterior wall of the third ventricle which has expanded associated with hydrocephalus.

Ethics Committee Approval: We conducted this study by retrospectively scanning patient data.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: S.H.; Design: A.S.; Data collection: S.A.; Analysis or interpretation: E.H.; Literature search: M.E.; Writing: A.E.K.

Conflict of Interest: None declared.

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