INTRODUCTION

Pineal cysts (PCs) are benign intracranial lesions that according to magnetic resonance imaging (MRI) studies account for 1.5–10.8% of the general population.\textsuperscript{12-428}

Accurately defining the natural course of PCs has been challenging due to their predominantly asymptomatic course that results in incidentally discovered lesions which are consequently lost to follow-up. While hydrocephalus associated with PC represents the most common-accepted surgical indication, decision-making in nonhydrocephalic PCs is left to individual clinical
judgment. A growing body of research concludes that nonhydrocephalic PCs can be related to headaches in the absence of hydrocephalus. However, there is no clear consensus on the most suitable clinical approach for symptomatic nonhydrocephalic cysts, nor do standardized guidelines exist for asymptomatic patients.

This retrospective study reports the experience in management of patients harboring PCs at a single neurosurgical center for more than two decades. The purpose of this report is to describe the clinical manifestation and radiographic characteristics of symptomatic patients; to evaluate the surgical results and complications; to define the natural course of PCs that do not require surgical treatment.

MATERIALS AND METHODS

We retrospectively reviewed that all cases of PCs consecutively operated by two senior surgeons Dr Alexander Konovalov and Dr David Pitskhelauri at the Burdenko Neurosurgery Center between 1995 and 2018. Cases were identified using the medical and neuroimaging databases. Apart from surgical cases, we also studied the series of patients managed conservatively (the natural course group). The study was performed with the approval of the ethics committee at the Burdenko Neurosurgery Center. Informed consent for surgery was obtained from all patients.

Surgical group

During this period, we operated on 103 symptomatic patients with PCs [Figure 1]. A confirmed histopathological diagnosis of a benign PC was obtained following operation in all cases. Out of 103 patients, we were able to evaluate long-term clinical outcomes in 71 patients. Among them, 23 presented with obstructive hydrocephalus. Thirty-six had nonhydrocephalic PCs with intracranial headaches, of which 30 were evaluated in our previous report. Twelve patients with nonhydrocephalic PCs underwent surgeries due to PC-imaging characteristics resembling tumor. Thirty-two patients were lost to a follow-up after discharge from the center for reasons mainly associated with contact information shift (n = 29), unexplained death (n = 2), and murder victim (n = 1).

Our primary surgical approach for PCs resection is represented by the supracerebellar infratentorial approach in the sitting position (96% of our cases). The surgical route to the pineal region is opened after a midline linear skin incision, a small suboccipital craniotomy (3 × 4 cm), and a paramedian supracerebellar approach. When possible, PC resection is performed by its cautious detachment from the posterior and habenular commissures with their preservation, unless the tight adherences of the cyst capsule are found.

Neuro-ophthalmological evaluation

Patients were categorized concerning the presence or absence of ophthalmological disturbances. Symptomatic patients were divided into mild and moderate groups depending on the severity of oculomotor and pupillary abnormalities. Patients with moderate ophthalmological disorders revealed on the preoperative examination were considered to be candidates for surgery. Mild disorders included: mild limitation of upward gaze, reduced pupillary light reflex, barely noticeable skew deviation, and no diplopia. Moderate disorders included: upward gaze palsy, eyelid-retraction, absence of pupillary light reflex, skew deviation, convergence-retraction nystagmus, and accommodation disorder. Subjective episodic diplopia alone was not considered as indication for surgery. We used our grading system for initial examination and after surgery in a short- and long-term follow-up period.

Headache assessment in patients without hydrocephalus

Particular caution was given during the initial workup of symptomatic patients with headaches and nonhydrocephalic cysts. None of these patients were offered surgical intervention on their first visit to the hospital. The headache's severity and impact on the patient's daily life were assessed by a team of neurologists and headache specialists. To determine headache impact on everyday life, Headache Impact Test was used. Surgical intervention was considered only in patients who did not experience relief after long-term medication, and other secondary conditions associated with headache were ruled out. When discussing the goals of surgery, technical challenges of the surgical procedure, potential disabilities, and clinical uncertainty in the headache outcome were acknowledged. Patients with different types of migraine, cluster headaches, and tension headaches were not considered as surgical candidates.

Radiological analysis

Available MRI sequences were studied and imaging characteristics were documented. To validate surgery in
patients with nonhydrocephalic PCs suffering from intractable headaches, we used the previously described method of cerebral aqueduct (CAq) morphometrics assessment. For this purpose, we measured the preoperative rostral and caudal CAq diameters and their ratio (Rd/Cd) on a midsagittal MRI.

Natural course group

The natural course group was composed of conservatively managed patients who had at least a 5-year clinical and radiological follow-up. Conservative management was focused on observation or symptomatic treatment with a specific emphasis on identifying the etiology of the headache. We opted for an observational strategy for patients with asymptomatic nonhydrocephalic PCs or clinical symptoms unrelated to the PC. Based on inclusion criteria, a list of 39 patients was generated. We reviewed initial clinical and radiological data for each patient and compared it with the last observation.

Statistical analysis

Statistical calculations were performed using GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, CA). The continuous variables were presented as mean and standard deviation. Categorical variables were described using counts and percentages. Categorical variables in subgroups were explored using Chi-square test. Comparison between continuous variables was made using Mann–Whitney U-test.

RESULTS

Surgical group

Characteristics of the population

Table 1 shows preoperative clinical findings in 103 patients. The male/female ratio was 1:4 (19 male and 84 female); there were 12 children (<18 years) (12%), the ratio of boys to girls was 1:3 (3 boys and 9 girls); the adult/children ratio was 8:1. The mean age was 28.3 ± 10.9 (ranging from 5 to 55 years). The most common presenting symptom was headache documented in 95 (92%) patients. Headache was not specifically localized: in 52 (55%) of the cases, patients noted bilateral diffuse squeezing pain; in 20 (21%) and 14 (15%) of cases, headache was localized in the occipital and temporal regions, respectively. In 9 (9%) of the cases, headache was migratory.

Neuro-ophthalmological examination findings were available in all cases preoperatively. In 79 (77%) patients, the preoperative ophthalmo-gological examination showed no disturbances. Twenty (19%) patients were identified to have mild disorders resulting in light-near dissociation of pupils. Four (4%) patients presented with moderate disorders with upward gaze palsy. In 7 (7%) patients, optic disc edema due to hydrocephalus was documented, three progressed to optic atrophy.

Radiological features

Detailed radiological data analysis was available for 71 patients [Table 2]. Hydrocephalus was present in 23 (32%) out of 71 cases, of which 7 (10%) cases were associated with intracystic hemorrhage. Surgically removed cysts were predominantly large – >2 cm (62%) [Figure 2a]. The average size of PC (1–2 cm) was present in 37% [Figure 2b], while small PCs (<1 cm) were seen in 1% [Figure 2c]. Evans’ ratio, anteroposterior, and craniocaudal cyst diameters appeared to be greater in hydrocephalic PCs when compared to nonhydrocephalic PCs (P < 0.001, P < 0.001, P = 0.04). We found no difference between PC anteroposterior sizes and gender or age (P = 0.64, P = 0.48).

The preoperative computed tomography (CT) scans were available in five cases, of which a thin rim of calcification along the cyst wall was observed in four cases.

| Table 1: Demographics and clinical symptoms of all surgically managed patients. |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Parameter                       | Nonhydrocephalic PCs (n=48) (%) | Hydrocephalic PCs (n=23) (%) | Total (n=103)* (%) | P-value         |
| Age (years)                     | 26.8 ± 10.7     | 27.3 ± 10.3     | 28.3 ± 10.9     | 0.88            |
| Sex: Females                    | 41 (85)         | 18 (78)         | 84 (82)         | 0.7             |
| Symptoms                        |                 |                 |                 |                 |
| Headache                        | 45 (94)         | 22 (96)         | 95 (72)         | 0.74            |
| Episodic loss of consciousness  | 5 (10)          | 0               | 6 (6)           | 0.11            |
| Ataxia and Dizziness            | 22 (46)         | 7 (30)          | 30 (29)         | 0.59            |
| Episodic diplopia               | 3 (6)           | 2 (9)           | 5 (5)           | 0.71            |
| Neuro-ophthalmo-gological findings |                |                 |                 |                 |
| No disturbances                 | 38 (79)         | 13 (57)         | 79 (77)         | 0.13            |
| Light-near dissociation of pupils | 9 (19)       | 7 (30)          | 20 (19)         | 0.3             |
| Upward gaze palsy               | 1 (2)           | 2 (9)           | 4 (4)           | 0.19            |
| Optic disc edema                | 0               | 7 (30)          | 7 (7)           | <0.001          |

*Including 32 surgically managed patients who were lost to follow-up, whose preoperative clinical symptoms were retrieved from the database. Categorization of presenting symptoms based on the presence or absence of hydrocephalus could be performed only in 71 patients who had follow-up.
In 77% of cases, on T1-weighted image, cysts were defined as typical ovoid lesions with smooth margins. It was noted that signaling intensity content was increased in 52 (73%) cases, while 19 (27%) patients’ signaling content was isointense relative to cerebrospinal fluid (CSF). On T1-weighted image enhanced with contrast, 55 (77%) cysts showed typical enhancement with a typical thin rim, while 16 (23%) had irregular margins with numerous intracystic septations and 7 (10%) showed nodular enhancement in the posterior aspect of the cyst. On T2-weighted image, 48 (68%) showed markedly increased signaling intensity and 23 (32%) were isointense relative to CSF. On FLAIR images, PCs appeared hyperintense relative to CSF in 67 (94%) cases and isointense in 4 (6%).

In 27 cases, sagittal FIESTA studies were available. According to this data, the cyst structure was classified into three types previously described by Pastel et al.:[29] in five cases, PCs appeared to lack internal structure and had a thin wall (Type 1); in five cases, there were multiple septations and small internal cysts (Type 2); and in six cases, PCs were composed of a combination of Type 1 and Type 2 (Type 3). In addition, in 11 cases, we identified a new type of PC with a diverticulum [Figure 3]. The diverticulum herniated in the third ventricle between the habenular and posterior commissures. Such herniation obstructed the CAq in six cases and narrowed it in five. The diverticulum was seen on FIESTA sequences and could not be visible on the standard T1-weighted image.

**Surgery and outcome**

Total resection of PC was achieved in all cases, which was confirmed by a postoperative MRI. In 99 (96%) patients, PC removal was performed in the sitting position through the supracerebellar infratentorial approach; 3 cases (3%) were operated through the anterior interhemispheric transcallosal approach; one (1%) patient underwent surgery through the occipital interhemispheric transtentorial approach. In 35 (35%) cases, when approaching the pineal region, 1–2 bridging veins were sacrificed. In 64 (65%), preservation of all bridging veins was achieved. While dissection of the quadrigeminal cistern, the precentral vein was preserved in 94 (91%) cases. In 9 (9%) cases, the precentral vein was coagulated and transected. Following resection of the PC, the posterior commissure was preserved in 63 (61%) cases.

### Table 2: Radiological characteristics of patients in the present study.

| Radiological features | Nonhydrocephalic PCs (n=48) (%) | Hydrocephalic PCs (n=23) (%) | Total (n=71) (%) | P-value |
|-----------------------|---------------------------------|-----------------------------|-----------------|---------|
| Evan’s ratio          | 0.25±0.04                       | 0.34±0.01                   | 0.28±0.02       | <0.001  |
| Anteroposterior cyst diameter (cm) | 2.4±3.6                     | 3.5±5.4                     | 2.7±4.4         | <0.001  |
| Cranio-caudal cyst diameter (cm)      | 1.2±1.3                      | 1.3±0.5                     | 1.2±1.1         | 0.04    |
| Intracystic hemorrhage | 0                              | 7 (30)                      | 7 (10)          | <0.001  |
| Typical appearance on T1-WI with contrast | 34 (71)                | 21 (91)                     | 55 (77)         | 0.05    |
| Atypical appearance on T1-WI with contrast | 6 (13)                  | 1 (4)                       | 7 (10)          | 0.28    |
| Intracystic septations on T1-WI with contrast | 14 (29)               | 2 (9)                       | 16 (23)         | 0.05    |
| Cyst intensity relative to CSF on T1-WI | 15 (31)                  | 4 (17)                      | 19 (27)         | 0.22    |
| Isointense            | 33 (69)                        | 19 (83)                     | 52 (73)         |         |
| Hyperintense          |                                |                             |                 |         |
| Cyst intensity relative to CSF on T2-WI | 15 (31)                  | 8 (35)                      | 23 (32)         | 0.77    |
| Isointense            | 33 (69)                        | 15 (65)                     | 48 (68)         |         |
| Hyperintense          |                                |                             |                 |         |
| Cyst intensity relative to CSF on FLAIR | 2 (4)                      | 2 (9)                       | 4 (6)           | 0.45    |
| Isointense            | 46 (96)                        | 21 (91)                     | 67 (94)         |         |
| Hyperintense          |                                |                             |                 |         |

CSF: Cerebrospinal fluid

**Figure 2:** (a) Midline sagittal FIESTA magnetic resonance imaging showing a large pineal cyst with an intracystic hemorrhage. (b) Midline sagittal FIESTA magnetic resonance imaging showing an average sized pineal cyst. (c) T1-weighted image with contrast-enhancement showing a small sized pineal cyst.
and partially damaged in 4 (4%). The habenular commissure was preserved in 48 (47%) cases and disrupted in 16 (15%) [Figure 4]. During mobilization of the PC, the posterior and habenular commissures were not clearly defined in 36 (36%) and 39 (39%) cases.

The mean discharge time after surgery was 8 ± 3 days. According to KPS scoring, 37 (36%) patients had a 100 score at discharge, 35 (34%) – 90 score, 29 (28%) – 80 score, 1 (1%) – 70 score, and 1 (1%) – 40 score.

The clinical follow-up period was 5.4 ± 3 years (ranging from 6 months to 15 years). Of the 71 patients available for long-term follow-up, headache completely resolved in 44 (62%) patients. Reduction in headache severity and frequency, defined as marked improvement, was observed in 20 (28%). In 7 (10%) patients, headache remained unchanged [Table 3]. Other neurological symptoms resolved in all cases.

Among 36 patients with nonhydrocephalic cysts who were operated on because of intractable headaches, 15 (42%) experienced total relief after surgery and 15 (42%) reported significant headache relief. In 6 (16%) patients, headache remained persistent. Patients with clinical improvement had a significantly lower preoperative Rd/Cd ratio (0.47 ± 0.15) when compared to patients with no improvements (0.75 ± 1.7) (P < 0.001).

Complications

There were no cases of postoperative mortality in our series. Thirty-seven (36%) out of 103 patients had some postoperative complications [Table 4]. Six (6%) patients suffered from minor venous air embolism during the operation, which was not clinically significant. One (1%) patient experienced severe paradoxical air embolism due to air aspiration through the damaged transverse sinus and a patent foramen ovale. Subsequently, he had an embolic ischemic event causing tetraplegia after surgery. One (1%) patient had intraventricular hematoma, which required an external ventricular drainage placement. Five (5%) patients developed meningitis and were successfully treated with broad-spectrum antibiotics. Twenty-four (23%) patients experienced moderate neuro-ophthalmological disorders.

Neuro-ophthalmological outcome

Neuro-ophthalmology examination results were available in 79 patients for the short- and long-term outcome. These examinations were completed first on a postoperative day 1 or 2 and, then on average 8 ± 3 days after surgery, and 4 ± 3 years after surgery [Figure 5a]. Optic disc edema resolved in all cases at discharge.

On postoperative days 1–2, we observed a tendency for a significant proportion of patients to decline in their neuro-ophthalmological status (P < 0.001). Of 62 (79%) patients presenting without initial neuro-ophthalmological disorders, 38 (48%) retained normal pupillary reflex and ocular motility on examination on a postoperative day 1–2; 41 patients deteriorated and had mild (13%) and moderate (39%) neuro-ophthalmological disorders. Transient moderate neuro-ophthalmological disorders in the short-term postoperative period were seen in 9 (11%) patients. We did not observe significant improvements in the neuro-ophthalmological status of patients by the postoperative day 8 ± 3, with a total of moderate disorders seen in 22 (27%) patients. The detailed

Figure 3: (a) Midline sagittal FIESTA magnetic resonance imaging demonstrating a typical pineal cyst. (b) Midline sagittal FIESTA magnetic resonance imaging showing a pineal cyst with the diverticulum, which herniates between the habenular and posterior commissures. (c) The diverticulum of the same pineal cyst is not visible on the T1-weighted image with contrast-enhancement. Abbreviations: arrow, the diverticulum; white arrowhead, habenular commissure; black arrowhead, posterior commissure.

Figure 4: Intraoperative illustration of the pineal cyst resection stage. After the pineal cyst (1) is emptied, its capsule is gently separated from the posterior (2) and habenular (3) commissures preserving their anatomical integrity. The third ventricle is exposed through the pineal (4) and suprapineal (5) recesses.
course of neuro-ophthalmological deficits in patients with moderate disorders in the short-term period is represented in Figure 5b. The most common symptoms at discharge were upward gaze palsy (27%) and skew deviation (17%).

Analysis of neuro-ophthalmological symptoms in the long-term follow-up period showed that most patients had mild (30%) or no deficit (62%), when compared to the short-term outcomes. Of 31 patients with moderate disorders on postoperative days 1–2, symptom resolution was observed in 82% in the long-term follow-up period. Overall, among patients with no neuro-ophthalmological symptoms before surgery, 79% were asymptomatic by the end of the long-term follow-up. The most common symptoms at last follow-up were upward gaze palsy (6%) and skew deviation (5%), followed by convergence disorders (3%) and eyelid-retraction (2%). There were no patients with moderate disorders who did not improve by 5 years after surgery.

Intraoperative injury of the posterior commissure was not associated with the presence of moderate neuro-ophthalmological disorders (P = 0.26). However, we found that patients with moderate neuro-ophthalmological disorders were associated with significantly greater anteroposterior cyst diameter, when compared to patients with mild disorders (21 ± 3.9 vs. 18.8 ±3.6, P = 0.03) and no disorders (21 ± 3.9 vs. 18 ± 5.2, P = 0.02) [Figure 5c]. Similarly, the patients with moderate neuro-ophthalmological disorders appeared to have significantly greater craniocaudal cyst diameter when compared to patients with no disorders (12.4 ± 4.8 vs. 9.3 ± 5.7, P = 0.04) [Figure 5d].

Natural course group

The male/female ratio was 1:3 (9 male, 30 female). The mean age at diagnosis was 35 ± 13.5 (ranging from 5 to 62 years).

The most common presenting symptom was headache (63%, n = 25). Other symptoms included dizziness (n = 6), nausea and vomiting (n = 6), numbness of fingertips (n = 3), tinnitus (n = 2), and memory disorders (n = 2). In all cases, after initial medical PCs were judged to be an incidental finding unrelated to the presenting symptoms. Five patients had reduced pupillary light response. None of the patients presented with moderate neuro-ophthalmological disorders or hydrocephalus. The mean anteroposterior cyst diameter was 1.5 ± 0.4 cm (ranging 0.7–2.4) and craniocaudal diameter – 0.9 ± 0.3 cm (ranging 0.4–1.4). PC size in the natural course group was significantly smaller than in the surgical group (P = 0.001).

The follow-up interval varied from 5 to 15 years, with the mean interval being 7 ± 2.5 years. Headache resolved in 14 (56%) of patients and improved in 11 (44%). Other nonspecific symptoms improved significantly or resolved in all patients. PC enhancement and signaling intensity characteristics did not change in the 39 patients on the last follow-up MRI. PC size remained stable during the follow-up in 34 (87%) out of 39 patients [Figure 6]. Five PCs enlarged in the anteroposterior diameter (3.2 ± 0.8 mm, ranging 2–4), of which in one case CAq obstruction and hydrocephalus developed eventually requiring surgery. The mean age of patients with PC enlargement was 15 ± 7.1 years, whereas the mean age of patients with stable cysts was 26.5 ± 10.1. The patient’s gender or age was not a significant predictor of cyst growth (P = 0.4, P = 0.56).

DISCUSSION

Clinical and radiological features

PC is one of the most common brain lesions diagnosed in predominantly young females and yet accompanied with nonspecific symptoms most of the time. Despite the high prevalence, identification of symptomatic cysts remains an unsolved problem.

Discrepancies in the incidence of preoperative neuro-ophthalmological symptoms occur throughout the published studies on surgically managed PCs, ranging between 2% and 72.5%. Visual symptoms in patients with

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**Table 3:** Headache outcome of patients in the present study.

| Headache outcome | Nonhydrocephalic PCs (n=48) (%) | Hydrocephalic PCs (n=23) | Total (n=71) |
|------------------|---------------------------------|--------------------------|--------------|
| Complete improvement | 15 (42) | 12 (100) | 17 (74) | 44 (62) |
| Marked improvement | 15 (42) | 0 | 5 (22) | 20 (28) |
| No improvements | 6 (16) | 0 | 1 (4) | 7 (10) |

PC: Pineal cysts

**Table 4:** Complications after microsurgical removal of pineal cysts.

| Complications | n (%) |
|---------------|-------|
| Neuro-ophthalmological disorders | 24 (23) |
| Venous air embolism | 7 (7) |
| Meningitis | 5 (5) |
| Intraventricular hematoma | 1 (1) |

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Konovalov, et al.: Pineal cyst management

PCs are mainly subjective and may lead to uncertainties in perception or interpretation by patients. The low incidence of visual abnormalities before surgery in our cohort (23%) is in agreement with the medical literature. In rare cases, PCs can be a source of tectal compression and CAq obstruction, resulting in Parinaud’s syndrome, hydrocephalus, and optic disc edema. In our cohort, we operated on patients who presented with some degree of Parinaud’s syndrome (4%) and hydrocephalus (32%). While these findings are well-established indications for surgical intervention, headaches remain the most common symptom in such patients occurring in 92% of symptomatic cases.

The previous studies deemed large cysts to have the potential to cause symptoms. Our analysis appeared to be consistent with these studies, as the surgically treated patients had significantly larger PCs compared to conservatively managed cases ($P = 0.01$). $^{[20,33]}$

PCs can have an atypical nodular enhancement in 11% of cases. $^{[3]}$ Such atypical signaling was observed in 10% of histologically confirmed cases in our study. Distinctly defining the internal structure of the PCs has been shown to aid in distinguishing cyst features from a tumor. $^{[29]}$ In our study, we evaluated the role of FIESTA for the visualization of the internal structure in PCs. We marked three types of different internal structures, previously described by Pastel $^{[29]}$ et al.

In addition, our analysis of FIESTA sequences discovered a new type of PC, which has never been reported previously in the literature. A feature of this type of PC is that the anterior

![Figure 5: (a) The course of neuro-ophthalmological symptoms in the short- and long-term follow-up periods. (b) Detailed course of neuro-ophthalmological signs among patients with moderate disorders in the short-term postoperative period. Postop, postoperative. (c) Comparison of the antero-posterior PC size to different grades of neuroophthalmological disorders. Bars indicate standard deviations. (d) Comparison of the craniocaudal PC size to different grades of neuroophthalmological disorders. Bars indicate standard deviations.](image)
One patient had a contraindication for the sitting position (n = 10), episodic loss of consciousness occurring in 1 (1%) case, which corresponds to the available literature data. The patient had suffered a wide damage of the transverse sinus and large amounts of air introduced in the circulation. Because of the existing right-to-left shunt in this patient, the air entered the arterial system and induced a bilateral cortical stroke. Subsequently, the patient was discharged with tetraplegia to a rehabilitation facility. Six (6%) remaining cases of the air embolism were promptly managed with teamwork, greatly reduces the risk of air embolism while allowing the surgeon to operate on pineal region lesions with gravity retraction and preservation of normal anatomy. In our study, from 99 surgeries in the sitting position, an episode of severe venous air embolism among patients operated in the sitting position occurred in 1 (1%) case, which corresponds to the available literature data. The patient had suffered a wide damage of the transverse sinus and large amounts of air introduced in the circulation. Because of the existing right-to-left shunt in this patient, the air entered the arterial system and induced a bilateral cortical stroke. Subsequently, the patient was discharged with tetraplegia to a rehabilitation facility. Six (6%) remaining cases of the air embolism were promptly managed during surgery and appeared to be clinically insignificant.

In three cases, the PC resembled a tumor causing hydrocephalus, and thus, an anterior interhemispheric transtentorial approach with a simultaneous microsurgical third ventriculostomy was preferred. One patient had a contraindication for the sitting position because of the patent foramen ovale and was operated on in a lateral park-bench position through an occipital interhemispheric transtentorial approach.

The preservation of bridging veins and the precentral vein was not possible in 35% and 9% of the cases, respectively. Despite this fact, we did not observe any neurological deterioration or cerebellar edema in these patients following surgery.

Neuro-ophthalmological outcome

Since one of the most common post-operative complications in our study was associated with moderate neuro-ophthalmological outcomes, it is important to note that the herniating part of the cyst herniates in the third ventricle above the caudate nucleus. We hypothesize that the herniating part can act as a ball valve, moving in the anterior-inferior direction with subsequent aqueductal stenosis and intermittent obstruction of the CSF flow. It is important to note that the herniating part is barely visible on the common MRI sequences. Given that herniating part may act as a ball valve, patients with this type of PC might experience symptoms related to the intermittent obstruction of CSF. In our cohort, this irregularly-shaped cyst was observed in 11 patients, all of whom presented with severe headaches (n = 10), episodic loss of consciousness (n = 1), and dizziness (n = 3), which resolved immediately after surgery. Therefore, FIESTA sequence is a valuable tool for PC management. The current observation of herniated PCs can aid in further investigations to substantiate the hypothesis.

Surgery and complications

The literature and acceptance for consideration of surgery in patients with hydrocephalus or Parinaud’s syndrome are not in question. The surgical approach to a PC that is large enough to cause hydrocephalus could be dealt with endoscopically or with the use of a microscope. In many cases, endoscopic strategies may include cyst fenestration with or without an endoscopic third ventriculostomy without cyst resection. Most neurosurgical centers, including our own, propose resection of PCs. While the exact degree of PC resection is not established, we usually adhere to a gross total resection. The rationale behind such strategy is to minimize potential recurrence and reoperation. Despite the role of the pineal gland in the circadian rhythms, we did not observe any patients with sleep disturbances either before or following surgery. Possible consequences of a melatonin deficiency after a pineal gland removal may be much more difficult to identify. The reported incidence of sleep impairments in patients with PCs reaches 5–40%.[11,21,23,24,34] However, the fact that sleep disturbances are not constantly observed in this patient group indicates that melatonin deficiency itself may not be the only causative factor. Noteworthy, it was previously concluded on the small sample size that a craniotomy in general, rather than pinealectomy itself, was associated with sleep impairment.[18] Considering that sleep disorders are rarely based on structural lesions, the PC’s relationship to sleep is yet to be revealed.[7]
disorders, we precisely evaluated its course in the short- and long-term postoperative periods. Available studies regarding neuro-ophthalmological outcomes after PC surgery are scarce and do not describe the course of symptoms in the postoperative period.\(^\text{[12,16]}\)

We found that long-term neuro-ophthalmological disturbances were more common and long-lasting than expected. Among patients with no or mild disorders before surgery, 34 (38%) had a marked increase in oculomotor and pupillary disorders on postoperative day 1–2. However, acquired disturbances showed a tendency to partially regress by the time of discharge – on review on postoperative day 8 ± 3. Noteworthy, the most common symptoms at last follow-up were upward gaze palsy (6%) and skew deviation (5%).

We found that moderate disorders were significantly related to the cyst size. Hence, the incidence of postoperative neuro-ophthalmological deficits reported in our study probably reflects the tense adhesion of relatively large PCs to the posterior commissure. Furthermore, surgeon’s diligence to a total resection and the number of manipulations that he performs while detaching the cyst from the posterior commissure may also play an important role in such disorders. The rostral intermediate medial longitudinal fasciculus decussates in the posterior commissure, conveys neuronal interconnections with the interstitial nucleus of Cajal, and is associated with the upward gaze control.\(^\text{[12,35]}\)

Our analysis did not reveal a significant relationship between the partial damage or complete anatomical preservation of the posterior commissure and the severity of postoperative neuro-ophthalmological deficits. Therefore, it can be assumed that the development of neuro-ophthalmological disorders might be caused by the violation of the anatomical integrity of the posterior commissure and its stretching during surgical manipulations. With regard to this, we decided to modify our surgical technique. When surgically managing a typical PC, it is rational to avoid complete resection of the capsule, leaving tiny portions attached to the posterior commissure. Nevertheless, resolution of moderate neuro-ophthalmological disorders can occur in 82% of patients by 4 years after surgery, with convergence disorders being the most long-lasting deficit.

**Headache outcome in non-hydrocephalic PCs**

Patients suffering from intractable headaches have a lower quality of life.\(^\text{[8,19]}\) Thus, surgical resection, if justifiable, could improve the quality of life in patients with non-hydrocephalic PCs. In addition, a better understanding of how surgery affects the mechanism of headache formation could play a significant role in determining which patients should undergo surgery. While the causal relationship between headaches and PC with hydrocephalus is inherent in mechanical obstruction and increased intracranial pressure, the link between headaches and non-hydrocephalic PC is still investigated. Recent popular explanations include compression of CAq and disturbances of the CSF flow.\(^\text{[6,34]}\)

Our previous study, which was conducted in 2016, hypothesized that PC-related CAq stenosis might cause intractable headaches in the absence of hydrocephalus. We described the method for CAq morphometrics measurement and investigated the clinical outcome concerning different aqueduct geometry.\(^\text{[30]}\) Our findings indicated that the configuration of the CAq in patients with clinical improvement regains its diameter in the postoperative period. A similar observation was highlighted in another study, which further supports that headaches in nonhydrocephalic PC can be associated with tectal compression.\(^\text{[14]}\) Since 2016, we have considered the Rd/Cd ratio as an additional tool to support decision-making in such controversial patients, and six more patients underwent surgery subsequently. Despite the <0.56 Rd/Cd ratio was observed in the newly operated patients, only five out of six had significant clinical improvement following surgery. Indeed, this further underscores that the cause of headaches remains a subject of controversy, and even exhaustive workup before considering patients for PC resection may not guarantee clinical improvement. In our cohort of surgically treated patients with nonhydrocephalic PCs and intractable headaches, the clinical improvement rate appeared to be 84%. Comparable symptom improvement rate was documented by other authors being 42.9–100%.\(^\text{[1,22]}\)

**Natural course group**

We found that the majority of patients with PCs remain clinically stable during follow-up, with a complete resolution or improvement in their symptoms. According to our analysis, patients with a newly diagnosed PC remain radiologically stable at least 5 years after diagnosis [Figure 6]. We were unable to identify the specific clinical or MRI features of PCs that would predict cyst growth. It is more likely that PCs in children and adolescents change their appearance than in adult cases.\(^\text{[2,3]}\) However, even cysts that change or grow are likely to remain asymptomatic.\(^\text{[2,3]}\) In contrast to other studies, we did not see a decrease in cyst size or its involution in any patients, which might be associated with an age-related difference within cohorts. PC involution may be observed in older patients.

It is important to note that in one patient hydrocephalus developed after 8 years of follow-up. This observation is an important finding regarding the aspects of PC’s natural course. Initially, asymptomatic PC can grow over the years and cause hydrocephalus.

**Management algorithm**

We have developed a management algorithm based on the patterns and distinguishing features of PCs obtained in the present study [Figure 7].
Patients with atypical MR characteristics of PC, such as atypical contrast-enhancement, irregular cyst shape, a predominance of the solid component over cystic, require first of all, differential diagnosis with lesions of the pineal region. Decision-making in the management of such patients can be addressed through a close follow-up with repeat imaging in 6 months and assessment of tumor markers (alpha-fetoprotein and beta-chorionic gonadotropin). In the cases of radiologically unstable atypical PC (cyst growth or change in radiological patterns) and negative tumor markers, surgical intervention could be considered.

In cases when a patient with nonhydrocephalic PC suffers from headaches, determining the cause of this symptom is paramount. A thorough neurological examination and other specialists aimed at excluding conditions associated with the primary and secondary nature of the headache are fundamental.

In addition, the algorithm addresses the preoperative Rd and Rd/Cd ratio, the two crucial factors in the management of patients with headache and nonhydrocephalic cysts. The first line of management in such patients should be an observational strategy with conservative therapy over a 2–3 month period of time. Resistance to medication during a given period, absence of any conditions associated with headache, and preoperative Rd/Cd ratio of the CAq ≤0.56 is positive indicators for surgical intervention.

Limitations

Several limitations should be acknowledged. The present study has a retrospective nature with an insufficient level of evidence and associated selection biases. Thirty-two surgically treated patients could not be recalled to assess their radiological features and outcome, which introduces the loss to follow-up bias. The prevailing reasons for the loss to follow-up occurred due to the migration of the patients or their “lack of time” to undergo follow-up evaluation (29 patients). In addition, some patients were operated in early 2000s, before the follow-up protocol was established in our center. The dropout rates could severely compromise the study's validity if reluctance to undergo follow-up screening is associated with mistrust due to poor clinical outcomes. Regarding the three patients with a loss to follow-up due to death, the association with surgery is less likely, since all three had KPS 100 at discharge. In addition, there is a selection bias for the natural course group, since only patients without indications for surgery were included in the group. The true natural history of PCs would be determined by a random inclusion of patients with diagnosed PC and subsequent prospective follow-up. Finally, the present population of surgically treated patients overlaps for 30 patients with our previous study on the analysis of CAq diameter. Nevertheless, we believe that this study highlights essential data on developing the right approach to a patient with a newly diagnosed PC.

CONCLUSION

In this study, we attempted to answer a series of questions regarding the symptomology, radiological features, natural course, postoperative follow-up, and complications in patients with PC. Patients with nonhydrocephalic PCs and intractable headaches experience significant relief in headache symptoms, but are at risk of mild-to-moderate neuro-ophthalmological disorders. Still, many aspects of PC's natural course remain unsolved. Further research should focus on prospective clinical trials combined with novel imaging tools.
Declaration of patient consent

Patients’ consent not required as patients’ identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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