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CLINICAL ARTICLE - BRAIN TUMORS

Clinical management of pineal cysts: a worldwide online survey

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Abstract
Background A pineal cyst is a benign affection of a pineal gland on the borderline between a pathological lesion and a variant of normality. Clinical management of patients with a pineal cyst remains controversial, especially when patients present with non-specific symptoms.
Methods An online questionnaire consisting of 13 questions was completed by 110 neurosurgeons worldwide. Responses were entered into a database and subsequently analysed.
Results Based on data from the questionnaire, the main indication criteria for pineal cyst resection are hydrocephalus (90 % of the respondents), Parinaud's syndrome (80 %) and growth of the cyst (68 %). Only 15 % of the respondents occasionally operate on patients with non-specific symptoms. If surgery is indicated, improvement is expected in 88 % of the patients. The vast majority of the respondents favour a supracerebellar infratentorial approach to the pineal region. Most (78 %) of the respondents regarded the patient registry as a potentially useful instrument.
Conclusions This survey sheds light on the current practice of pineal cyst management across the world. Most of the respondents perform surgery on pineal cysts only if patients are presenting with symptoms attributable to a mass effect. Surgery for patients with non-specific complaints (headache, vertigo) is not widely accepted, although it may prove effective. A prospective patient registry might be useful in the decision-making process in the clinical management of pineal cysts.

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Introduction

A pineal cyst (Fig. 1) is a benign affection of the pineal gland on the borderline between a pathological lesion and a variant of normality [1]. Symptoms of patients with a pineal cyst are often non-specific and vague (headache, sleep disturbances, vertigo, nausea, etc.), which makes it difficult to attribute them to the cyst [2]. According to large magnetic resonance (MR) studies, the prevalence of pineal cysts in the general population is 1–1.5 % [1, 3, 4], reaching 2-2.5 % in young adults and decreasing with age. Women are affected more often than men [3, 4].

Lately, we were intrigued by the increasing number of patients that are referred to our outpatient clinic for pineal cysts. However, guidelines for their management are lacking. Asymptomatic patients need no treatment and are subjected to clinical and/or radiological follow-up. Patients presenting with symptoms related to a mass effect of a large cyst compressing the tectum (Parinaud's syndrome) or symptoms related to the hydrocephalus due to stenosis of the aqueductus Sylvii are strong candidates for surgery. Between these two extreme categories lies a "grey zone" of patients that are "oligosymptomatic". Their complaints are somehow non-specific and detecting pineal cysts could be just a coincidence as well as a causative factor. In our opinion, this third group of patients deserves particular attention.

In our own series of 80 patients, we operated on 20 with good results. Only one of these patients had Parinaud's syndrome and none presented with hydrocephalus. In some cases, an indication for surgery was based on patient preference and the experience of the clinician, and not on objective criteria.

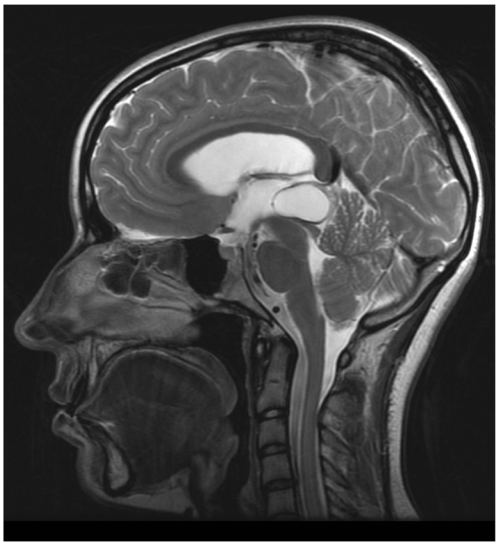

Fig. 1 Sagittal MR imaging of the brain: pineal cyst

We used an online questionnaire to gather expert opinions (level of evidence V) from neurosurgeons worldwide. A goal of our study was not to define one correct algorithm for decision-making, but rather to present the diversity of clinical practice concerning pineal cysts. We believe that this paper could serve as a basis for future discussion on this challenging topic.

Material and methods

A simple online questionnaire (13 questions) was designed through Google Forms Freeware (Google, Mountain View, CA, USA) (Appendix 1).

The first three questions concerned personal information and career background, followed by ten questions (Q) related to pineal cysts. The survey mainly focused on indication of surgery (Q4, Q5 and Q7). The remaining questions assessed the caseload of patients with pineal cysts in the respective respondents' departments (Q6 and Q9), the preferred surgical approach (Q10), personal experience with the results of surgery (Q11) and follow-up strategy (Q8). The potential advantage of an international registry was discussed in Q12. Q13 provided space for any final comments and thoughts on the content of the survey. Some questions were designed for one answer only (Q1-4, Q6-9 and Q12), whereas others had check boxes with the possibility of multiple answers (Q5, Q10 and Q11).

A brief cover letter with a link to the survey site was sent to the respondents via email. The recipient list was based on the list of invited speakers to the EANS 2014 Congress in Prague (Czech Republic). The survey was anonymous and conducted over 6 weeks in March and April 2015.

Only those questionnaires that were completed on or before 30 April 2015 were included in the analysis.

Results

In total, 119 out of 457 neurosurgeons completed the survey (response rate 26 %). Of these 119 neurosurgeons, 9 were excluded because their responses were either incomplete (8 responses) or submitted too late (1 response). Therefore, the responses from 110 neurosurgeons were analysed. The results are graphically summarised in Fig. 2. Most responses were from the USA (15 responses) and Germany (14), followed by Italy (8), The Netherlands (5), France (5), Brazil (5) and Israel (5). We also registered responses from such countries as Oman, Angola, Egypt, Chile and Lithuania. The majority of respondents were qualified clinicians from academic institutions (85 %) with 20 or more years of experience (53 %).

Some 56 % of the respondents considered the pineal cyst to be consistent with a surgical lesion. An indication for surgery (Q5) (sorted in decreasing order) is obstructive hydrocephalus (90 %), Parinaud's syndrome (80 %), growth of the cyst (68 %), diplopia (46 %), headache (25 %), endocrinological disturbances (12 %), vertigo (7 %), other (5 %) and the "clinician's gut feeling" (3 %). Fifteen percent of the respondents were willing to operate even if the patient presents with only non-specific complaints (Q7). The preferred surgical approach is a microscopic supracerebellar infratentorial craniotomy (62 %), followed by endoscopic transventricular (19 %), occipital transtentorial (13 %) and an endoscopic supracerebellar infratentorial approach (10 %). Less frequently employed procedures are stereotactic aspiration (5.5 %) and the standard transcallosal interforniceal approach (1.8 %). Nine percent of the respondents selected "other approach". Most of the respondents followed-up the patients clinically and radiographically (72 %), 8 % only clinically and 20 % did not follow-up the patients (Q8). Seventy-eight percent of the respondents considered an international patient registry as a potentially useful tool (Q12). Thirty-eight neurosurgeons wrote comments in response to Q13. Some examples of these remarks are listed Table 1.

Discussion

Most of the respondents agree that pineal cysts which cause symptoms due to the compression of the surrounding structures should be subjected to resection. Some 90 % of the neurosurgeons consider obstructive hydrocephalus as an indication. Eighty percent consider Parinaud's syndrome caused by midbrain tectum compression as an indication for surgery.

Sixty-eight percent of the respondents indicated surgery in case of cyst growth. The literature suggests that the natural

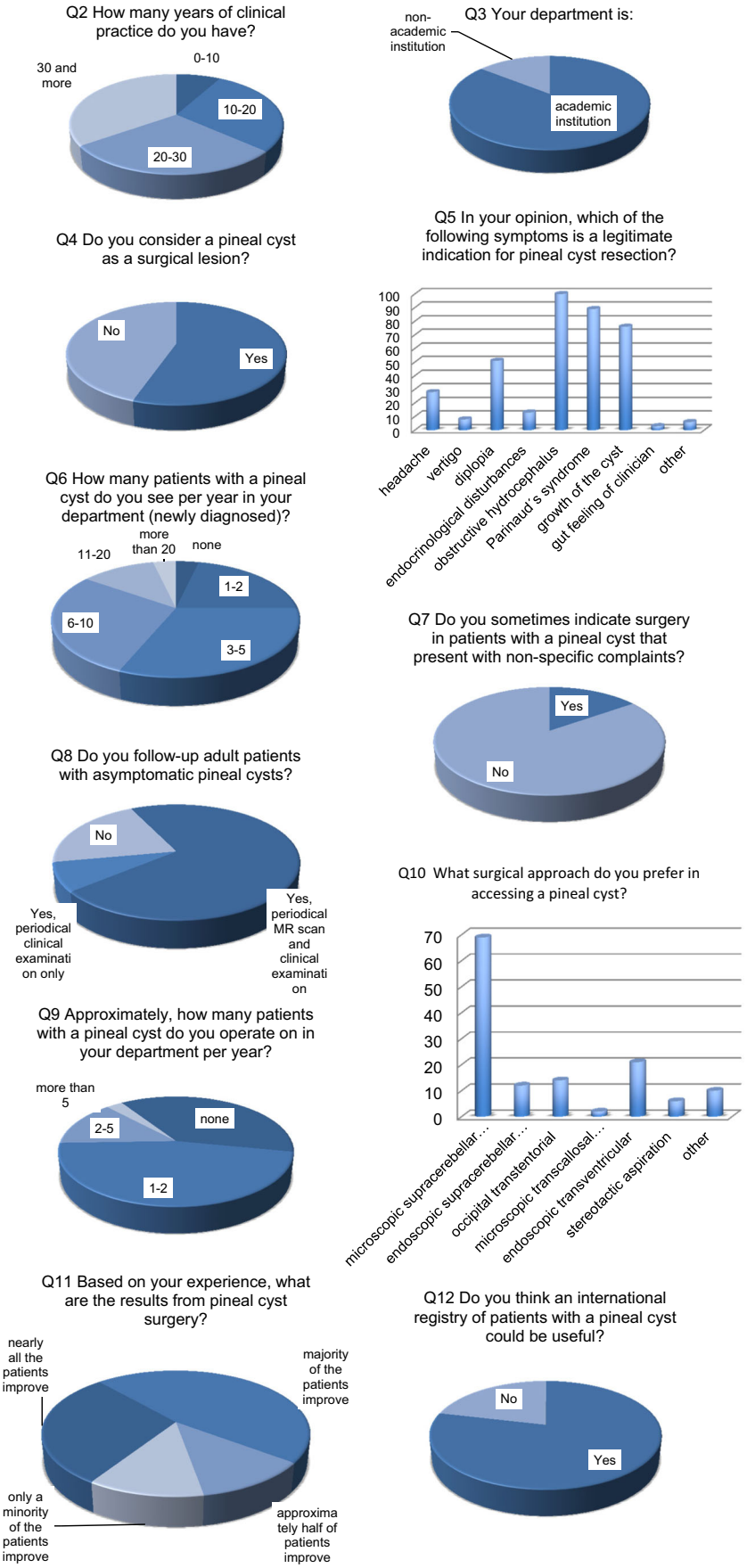

Fig. 2 Responses on selected questions depicted in charts

Table 1 Selected comments in response to the question 13

"*We regard intermittent nausea as an important clinical sign fixing the indication for surgery.*"
"*I think the main issue is to exclude those lesions that are in fact malignant tumours.*"
"*The most common indication for surgery in my experience is disabling headache refractory to medications. Rankin score = 0-1 (with or without anti-migraine medication) makes surgery useless.*"
"*I operated on pineal cysts much more often some years ago (just because of headaches), but most patients still complained about having headaches after surgery, so I quit operating just because of headaches.*"
"*Surgery for non-specific symptoms rarely improves the patient. Complications of such surgery far outweigh the benefits.*"

course of pineal cysts is steady growth during late childhood and adolescence, followed by slow involution [3, 5]. No statistically significant change in the clinical picture was observed during these changes [3, 6]. In our department, simple growth of the cyst in the first decades of life with no change in contrast enhancement is considered normal and does not justify surgery per se.

Only 15 % of our respondents reported operating on patients with non-specific symptoms (headache, vertigo, sleep disturbances, etc.) and even less (3 %) were willing to perform surgery based on intuition rather than hard evidence. In Q4 ("Do you consider a pineal cyst as a surgical lesion?"), 56 % of respondents produced a "yes" response. This question was maybe more ambiguous than intended. By "surgical lesion", we meant a lesion that might be considered for surgical treatment at some point, including all available surgical procedures (i.e. not only resection). Answer "yes" was not meant that every pineal cyst should be resected.

The role of pineal cysts in the aetiopathogenesis of headache remains undetermined. A relatively high prevalence of both cysts and headache suggests that in many cases their coexistence is incidental. Some authors will not operate on patients with headache as a sole presenting symptom of pineal cysts (i.e. without hydrocephalus) [3, 7, 8]. One of our respondents reported that, because of unsatisfactory outcome, he no longer operated on these patients (Table 1).

Seifert et al. [9] showed that pineal cysts might be the causative factor for headache. The authors compared 51 patients with a pineal cyst with 51 healthy matched controls and found that patients with a cyst had headaches twice as often as the controls. The literature contains many cases in which headache as the only symptom was resolved by pineal cyst resection [10–12]. One of our respondents confirms this observation: "The most common indication for surgery in my experience is disabling headache refractory to medication…" (Table 1).

Differential diagnosis of headache is extensive and beyond the scope of this paper. During the management of patients, secondary causes of headache need to be ruled out. In our experience, headache in patients with a pineal cyst does not have any characteristic pattern, though it often mimics migraine or tension-type headaches. Some authors speculate that the causative factor might be the intermittent obstruction of the aqueduct [13] or melatonin-level disturbance [14].

Sometimes unusual or even bizarre symptoms such as monoparesthesia, tremor or skin numbness become less intense or even disappear entirely after surgery [2, 13], an observation consistent with our own experience.

Considering the relatively high prevalence of pineal cysts (1-2 %) in combination with improved diagnostic methods (MR), patients with cysts rarely seek neurosurgical consultation. Only 4 % of our respondents have a case volume of more than 20 patients per year in their department outpatient clinic (this figure refers to the whole department and not just the individual respondent's caseload, see Q6). The usual caseload in the department per year varied from 1–2 patients (21 % of departments) to 3–5 patients (32 %) and 6–10 patients (27 %). One possible reason for this discrepancy is that most of the patients are asymptomatic and therefore do not seek medical attention. Another possible explanation is that neurologists do not refer their patients to neurosurgeons, as neurologists often do not consider surgery as a treatment option.

The operative caseload is one to two cases per year in 46 % of the departments from the survey study, three to five cases in 14 % and more than five cases in 3 %. Thirty-seven percent of the departments do not perform surgery for pineal cysts at all. Keeping in mind the above-mentioned data, a rough estimation is that 25 % of all patients seen in outpatient clinics undergo cyst surgery. In our own series consisting of 80 patients, 20 (or 25 %) underwent surgery for pineal cysts. It should be stressed that the population seen in neurosurgical departments is already a selected group of patients often seeking a second or third opinion. In reality, the proportion of patients with a pineal cyst that undergo surgery is significantly smaller.

Another observation is that surgery for pineal cysts is rare and is primarily indicated for patients with severely debilitating symptoms. As noted above, only a few procedures per year are performed in the majority of the neurosurgical departments. Considering that the pineal gland is one of the central structures of the brain, surgery in this region is associated with some serious complications [7, 15] (*see* below). This makes it appropriate to suggest that only a few surgeons per department specialise in surgery in this area. Regionalisation of this type of surgery to fewer centres may be even more reasonable [16]. However, we realise that the pineal region case-load per department/surgeon is likely higher than indicated by our survey, since also other kinds of pathologies in this specific area need to be taken into consideration (e.g. tectum glioma, pineal tumours) making the need for regionalisation perhaps less important.

Routine follow-up is usually recommended, even in asymptomatic cases. In Q8, 80 % of the respondents reported examining patients periodically (72 % included MRI), whereas 20 % did not examine their patients periodically. Al-Holou et al. [3] do not recommend periodical follow-up in asymptomatic adult patients if the cyst looks typical on MR imaging. Nevertheless, cyst growth has been described [6] and sometimes cystic tumorous growth could be misdiagnosed as a simple cyst (see comment in Table 1). For these reasons, we advocate routine clinical and radiological examination.

The preferred surgical procedure for resection of pineal lesions is undoubtedly the supracerebellar infratentorial approach, which was first described in 1911 by Krause [12]. Its main advantage is that access to the pineal region is done completely extracerebrally. Possible complications include venous sinus injury, cerebellar venous infarction and cerebellar swelling [17]. When performed in a sitting position, caudal retraction of the cerebellum by gravity is advantageous, but potential air embolism is an additional risk.

The alternative occipital transtentorial approach was used by 13 % of the respondents. Berhouma et al. [7] applied this approach to 20 patients with a pineal cyst. Total removal of the cyst was achieved in only 70 % of the patients. Unfortunately, the authors did not specify exact circumstances. A possible explanation is that deep cerebral veins are typically running above the pineal cyst and therefore block the surgical corridor when accessed supratentorially. A potential risk is transient hemianopsia, which occurred in four cases (20 %) in this series.

The pineal region could also be accessed from the opposite side, i.e. anterior and superior aspect using the transventricular endoscopic approach; 19 % of the respondents reported using this approach. A major drawback with this technique is recurrence, because a large portion of the cyst wall is left in situ. In the largest published cohort study (nine patients) [18], recurrence occurred in one case (11 %). However, associated obstructive hydrocephalus could be treated by a third ventriculostomy during the same procedure.

Stereotactic cyst aspiration (used by 5.5 % of the respondents) was reported in several papers in the 1990s [19–22]. The largest cohort study, comprising 14 patients, was done by Kreth et al. [20]. In this study, symptom relief was achieved in six patients (43 %). One obvious advantage is that this technique is less invasive; however, patients can present regrowth of the cyst [22].

In patients presenting with obstructive hydrocephalus, different surgical strategy than cyst removal is possible. Some authors advocate treating hydrocephalus by cerebrospinal fluid (CSF) diversion using ventriculoperitoneal (VP) shunting or endoscopic third ventriculostomy (ETV) [7]. We believe that surgical treatment should be causative and, therefore, we aim primarily towards resection of the cyst and restoration of the natural CSF pathway. A simple CSF diversion without cyst management would not be advisable, because a persistently expanding cyst may result in progressive gaze palsy [23]. Furthermore, no histological material is obtained during shunting procedures, which might be regarded as a potential drawback [24]. Sajko et al. [25] reported combined surgical treatment by insertion of a VP shunt in ten patients with acute obstructive hydrocephalus before the cyst resection. In emergency situation, we prefer temporary external ventricular drainage as a bridging therapy to the cyst resection. VP shunting carries significant risk of long-term complications and is unnecessary when CSF pathway is restored by the cyst removal. From this perspective, ETV may be a less invasive option to treat the hydrocephalus. Berhouma et al. [7] were able to perform ETV and pineal cyst marsupialisation in one procedure. Spontaneous resolution of the cyst following ETV is reported in the literature [26].

A notable finding in the present study concerns a point raised by one of the respondents, who suggested that intermittent nausea is a specific sign and an important criterion for surgery indication (Table 1). The phenomena of transient headache and nausea are traditionally explained by intermittent obstruction of the aquaeductus caused by a pineal cyst similar to what is observed in patients with a colloid cyst in the anterior aspect of the third ventricle [27]. A valve-like mechanism is suggested when periods of obstruction in combination with increased intracranial pressure (ICP) are followed by periods of normal cerebral aquaeduct patency and normal ICP. Such changes are believed to be caused by posture and position of the head [13]. Relevant data supporting this hypothesis are lacking, however. Kalani et al. [13] attribute many of the non-specific symptoms, including syncope and visual and sensory disturbances, to this phenomenon.

Despite all the uncertainties and drawbacks associated with pineal cyst surgery, the perception of results of the surgery for most neurosurgeons is optimistic. Indeed, 64 % of the respondents think that the majority of the patients improve after surgery. On the other hand, 10 % of the respondents believe that only a minority of patients present any amelioration. It is obvious that these data are very subjective and self-perception of one's work could be distorted by bias. Trying to find more objective surgical results, the literature does offer several case series. Symptom relief in patients presenting with elevated ICP due to hydrocephalus reaches levels up to 100 %. When total resection of the cyst was achieved, no recurrence was reported [13, 24].

In patients with headache as the only complaint, surgery is curative in 25-100 % of the cases [8, 11, 15, 24]. In their recent paper, Kalani et al. [13] focused on patients with non-specific symptoms and found a 94 % resolution or improvement of the symptoms. Even unusual rare presentation of pineal cysts (monoparesthesia, face numbness, tremor, ataxia, hemiparesis, syncope, etc.) resolved after cyst resection [2,

10, 13]. A significant part of the success in patients with non-specific symptoms might be related to the "placebo effect". In neurosurgery, a placebo effect was demonstrated on several occasions [28, 29], and neurosurgeons should be aware of this when indicating relatively invasive operation such as pineal cyst removal.

A prospective randomised trial is greatly needed to elucidate this interesting topic of pineal cysts. However, a major issue in such a trial would be the selection of inclusion criteria and the randomisation process. Therefore, an international patient registry could serve as a compromise. Clinical and radiological findings as well as surgical results could be collected in this way. The majority of our respondents (78 %) consider a patient registry as a potentially useful tool.

Conclusions

The clinical approach to pineal cysts is highly controversial within the neurosurgical community. Some neurosurgeons do not consider pineal cysts as pathological lesions, whereas others do and occasionally indicate cyst resection. The majority of patients are asymptomatic and observation is indicated. Most of our respondents have operated on patients with a pineal cyst only if they present with symptoms attributable to a mass effect. Surgery for patients with non-specific complaints is not widely accepted, although such surgery may be effective. Clinical guidelines are lacking because no prospective trial has thus far been conducted. We believe that an international patient registry would be helpful in the decision-making process in the clinical management of pineal cysts.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organisation or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study by submitting the online questionnaire.

Appendix 1

1. Where do you come from?
2. How many years of clinical practice do you have?
(a) 0–10 years
(b) 10–20 years
(c) 20–30 years
(d) 30 years and more
3. Your department is:
(a) an academic institution
(b) a non-academic institution
4. Do you consider a pineal cyst as a surgical lesion?
(a) yes
(b) no
5. In your opinion, which of the following symptoms is a legitimate indication for pineal cyst resection?
(a) headache
(b) vertigo
(c) diplopia
(d) endocrinological disturbances
(e) obstructive hydrocephalus
(f) Parinaud's syndrome
(g) growth of the cyst
(h) clinician's "gut feeling"
(i) other
6. How many patients with a pineal cyst do you see per year in your department (newly diagnosed)?
(a) none
(b) 1–2
(c) 3–5
(d) 6–10
(e) 11–20
(f) more than 20
7. Do you sometimes indicate surgery in patients with a pineal cyst that present with non-specific complaints (i.e. headache, sleep disturbances)?
(a) yes
(b) no
8. Do you follow-up adult patients with asymptomatic pineal cysts?
(a) yes, periodical MR scan and clinical examination
(b) yes, periodical clinical examination only
(c) no
9. Approximately, how many patients with a pineal cyst do you operate on in your department per year?
(a) none
(b) 1–2
(c) 3–5
(d) more than 5
10. What surgical approach do you prefer in accessing a pineal cyst?
(a) microscopic supracerebellar infratentorial
(b) endoscopic supracerebellar infratentorial
(c) occipital transtentorial
(d) microscopic transcallosal interforniceal
(e) endoscopic transventricular
(f) stereotactic aspiration
11. Based on your experience, what are the results from pineal cyst surgery?
(a) nearly all the patients improve
(b) the majority of the patients improve
(c) approximately half of the patients improve
(d) only a minority of the patients improve
12. Do you think an international registry of patients with a pineal cyst could be useful?
(a) yes
(b) no
13. Would you like to make a comment?

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