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Original Article

The microsurgical management of benign pineal cysts: Helsinki experience in 60 cases

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ABSTRACT

Background: Microsurgical resection represents a well-accepted management option for symptomatic benign pineal cysts. Symptoms such as a headache, hydrocephalus, and visual deficiency are typically associated with pineal cysts. However, more recent studies reported over the past years have characterized additional symptoms as a part of the clinical manifestation of this disease and represent additional indications for intervention.

Methods: We present a retrospective review of patients with histologically confirmed benign pineal cysts that were operated on in our department between 1997 and 2015. A demographic analysis, evaluation of preoperative status, surgical treatment, as well as immediate and long-term clinical and radiological outcomes were conducted.

Results: A total of 60 patients with benign pineal cysts underwent surgery between 1997 and 2015. Gross total resection was achieved in 58 cases. All patients except one improved in their clinical status or had made a full recovery at the time of the last follow-up. The key steps for surgical resection of pineal cysts are reported, based on an analysis of representative surgical videos.

Conclusions: We describe in this paper one of the largest series of microsurgically treated pineal cysts. In our opinion, judicious microsurgery remains the most suitable technique to effectively deal with this disease.

Keywords: Microneurosurgery, Pineal cysts, Pineal region lesions, Sitting position, Supracerebellar infratentorial approach

INTRODUCTION

Benign pineal cysts are usually incidental findings on magnetic resonance imaging (MRI). Microsurgical resection represents a well-accepted option for symptomatic benign pineal cysts. [4,15,29] Symptoms such as headache, hydrocephalus and visual deficiency have been described in classic cases. However, more recent reports collected over the past years have incorporated new symptoms as a part of the clinical manifestation of this disease. [4,6,14,16,29]

The supracerebellar infratentorial paramedian approach in the "sitting praying position," a well previously described variant of the classic sitting position, [10] represents our standard route for dealing with pineal region lesions. This approach, together with a judicious microsurgical technique, achieves excellent results with a low rate of complications. [9,10]

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In this paper, we report the surgical outcome of our series of benign pineal cysts encountered in Helsinki, which constitutes one of the largest cohorts investigated, while also describing in detail "tips and tricks" which allow for simple, safe, and effective microsurgical management of these lesions. Moreover, we analyze in detail the surgical indications for pineal cyst surgery.

METHODS

Patient population

We retrospectively reviewed the patients with histologically confirmed benign pineal cysts that were operated on in our department between 1997 and 2015. A demographic analysis, evaluation of preoperative status, and surgical treatment were conducted together with an assessment of immediate and longterm clinical and radiographic outcomes. Finally, the currently available patient information was reviewed in the Finnish Population Registry (as of July 2018) to determine the current clinical status of individuals. Chi-Square test and ANOVA test were used for the statistical analysis of qualitative and quantitative variables.

Pineal cyst surgery

The protocol for surgical treatment of pineal cysts in Helsinki was defined by the neuro-oncological and neurosurgical teams on the basis of the existing literature in 1997, when the senior author (JH) became the chairman of the department. The protocol was subsequently revised according to most recent data.

The following criteria included were used as an indication for surgery: (1) vertical gaze paralysis or double vision of unknown origin with midbrain compression observed in the imaging; (2) obstructive hydrocephalus; (3) cyst growth on sequential imaging studies with 1.5-2 cm as a cut of size to intervene; (4) presence of a solid component suggestive of a pineal tumor; and (5) largest cyst diameter >20 mm, associated to unspecific symptoms such as headache, visual disturbances, psychiatric symptoms, or sensory deficits among others. The threshold size of 20 mm to surgically treat pineal cysts in this last group was determined based on the average size of symptomatic pineal cysts published in literature. [6,16,17,19,33,34]

The goal of surgery was always to achieve a total removal of the pineal cyst. In fact, our and other surgical teams experiences demonstrated that partial resection might still progress to obstruction of the cerebrospinal fluid (CSF) pathway, and it has been reported that puncture of the cyst alone results in less effective treatment.[26]

Positioning and approach

The "sitting praying position" represents our standard position. [9,10] However, few other surgical positions to approach the pineal region in Helsinki Neurosurgery included the lateral park bench position or the supine position in case of endoscopic or stereotactic procedures.[9-11,27]

Risks and benefits as well as the exclusion criteria for the sitting position have been reported on detail previously.[9-11] However, we did not encounter complications related to the sitting position in elderly patients nor patients carrying cardiovascular diseases. Moreover, we especially recommend the sitting position for heavily obese patients.[9,11]

Regarding meticulous surgical access, the reported supracerebellar infratentorial approach is our standard approach. [10] Exceptionally, a suboccipital transtentorial route or endoscopic or stereotactic procedures might be employed in Helsinki Neurosurgery.^[27]

Microneurosurgery

In addition, we carried out a retrospective review of microsurgical videos of the past 22 consecutive cases of benign pineal cysts operated by the senior author (JH), with the aim to identify the key microsurgical steps and potential pitfalls of the procedure. In general, neuromonitoring was not employed for these cases and endoscopic-assisted procedures were not pursued either. Gross total resection of the lesions was achievable in most cases. [9-11]

Ethical aspects and analysis of the data

Following Institutional Ethics Board approval (#HUS/2772/2017), we accessed the hospital register and an authorized coauthor (R.R.) accessed the Finnish Population Register. We collected information about the clinical status, histopathology, imaging, and surgical treatment and follow-up from the medical records. IMPAX version 6.5.5.1608 (Agfa, Mortsel, Belgium) was employed for qualitative radiological analysis. Cranial computed tomography (CT) in patients with head trauma or drowsiness was useful to reveal incidental pineal cysts or acute hydrocephalus, respectively. Preoperative MRI studies were used to describe anatomic features of the cyst such as the size, the presence of solid components, contrast enhancement, midbrain compression, and presence of hydrocephalus. T1-weighted images (slice thickness 3-7 mm), T2-weighted images 5-7 thick, fluid-attenuated inversion recovery (FLAIR), and post contrast T1 MRI sequences had been obtained with spin-echo sequences through a number of 0.2 T, 1T, 1.5T, and 3T MRI machines. Preoperative aqueductal CSF flow measurements by phase contrast MR were not acquired. The cyst size was determined in sagittal anteroposterior dimension (SAPd), in sagittal craniocaudal dimension (SCCd), and in axial width (AW). For the postoperative radiological outcome, we reviewed immediate postoperative cranial CT scans without contrast obtained within the first 24 h, and long-term MRI studies acquired after few weeks from surgery. When postoperative MRI showed complete pineal cyst removal, further MRI studies were performed only if the patient experienced new symptoms.

RESULTS

rankin scale

The characteristics of 60 patients (44 females and 16 males) with a mean age of 29.1 \pm 12.4 (4–55) years, as our cohort of surgically treated pineal cysts, are presented in Table 1. Patients were usually referred from the department of neurology or other hospitals. However, our data analysis was mainly based on the neurosurgical evaluation in Helsinki Neurosurgery and the pre- and postoperative imaging of our department. At the last clinical evaluation, 58/60 patients had improved after surgery of which 49/58 patients were no longer presenting with any neurological deficit. One patient had postoperatively new onset double vision, and one other patient was lost during follow-up. According to the Finnish Population Register, 59 patients in this cohort were alive in July 2018 with a follow-up of 149 \pm 62 (47–244) months. It is possible that the one patient who was lost at follow-up had

Table 1: Characteristics of	f the 60	natients with	surgically	treated ninea	Cycte
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Population	60 patients; Age (years): 29.1±12.4 (4–55); 44 females and 16 males
Symptoms of presentation	Headache 73%, visual disturbances 27% (double vision 12%), nausea-vomiting 19%, vertigo 17%, psychiatric disorders 12%, sensory disorders 10%, memory deficit 8%, balance problems 5%. Other associated symptoms: loss of consciousness, ocular pain, tremor, galactorrhea, dysphasia, muscle cramps, and lack in speech development. 9 pineal cysts patients were minimally symptomatic, 4 of them incidentally found cases.
Bone flap (cm)	Height: 3.9±0.6 (2.5–5.3); Length: 3.4±0.6 (2.1–4.6)
Pineal cyst size (cm)	Length: 1.98±0.7 (1.1–5); Height: 1.34±0.4 (0.6–3.9); width: 1.55±0.4 (0.7–2.9)
Pineal cyst volume (cm³)	$2.7\pm4(0.4-28.3)$
Pineal cyst MR	T1-Weighted compared to CSF: isointense: 20%; Hyperintense: 80%
characteristics (available in 56 cases)	T2-Weighted compared to CSF: isointense to water: 100% of cystic component
	T1 Post contrast: ring enhancement: 49%, solid component: 47%
	FLAIR (available in 41 patients) compared to brain tissue: Isointense: 30, Hyperintense: 9,
	Hypointense: 3
Operative time of the past 22	Skin to skin: mean: 86.7±19 (60–130)
consecutive cases (minutes)	Microsurgery: mean: 24.9±9.8 (9.8–52.17)
Surgical resection	Complete: 58
	Residual: 1
	Stereotactic biopsy and puncture: 1
Surgical approach	Paramedian supracerebellar infratentorial: 29
	Midline supracerebellar infratentorial: 29
	Right suboccipital transtentorial: 1
	Right frontal stereotactic puncture: 1
Number of surgical procedures for	Unique procedure: 55
patient	Ventriculoperitoneal shunt before surgery in other center: 1
	Third ventricle endoscopic fenestration for a small residual cyst: 1
	Biopsy of an aseptic reaction in the surgical bed: 1
	Closure of a cerebrospinal fluid leak: 2
Surgical position	Sitting position: 58
	Park bench position: 1
	Supine position: 1
Postoperative	Postoperative infections: Bacterial meningitis: 4, wound infection: 2
complications	Cerebrospinal fluid leak without infection: 2
1	Aseptic inflammation in operative bed: 1
	Hematoma in the operative bed 1
	Slight double vision: 1
Final status at the last clinical	Symptom free: 49
evaluation * 14.6±30.2 months (0–180)	Improved: 9
,	New slight double vision: 1
mRS at the last clinical evaluation*	mRS 0: 48
	mRS 1: 10 (6 occasional headache, 3 slight double vision, 1 post trauma stress)
	mRS 2: 1 (memory deficit and right-hand clumsiness)
Last follow up in July 2018	Alive: 59
149±62 (47–244) months	Lost at follow-up: 1

changed his/her name and could not be retrieved from the registry according to existing privacy protection regulations.

Most frequently reported preoperative symptom was a headache which showed a variety of characteristics ("exercise headache" after physical activity in some patients, long-term migraine with acute exacerbations for several years before surgery, or intense headaches due to acute or subacute hydrocephalus events in a third group). Visual disturbances were reported with "nonspecific" symptoms, reduction of the visual acuity, and tubular vision. Unfortunately, data from formal neuro-ophthalmology examinations were only partially available for the current project. As mentioned above, only double vision was considered a symptom related to the compressive effect of the tectum. Details about symptoms in our study group are described in Table 1.

Selection criteria for surgery

Indications for surgery are listed in [Table 2 and Figures 1-5]. Forty-one (70%) patients had just one of the five surgical indications considered. The rest of the patients met two or more criteria to qualify for surgery.

Criterion 1 was compressive effect on the tectal plate presenting as double vision. This was the surgical indication in seven patients. However, only a patient, with a pineal cyst and a few

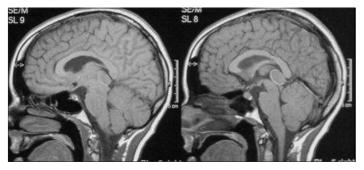


Figure 1: Pineal cyst with a compressive effect on the midbrain.

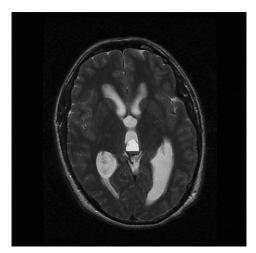


Figure 2: Pineal cyst with obstructive hydrocephalus.

months history of double vision, quickly worsened with a sudden temporary visual deficit associated with headache and was operated due to this specific reason. The other six patients showed more than one criterion that was considered an indication for surgery.

Criterion 2 was obstructive hydrocephalus. This was found in 21 of our patients, and nine of them were operated on for this criterion alone. Only a patient had a ventriculoperitoneal shunt

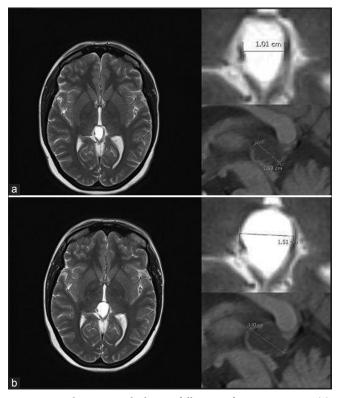


Figure 3: Pineal cyst growth during follow-up, from 1×1.5 cm (a) to $1.5 \times 1.9 \text{ cm (b)}.$

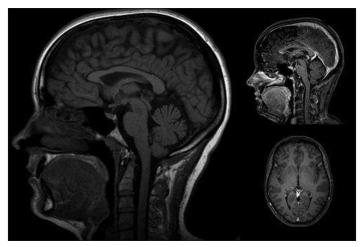


Figure 4: Pineal cyst with the presence of a solid component suggestive of a pineal tumor.

Table 2: Inclusion criteria for pineal cyst surgery: from 60 patients, 42 (In bold) underwent surgery on the basis of only one exclusive inclusion criteria. Another 17 patients had at least two different surgical inclusion criteria. In a patient, information was unavailable.

Inclusion criteria for surgery	N1. Compressive effect on the tectal plate	N2. Obstructive hydrocephalus	N3. Cyst growth during follow-up	N4. Cyst that simulated a solid tumor	N5. Cysts greater than 20 mm with nonspecific symptoms
N1. Compressive effect on the tectal plate	1	4		2	
N2. Obstructive hydrocephalus	4	9		2	3
N3. Cyst growth during follow-up			9	1	
N4. Cyst that simulated a solid tumor	2	2	1	13	3
N5. Cysts greater than 20 mm with nonspecific symptoms		3		3	10
Three cases with multiple inclusion criteria: N5+N4+N2 and N3 more		3	1	3	3
in a case Total	7	21	11	24	19

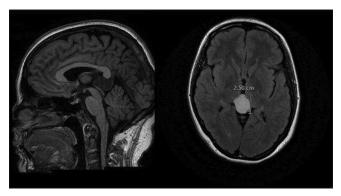


Figure 5: Pineal cyst larger than 20 mm associated with unspecific symptoms.

placed before surgical excision of the cyst. This patient, that still had persistent headache and nausea after a ventriculoatrial shunt without evidence of ventriculomegaly on multiple postoperative CT scan evaluation, required cyst removal for complete recovery and resolution of the symptoms. None but one of the other patients developed hydrocephalus during follow-up or required a shunt after surgical excision of the pineal cyst. One patient with hydrocephalus and a small postsurgical residual cyst subsequently underwent a third ventricle endoscopic fenestration without complications. Finally, one patient who had hydrocephalus preoperatively and who underwent a stereotactic procedure for aspiration of the cyst content did not require any future procedure. Rapidly progressive hydrocephalus events were associated with severe headache, nausea, vomit, double vision, papilledema, and unconsciousness in few days, while patients with less progressive hydrocephalus presented headache, double vision, ataxia, vertigo, incontinence, hand cramps, panic attacks, psychotic symptoms,

sensory deficits, and neurocognitive and memory deficiencies. Only a previously healthy patient was reported to have sudden nausea, vomiting, headache, and visual disturbances in the lateral gaze associated with acute hydrocephalus due to a 1.8 cm pineal

It is worth noting that six patients presented with symptoms associated with physical activity such as moderate to intense exertional headache, vertigo, and nausea. They were considered as cases with probable fluctuant hydrocephalus. The average size of these six cysts was 1.75 \pm 0.18 (1.5-2) cm in SAPd, 1.05 \pm 0.20 (0.7–1.3) cm in SCCd, and 1.36 \pm 0.34 (0.8–1.8) cm in AW. In two cases, data were not available, and in the remaining 13 pineal cysts associated with hydrocephalus, the average size was 2.49 ± 0.96 (1.3–5) cm in the SAPd, 1.62 ± 0.85 (0.9–3.9) cm in SCCd, and 1.92 ± 0.48 (1.4–2.9) cm in AW.

Criterion 3 was cyst enlargement during follow-up and was observed in 10 patients (9 females) with ages ranging between 15 and 37 years old. The average size of the cysts at the last preoperative evaluation was 1.91 ± 0.30 (1.4–2.4) cm in SAPd, 1.27 \pm 0.38 (0.6–1.9) cm in SCCd, and 1.46 \pm 0.45 (0.8–2) cm in AW. The average size of the cysts at the initial preoperative evaluation was 1.58 ± 0.26 (1.2–2.0) cm in SAPd, 1.06 ± 0.25 (0.5–1.3) cm in SCCd, and 1.21 \pm 0.43 (0.8–2) cm in AW. Regarding symptoms in this group, one pineal cyst was incidentally found, and the other two had minor headache. Three patients had depression, numbness in the lower extremities, and visual disturbances with dysphasia and vertigo, associated with headache. All the rest had moderate to severe headache. Patients of this group were followed every 6 months/1 year. The average time between the initial diagnosis and the surgical date was 3.3 ± 2.32 (0.5–7) years.

Six patients met indication criteria for surgery during the past 5 years of the study with an average observation time before surgery of 4 ± 2.4 (1–7) years. The four cases that were operated earlier than 2011 had an average observation period before operation of $2.1 \pm 2 (0.5-5)$ years. This finding reflected the progressively more conservative management of enlarging pineal cysts over the years.

Criterion 4 - 24 of the 60 pineal cysts presented with a solid component. The decision to proceed with surgery was based on a careful case by case evaluation by neurosurgeons and neuroradiologists. 13 (54%) patients with symptoms such as persistent headache, vertigo, dysesthesia, insomnia, changes in the personality, nausea, lack of speech development, galactorrhea, and visual disturbances had a radiographic evaluation concerning for an underlying neoplasm of unclear pathology, and they were operated on mainly due to this reason. The average size of these pineal lesions was 1.62 ± 0.36 (1.1-2.3) cm in SAPd, 1.10 \pm 0.26 (0.6–1.66) cm in SCCd, and 1.32 \pm 0.30 (0.7–1.93) cm in AW. Details about the solid components may be found in the radiological features section and the discussion.

Criterion 5 - 19 patients harboring large cysts presented with rather unspecific symptoms as follows: headache, not well defined visual disturbances, depression, psychosis, disorientation, nausea, memory deficits, balance instability, vertigo, episodic loss of consciousness, exertional headache, periorbital pain, tremor in a 8-year-old patient, and corporal or facial sensory deficits. Some symptoms without correlation to the disease such as epilepsy, hemifacial edema, tinnitus, cervicalgia, and sarcoidosis, were also encountered. The average pineal cyst size in this group was 2.13 \pm 0.37 (1.6-3.1) cm in SAPd, $1.41 \pm 0.32 (0.9-2)$ cm in SCCd, and 1.56 ± 0.41 (0.8–2.3) cm in AW.

Ten patients did not display any other criterion. Seven patients with very disabling symptoms had cyst diameters smaller than 20 mm: in 4 cases, the maximum diameter was 18 mm, 19 mm in 2, and 16 mm in one case.

Table 3 describes the size of pineal cysts according to the different criteria for intervention applied in this series.

Surgical treatment

Gross total removal was achieved in 58 cases. A patient had a small residual cystic remnant that after few weeks compressed and occluded the aqueduct below the tectal plate and required an endoscopic third ventriculostomy, and one other pineal cyst was punctured by a stereotactic procedure with the aspiration of the cyst content without postoperative complications. Most patients were operated on by the senior author (JH). Three patients were operated on by other surgeons, including the one case of the stereotactic procedure in the supine position as a less invasive technique instead of the more demanding microsurgical approach. Two of these cases followed a paramedian supracerebellar infratentorial approach in a sitting position, and a suboccipital transtentorial approach. The supracerebellar infratentorial approach in the "sitting praying position" was chosen as the standard approach.

Before 2008, a straight midline approach was almost always used over the current paramedian supracerebellar route.[10] Under our protocol, a normal weight patient might be positioned in a sitting position in about 5 min as video-illustrated in previous papers.[9,11] As also detailed in a previous paper,[10] thanks to the straight supracerebellar trajectory to the pineal region, intraoperative image guidance was not required. The size of the bone flap of the craniotomy was usually <4 cm in diameter, and the average skin to skin surgical time was <11/2 h, while the average microsurgical time required by the surgeon to open the

Table 3: Pineal cysts size according to the different inclusion criteria applied in this series. ANOVA test, p<0.05 (p value was calculated between the sagittal anteroposterior dimensions of the subgroups measured in milimeters)

	SAPd (cm) Mean±SD (min-max)	SCCd (cm) Mean±SD (min-max)	AW (cm) Mean±SD (min-max)
All PC in the series	1.98±0.7 (1.1-5)	1.34±0.4 (0.6-3.9)	1.55±0.4 (0.7-2.9)
PC with hydrocephalus	2.49±0.96 (1.3-5)	1.62±0.85 (0.9-3.9)	1.92±0.48 (1.4-2.9)
Large PC with unspecific symptoms	2.13±0.37 (1.6-3.1)	1.41±0.32 (0.9–2)	1.56±0.41 (0.8-2.3)
PC with Probable fluctuant hydrocephalus	1.75±0.18 (1.5–2)	1.05±0.20 (0.7–1.3)	1.36±0.34 (0.8-1.8)
PC with double vision	1.97±0.64 (1.4-3.2)	1.36±0.69 (0.9-2.6)	1.71±0.54 (1.2-2.8)
PC with solid components	1.62±0.36 (1.1-2.3)	1.10±0.26 (0.6-1.66)	1.32±0.30 (0.7-1.93)
PC enlargement during FU (last preoperative measurement)	1.91±0.30 (1.4–2.4)	1.27±0.38 (0.6–1.9)	1.46±0.45 (0.8–2)
PC enlargement during FU (initial preoperative measurement)	1.58±0.26 (1.2–2.0)	1.06±0.25 (0.5–1.3)	1.21±0.43 (0.8–2)

AW: Axial width, FU: Follow-up, Max: Maximum, Min: Minimum, PC: Pineal cysts, SAPd: Sagittal anteroposterior dimension, SCCd: Sagittal craniocaudal dimension, SD: Standard deviation

dura, remove the cyst, and perform the hemostasis before closing the dura, was <25 minutes. Finally, an assistant surgeon usually closed the small lateral durotomy under the microscope. Sutures, surgical, glue, and Tachosil were commonly used as needed. However, a synthetic dural graft was very rarely required. The bone flap was repositioned and reaffixed firmly with a titanium clamping system (CranioFix). Suboccipital muscles and the epicranial aponeurosis were closed properly. Surgical staples were routinely used to close the skin wound. Differently, from the midline approach, the morphology of the tentorium did not affect the lateral supracerebellar access in the paramedian approach. Moreover, midline veins draining to the straight sinus are not harmed, but small lateral veins might be coagulated and cut.

Based on the analysis of several surgical videos, we were able to determine some key steps in the surgical resection of pineal cysts as described in Table 4 (Link for a pineal cyst surgical video http://surgicalneurologyint.com/videogallery/pineal-cyst/).

Pathophysiology

All cases in our cohort had histological confirmation of benign pineal cysts (WHO I) by an experienced pathologist. As reported in literature, histologic features were characteristic for inner glial tissue surrounded by outer pineal gland tissue. The cyst cavity was usually unilocular or multilocular without epithelial lining. Fibrillary astrocytes were immunopositive for antibody stains to glial fibrillary acidic protein (GFAP) and S100 protein. The peripheral pineal cells were positive to synaptophysin and neurofilament protein. A small interstitial component of the pineal cells was positive for GFAP and S-100 protein.[33] Chromogranin stain, which is positive in most pineal parenchymal tumors, does not demarcate pineal cysts [Figure 6].[36]

Radiological characteristics

A CT scan was usually the first examination performed in head injured patients and acute hydrocephalus cases. Nevertheless, MRI remains our gold standard for both initial assessment and follow-up imaging. MRI was available in 56 cases. Most of the pineal cysts had a typical MRI appearance of a well-defined T1-hyperintense and T2isointense round-shaped lesion, with homogenous interior signal characteristics, a rim of contrast-enhancement with <2 mm wall thickness, and no infiltration of the surrounding structures [Figure 7].[3,7] Around 50% of the pineal cysts presented as lesions with fine rim enhancement after intravenous contrast administration, and five patients presented fluid-fluid level on axial MRI sequences. Forty-one patients had FLAIR MRI sequences, where we identified three different cystic content appearances compared to the brain tissue: (a) an isointense image in 30 cases, where a large number of them resembled the gray matter and others matched similar aspects to the white matter or mixed components. Five of these cases tended to be hyperintense; (b) a clearly hyperintense aspect in 9 cases, and (c) a hypointense appearance in 3 cases, one of them

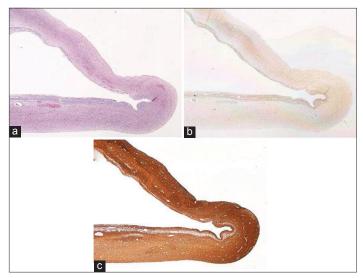


Figure 6: Microphotographs of a surgically treated benign pineal cyst. (a) Hematoxylin and eosin stain, (b) chromogranin stain, and (c) glial fibrillary acidic protein stain.

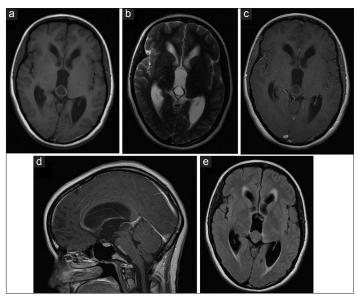


Figure 7: Classic MRI appearance of a benign pineal cyst. (a) T1-hyperintense lesion compared to CSF in axial view, (b) T2-isointense lesion compared to CSF in axial view, (c) ring enhancement lesion after intravenous contrast administration in T1 axial view, (d) ring enhancement lesion after intravenous contrast administration in T1 sagittal view, and (e) isointense lesion compared to brain tissue in FLAIR axial view.

similar to CSF. Regarding the cysts that enlarged at the follow-up, besides the cyst size and shape, we did not find changes in T1, T2, or post contrast T1 MRI sequences. However, FLAIR sequences obtained in 7 cases, demonstrated ununiformed variations in the cystic appearances between the initial and the last preoperative imaging in five patients.

Stage of the microsurgery	microsurgical resection of pineal cysts. Analysis of 22 conso Cornerstone	Frequency	Instruments
24.9±9.8 min (9.8–52.17)	Cornerstone	of use	mstruments
Dura opening and access to the pineal region 7.3±2.3 min (2.3–12.5)	 Opening of the dura under the microscope to recognize small tears and preventing to damage the venous sinuses Cerebrospinal fluid release before access 	22/22 1 and 10//22	a. Irrigation needle, b. dural forceps, c. dural scissors, d. needle-holder, e. long microscissors, f. scalpel, g. short and
	the quadrigeminal cistern (Cisterna magna – supracerebellar cistern)	1 and 10//22	long bipolar forceps (usually sharp tips), h. short and long thumb controlled suction tube
	3. Careful hemostasis of dural tears with bipolar electrocoagulation	14/22	
	4. Hemostasis of the epidural space with strong dural retraction with vicryl stitches along with the opening. Only 2 cases required surgical and Tachosil to seal the epidural space	22/22	
	5. Suturing of the superior dura opening angles to prevent air embolism and small bleedings	10/22	
	 Wide gap between the tentorium and the superior surface of the cerebellum under the effect of the gravity (11 only after releasing Cerebrospinal fluid) 	22/22	
	7. Straight paramedian access along the superior surface of the cerebellar hemisphere	22/22	
	8. Retractor-less approach (6 cases required coagulation and cut of a superior cerebellar vein close to the tentorium)	22/22	
Dissection and removal of the cyst 11.1±4.8 min (423.7)	 Lateral opening of the quadrigeminal cistern with high magnification along with all the procedure (approximately×15) 	22/22	a. Irrigation needle, b. long thumb controlled suction tube, c. long bipolar forceps (sharp and blunt tip), d. long
	2. Identification of the deep venous system (dark blue colorship). However, in only 15 cases we recognized clearly the precentral, basal or internal cerebral veins	22/22	straight microscissors, e. long small and medium size ring microforceps, f. microdissector
	3. Focused opening of the quadrigeminal cistern	22/22	
	4. Ipsilateral dissection of the cyst following the cleavage plane between the lesion and its vicinity	22/22	
	6. Internal debulking of the cyst	12/22	
	7. Coagulation and cut of fine vessels running on the cyst×s wall	20/22	
	8. Traction of the anterior wall of the cyst with bipolar forceps/ring forceps and harmless peripheral aspiration-dissection of the cyst from de surroundings	22/22	
	9. Opening of the posterior third ventricle and additional releasing of Cerebrospinal fluid	22/22	
	10. Cyst attachment to the internal cerebral veins (in 16 cases strong attachment that required coagulation and cut of part of the cyst's wall)	22/22	
Hemostasis 6.6±5.7 min	No hemostatic procedure	5/22	
(1–18.5)	2. Bipolar coagulation+tachosil-Surgicel	10/22	
	3. Only bipolar coagulation	6/22	
	4. Only Tachosil-Surgical	1/22	
	Water irrigation for confirmation of the bleeding absence	22/22	

As mentioned, 24 lesions showed some solid component among small thickenings of the cystic wall and large fragments of the eccentrically solid portions. The solid components were also characterized by irregular inner limits - one of them even confused as a parasitic lesion - with usually consistent enhancement after intravenous contrast administration. Intracystic septations were also visible in 11 cases, and three patients presented fluid-fluid level on the axial T2 sequence signing the pineal apoplexy.

Outcome

Clinical outcome

All patients except one improved clinically at last follow-up with most showing a complete recovery. All patients except one were functionally independent postoperatively. The one impaired patient remaining unfit to carry out activities due to a persistent though improved memory deficit and slight right-hand clumsiness (modified Rankin Scale 2). No other persistent perioperative complications were encountered. However, during an early postoperative assessment, three Parinaud's syndromes were observed in our patients. Two of them resolved completely, while the third one improved substantially with very minimal residual double vision present at last evaluation 7 months after surgery.

Complications such as postoperative bacterial meningitis (4), wound infection without meningitis (2), and CSF leak without infection (2) were observed in 8 of our patients, with the last case presented in 2005. All cases were successfully managed with antibiotics, though two of them required reoperation. The longterm evaluation of our patients revealed no significant sequelae with only occasional headaches in a few of them.

Radiological outcome

One patient with a small hematoma in the operative bed was managed conservatively. She initially presented with newonset postoperative visual disturbances and depression, which progressively resolved with the resorption of the hematoma. A second patient developed an aseptic granulomatous reaction following an open surgical biopsy. For this, she was treated medically and continued to follow-up.

DISCUSSION

In this paper, we present our microsurgical management of 60 consecutive patients presenting with benign pineal cysts. We assessed our indications and categorized them into specific criteria for pineal cysts surgery, and we evaluated the surgical outcome, and we analyzed the key steps for microsurgery. Table 5 lists the most relevant series (series with >10 pineal cysts) of the surgically treated pineal cyst from literature. [4,15,17,18,25,29-31,33] Similarly to the previously published series, our surgically treated pineal cysts are predominantly encountered in young females between the second and the third decades of life.[22,32,34,44] Four patients were <10 years

old and were operated on due to the solid appearance of their pineal lesion which was suspected to be a solid primary tumor. Moreover, these particular patients presented with double vision or other visual disturbances, language impairment, and one of them had a lesion with a diameter of 24 mm. The retrospective analysis of our radiographic data suggests that pineal cysts with solid components are well-defined round lesions with uniform borders and without infiltration of surrounding structures, compared to other tumors with cystic components harboring undefined borders and nonuniform morphology. However, it may be challenging to determine a precise radiological differentiation between the pineal cyst and cystic pineocytomas, gliomas or even pineoblastomas. [21,13]

As concluded by some authors, despite the advances in highresolution MRI, there are not definite radiological methods to distinguish benign pineal cysts from pineal region malignancies containing cystic components such as pineocytomas, pineoblastomas, germinomas, or mature teratomas. [21,38]

Inclusion criteria for pineal cyst neurosurgery

The symptoms in our surgically treated pineal cyst patients do not differ from those reported in other series: headache being the most common symptom (with or without hydrocephalus) besides other nonspecific symptoms such as numbness, visual disturbances, vertigo, balance disturbances, and memory deficits. Although some symptoms might be clearly explained by hydrocephalus or the compressive effect of the tectum, the association between the symptoms and the cyst becomes hard to define in the absence of ventriculomegaly or Parinaud's syndrome. Radoš et al. hypothesize that CSF can be permanently produced and absorbed inside the brain ventricles, as well as inside the entire CSF system, as a consequence of water filtration and reabsorption through the capillary walls into the interstitial fluid of the surrounding central nervous system tissue. Thus, the obstruction of the aqueduct of Sylvius cannot be the only cause of hydrocephalus development, but the association with other pathological processes that impair filtration and reabsorption of fluids on the capillary level such as bleeding, infection, tumor, and toxic substances, among others.[37] Kalani et al. postulate that intermittent occlusion of CSF pathways may cause small pineal cysts to become intermittently symptomatic. [23] Bezuidenhout demonstrated an inverse correlation between the aqueductal CSF flow and pineal cyst size even in the absence of objective neurological findings or hydrocephalus. Thus, large pineal cysts might already display decreased CSF flow through the cerebral aqueduct in patients with nonevident hydrocephalus. [5] Eide and Ringstad hypothesized that pineal cysts-induced crowding of the pineal recess may compress deep cerebral veins causing a central venous congestion/hypertension syndrome.[14] They demonstrated increased pulsatile intracranial pressure and imaging evidence of central venous hypertension in symptomatic patients with nonhydrocephalic pineal cysts. Thus,

Author	Mean age (min-max) (years)	Number of cases	Average major cyst diameter (mm)	Mean follow-up (months)	Surgical complication	Improvement (cases)	Treatment	Grade of resection
Fain <i>et al</i> . 1994 ^[17]	28.7 (15–46)	24	17	3–120	1 transient ocular deficit, 1 transient Parinaud's syndrome, 1 cerebellar infarction	Nai	23 SCIT, 1SB	GTR: 22
Kreth <i>et al</i> . 1996 ^[30]	30	14	Nai	48.0	Nai	symptom free or improvement: 6	14 SB	Nai
Mena <i>et al</i> . 1997 ^[33]	33 (7–69)	15	20	91.1	1 seizure, 1 death	symptom free or improvement: 12	13 SCIT, 1 OTT, 1 SB	1 recurrence 60 months after biopsy
Hajnsek <i>et al.</i> 2013 ^[25]	Nai	56	Nai	Nai	Nai	symptom free or improvement: 56	56 SCIT	Nai
Kalani <i>et al</i> . 2015 ^[29]	24 (4-47)	18	15	19.1	12 transient disconjugate eye movements	symptom-free or improvement/17	18 SCIT or OTT	GTR: 18
Berhouma et al. 2014 ^[4]	23.5 (7–49)	24	Nai	144.0	2 occipital pseudomeningoceles	Nai	20 OTT, 4EF+third ventriculostomy	GTR: 14, PF 6, EF: 4
Eide and Ringstad 2017 ^[15]	30.9 (16–59)	27	MSR: 20.8, MSF: 16.0, VPS: 16.1	MSR: 2.9, MSF: 6.2, VPS: 3.5 (years)	1 sudden coma four years after MSF of the cyst	improvement or symptom free: 67% (MSF), 17% (VPS), 100% (MSR)	6 MSF (SCIT+ OTT), 15 MSR (SCIT), 6 VPS	4 VPS required ne procedures
Majovsky et al. 2017 ^[31]	39.7 (20–63)	21	18	71.2	1 third ventricular hematoma, 1 wound infection and osteomyelitis (9.5%)	symptom free: 10, improved 10,	21 SCIT	Nai
Fedorko 2018 ^[18]	Nai	12	Nai	Nai	3 transient neurological deterioration	symptom free: 5 Improved: 7	12 SCIT (2 biopsy and fenestration)	Nai
Present series	29.1 (4–55)	60	20	149.0	4 bacterial meningitis, 2 wound infection, 2 Cerebrospinal fluid leak without infection, 1 aseptic inflammation in operative bed, 1 small hematoma in the operative bed	symptom-free: 49, improved: 9, new slight double vision: 1 lost at FU: 1	29 SCIT paramedian, 29 SCIT midline, 1 OTT, and 1 SB (1 residual lesion)	GTR: 58, PI 1, SB: 1

EF: Endoscopic fenestration, GTR: Gross total resection, Max: Maximum, Min: Minimum, MSF: Microsurgical fenestration, MSR: Microsurgical removal, Nai: No available information, PR: Partial resection, OTT: Occipital transtentorial approach, SB: Stereotactic biopsy, SCIT: Supracerebellar infratentorial approach, VPS: Ventriculoperitoneal shunt

symptomatic pineal cysts without hydrocephalus or Parinaud's syndrome would fit such an explanatory mechanism. We did not determine the exact same variables employed in their study; however, the average value of the tectum-splenium-cyst ratio in

our nonhydrocephalic patients with large cysts and unspecific symptoms (Criterion 5) was 0.9 which was comparable to that previous report.[14] This measure expresses quantitatively the risk of compression of the deep venous system, especially the internal cerebral veins with a consequent symptomatic central venous hypertension.

Another indication for pineal cyst surgery was the presence of nonspecific symptoms in the context of a radiographically detected lesion with a solid component. It is well known that pineal cysts frequently contain solid structures and these may even enhance after contrast injection. [8,32,44] Pineal parenchymal tumors may less frequently mimic pineal cysts due to the post contrast enhancement of specific cyst components.^[16,40] In this regard, careful case-by-case evaluation and cooperation between the neuroradiologist and the neurosurgeon are well advised.

During the past years, evidence about the natural history of this benign lesion, which includes spontaneous shrinkage, have led to the development of more stringent indications for the surgical treatment of pineal cysts. [1,4] Al-Holou et al. reported an extensive epidemiological study with a population of 48,417 consecutive patients older than 18 years, who underwent brain MR imaging for a variety of reasons. Pineal cysts ≥ 5 mm were found in 1% of the study population (162 males and 316 females). On follow-up, MR imaging at a mean interval of 3.4 years from the initial study of 151 of these patients who were diagnosed with a pineal cyst, 124/151 pineal cysts remained stable, and only four increased in size, whereas 23 decreased in size. At the time of the initial diagnosis, the mean pineal cyst size was calculated to be 9.7 ± 3.8 mm. Of note, 50% of the pineal cysts were <10 mm in maximum dimension. Interestingly, cysts that were larger at the time of initial diagnosis were more likely to decrease in size over the follow-up interval than smaller cysts. Patient sex, patient age at diagnosis, and the presence of septations within the cyst were not significantly associated with cyst size change on follow-up.^[1]

Interestingly, our results showed that the mean pineal cyst diameters in patients with clinical and radiographic hydrocephalus were $2.5 \pm 0.96 \text{ (SAPd)} \times 1.6 \pm 0.85 \text{ (SCCd)} \times 1.9 \pm 0.48 \text{ (AW)}$ cm. On the other hand, large cysts with unspecific symptoms had a mean size of 2.1 \pm 0.37 (SAPd) \times 1.4 \pm 0.32 (SCCd) \times 1.6 \pm 0.41 (AW) cm and pineal cysts - in patients harboring mainly headache – that increased in size along the years – up to 1.9 \pm $0.30 \text{ (SAPd)} \times 1.3 \pm 0.38 \text{ (SCCd)} \times 1.5 \pm 0.45 \text{ (AW)} - \text{measured}$ initially 1.6 ± 0.26 (SAPd) $\times 1.1 \pm 0.25$ (SCCd) $\times 1.2 \pm 0.43$ (AW).

In this regard, our findings might suggest that pineal cysts have progressive clinical evolution with obstructive hydrocephalus at the latest stage in acute or progressive diseases, with a mean cysts size of 2.5 cm. However, cysts with minimal symptoms such as headache and those cysts that will probably require surgery during the follow up period might initially present with a mean SAPd of only 1.6 cm (1.2 cm at minimum). In contrast to Al-Holou et al., who had in their extensive series a large number of pineal cysts that decreased in size at the follow-up, we hypothesize that once a minimally symptomatic cyst is equal or larger than 1.5 cm, the risk to increase in size, worsening the symptoms, and requiring surgery in the future is high, particularly in people with ages ranging between 15 and 40 years old.[1]

Furthermore, we noted that more conservative management has been adopted in our department over recent years for pineal cysts that are not clearly symptomatic, even if they were growing during the follow-up period. However, we continue to believe that symptomatic lesions clearly meet indication criteria for surgery, and especially tumors with mixed radiographic components should be carefully evaluated in cooperation with the neuroradiologists.

Surgical outcome

Our cohort study is the largest reported series of surgically treated pineal cysts thus far.[4,14,17,25,28,29,30,33] Even though our clinical outcome was overall satisfactory in 59 out of 60 cases, we still encountered a considerable number of postoperative infections and CSF leaks. We believe that the more recent use of the paramedian supracerebellar infratentorial approach instead of the earlier an more traumatic midline approach was the likely relevant factor in this regard [Table 6 and Figure 8]. Microscopic wound closures of lateral durotomies and the more recent use of new dural sealing agents are factors to be considered as well.

Pitfalls in pineal cyst microsurgery

The rather short surgical and microsurgical time of our operative procedures reflect the efficiency of our operative technique. The

Table 6: Postoperative complications related to the approach in 60 pineal cyst surgeries (Chi-Square, p<0.05).

1 , 0 . 1		
Approach	Postoperative complications related to the approach	%
Midline supracerebellar infratentorial approach (number of patients: 29)	Post operative infections: Bacterial meningitis: 3, wound infection: 2 Cerebrospinal fluid leak without infection: 2 Hematoma in the operative bed: 1	28%
Supracerebellar infratentorial paramedian approach (number of patients: 29)	Aseptic inflammation in operative bed: 1 Bacterial meningitis: 1	7%

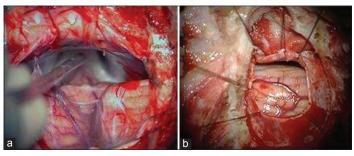


Figure 8: A midline supracerebellar infratentorial approach (a) and a right supracerebellar infratentorial paramedian approach (b).

paramedian supracerebellar infratentorial approach in a sitting position is a standard procedure that was perfected over many the years by the senior author (JH). The key steps of this particular approach are described in detail in previous papers. [9,10]

The pivotal microsurgical steps may be divided into three groups:

- The dura opening and access to the pineal region
- The microsurgical removal of the cyst
- The hemostasis.

All the microsurgical features were meticulously reviewed and optimized according to these three steps. Other authors have also presented general data from their retrospective reviews of traditionally written surgical reports. However, we believe that a careful analysis and review of surgical videos on the topic may reveal some pertinent aspect of the technique that escaped prior reporting. By submitting a link to our surgical recording (http:// surgicalneurologyint.com/videogallery/pineal-cyst/), we this hope to better describe the different steps of the microsurgical removal of pineal cysts.

Future perspectives

This is a retrospective study based on the experience of a single institution over the past 20 years; however, new protocols and new approaches are continuously evolving. Endoscopic procedures have been reported in the more recent literature for the management of pineal cysts. [20,24,26,42] In 2008, the first pure endoscopic supracerebellar infratentorial approach for a pineal cyst was reported.^[23] We remain hesitant to advocate for such minimal invasive approaches, since potential bleeding complications originating from bridging veins and/or highly vascularized lesions may be extremely hard to control in the endoscopic setting. Sometime more recently, endoscope-assisted procedures of the pineal region were introduced. [41,43] In this modification of the approach, surgical instruments for resection are used independently from the endoscope which is positioned over the cerebellar surface to reduce the risks of potential complications. In a recent cadaveric demonstration, we proposed a modified pure endoscopic approach to the pineal region and an incidental apoplectic pineal cyst was completely resected by a supracerebellar infratentorial approach.[12]

Similarly, a variety of stereotactic procedures have been reported. [2,30,35,39] These are minimally invasive procedures, but may be associated with possible cyst re-expansion and with a higher risk of sampling error from the surgical tissue. Kreth et al. published a series of 14 stereotactically managed pineal cysts, but in eight out of these 14 patients, symptoms did not completely resolve.[30] Therefore, the stereotactic treatment of pineal cysts requires further investigation and long-term follow-up data to prove its efficacy.

Our results from this large series demonstrate how the microsurgical management performed particularly under the small paramedian - instead of a midline - supracerebellar infratentorial

approach in a sitting position, is currently our most effective and safest approach symptomatic pineal cysts. Thus, virtually atraumatic procedures with small craniotomies and small dura openings can yield a reduction of postoperative complications. Needless to say, the development of excellent microsurgical skills is required for dealing with these deep-seated lesions.

CONCLUSION

We describe in this paper the largest series of microsurgically treated pineal cysts and report excellent clinical outcomes with our approach. A judicious microsurgical technique is in our eyes the most suitable technique to effectively deal with these benign lesions in a complex location.

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Conflicts of interest

There are no conflicts of interest.

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