**Title:** Incidental pineal cysts: is surveillance necessary?

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**Introduction:**

Pineal cysts were once thought to be rare, but the advent of higher resolution MRI scanning has resulted in more frequent identification of these lesions. The reported incidence of pineal cysts in MRI studies ranges from 1-23%.1–14 The natural history of this pathological entity is not well understood; most of the literature supports a benign course however there are a number of reports of patients developing headaches, hydrocephalus, extraocular movement abnormalities, Parinaud syndrome, pineal apoplexy and sudden death as a direct result of their pineal cyst.5,15–25

As the reported prevalence of pineal cysts continues to rise, and the natural history is not defined, there is increasing pressure on neurosurgical and neuro-radiological services to develop follow up strategies for these patients. The aim of this study was to investigate the prevalence and natural history of pineal cysts and to develop a pragmatic approach for clinical and radiological surveillance for these patients.

**Materials and methods**:

The radiological reports of all patients, aged greater than 16, who underwent MRI brain at The Walton Centre NHS Foundation Trust, between June 2007 and January 2014, were reviewed. The search tool CRIS (Computerised Radiological Information System) was used to identify reports containing the term “pineal cyst.”

Scans were reviewed by experienced consultant neuro-radiologists (K.D, M.B), to confirm the radiological diagnosis of pineal cyst. Patients were excluded if they had enhancing regions on MRI suggestive of non-benign pineal lesions such as primary pineal tumours. There was no exclusion criteria related to pineal cyst size. The MRI sequences T2 axial, FLAIR coronal, T1+gadolinium were reviewed to record the maximum cyst diameter. Measurements were made by both neuro-radiologists to determine pineal cyst size. The baseline MRI was used to confirm the diagnosis and subsequent follow up imaging was reviewed to assess for any interval change in the measurements. Non-volumetric measurements were used, and the longest diameter was taken to be the cyst size.

Due to the clinical set up at our centre, both baseline and surveillance imaging was performed on a variety of scanning platforms from various manufacturers at field strengths including 0.35T, 1.5T and 3.0T. Statistical analysis was performed using SPSS 20.0. Mann-Whitney U test was used to compare medians where appropriate. The institutional review board determined that formal ethical approval was not required for this study.

**Results**:

During the study period all 42,099 MRI head (elective and emergency) radiology reports were reviewed, identifying 281 patients with incidental pineal cysts (prevalence =0.667%). The median age at diagnosis was 38 years (range =16-84 years) (See Figure 1). 63.3% (n =178) of patients were female. The main indication for MRI was headache (50.2%), seizure (12.8%), and miscellaneous (36.7%), encompassing other neurological symptoms including tremor, visual disturbance and sensory disturbance. Median pineal cyst diameter at time of diagnosis was 10mm (range =2-28mm).

181 patients (64.4%) had at least 1 follow up MRI (mean =2.12, range =1-7), and median length of follow up was 6 months (range =1-68 months). Only 11 patients (6%) had pineal cysts that changed size at subsequent scan. No patients developed symptoms or complications attributable to their pineal cyst.

7 cysts increased in size with a median change of 2mm (range =1-2mm). At time of diagnosis these patients were aged 30-62 (median =44), with cysts ranging from 6-17mm (median =13mm). Additional information regarding these patients can be seen in Table 1. The median time to increase in size was 9 months (range =2-26). 4 patients aged 25-58 (median =30) had cysts which reduced in size. The cysts measured between 10-16mm (median =15mm), and the median change was 2.5mm (range =2-8mm). The median time to reduction in size was 10.5 months (range =6-14 months). An example patient MRI scan can be seen in Figure 2.

Cyst size did not correlate with age at time of diagnosis. Although all 5 patients with very large cysts (>19mm) were aged between 23 and 54.

100 patients did not have a surveillance MRI. Of the patients with no follow up, the median size of pineal cyst was 10mm (range =2-20mm), and their age ranged from 17-84 (median =40). There was no statistical difference in the demographics of this group when compared with those whom had surveillance (p>0.05 for both age and size of pineal cysts at diagnosis).

**Discussion:**

With increased availability of MRI there is an increasing referral of patients with incidental findings, so-called Victims Of Modern Imaging Technology (VOMIT).26 This increase in access to high quality imaging is likely the reason for incidental pineal cysts being increasingly reported.2,4,6,12,17,27–32 It is therefore necessary to identify patients who are at risk of developing symptoms, this will reduce the burden of unnecessary follow up appointments on neurosurgical and neuro-radiological institutions.

This study is one of the largest reported cohorts of adult patients with pineal cysts to date. It has demonstrated that a very small proportion (6%) of pineal cysts changed in size, but that all patients remained without complication. Importantly, no patients required surgical intervention at any point throughout the surveillance period.

Epidemiology

There have been multiple studies which have explored the prevalence of pineal cysts in patients presenting with neurological symptoms; they have all demonstrated greater incidence rates than the present study (0.667%), ranging from 1-23%.1–14 Autopsy data has demonstrated prevalence rates of 18-41%, although many of these publications include microscopic cysts.8,9,33,34

A recent MRI study demonstrated 23 of 100 individuals without neurological symptoms had pineal cysts (>2mm) when using a 1.9T MR scanner. A further 13% of these individuals demonstrated cystic lesions less than 2mm in size.8 Cystic changes may therefore represent a spectrum of disease from microscopic cystic lesions to large pineal cysts. If this is the case improvements in MRI resolution will inevitably result in more pineal cysts being identified.

Variation in quoted incidence rates may also be due to inconsistencies in exclusion of pineal cysts due to size. In the present study cyst size was not an exclusion criteria, with the smallest cyst measuring 2mm. Unfortunately, small cysts may have not been commented upon by the original reporting neuro-radiologist and therefore were not identified using the our search technique. Consequently, this may be the reason for the decreased incidence in the present study.

Pineal cysts are more prevalent in females in this population. This has been unanimously reported in the literature and may indicate a hormonal contribution to the disease.1,2,5,6,8,17,19,20,24,28

Change in prevalence throughout age groups

From the current study, we found pineal cysts to be more common in the younger age groups in both males and females (Figure 1). Whilst this may reflect a selection bias whereby younger persons are more likely to undergo brain imaging for trivial symptoms; nonetheless our findings support that already reported in the literature.2,4,10,12,28 Al-Holou and colleagues demonstrated that prevalence peaks in late childhood and then falls.2

Sawamura et al and Sener et al suggested that cysts may form in adolescence as they found no cysts in 73 children below the age of 10, and 332 children below 12 respectively.6,7 However a large study of patients aged under 25 years, using 1.5 and 3T MRI, demonstrated that pineal cysts were present in 0.5%, 1.6% and 2.7% of patients aged <1, 1-5, 6-12 years respectively.1 Sawamura et al also found that peak incidence occurred in females in their third decade of life again suggesting that pineal cysts may form early in life and regress.6

This suggestion is supported by larger cysts being rare in elderly patients,6,9,30 and those under ten years.30 Our findings would concur with this, although no correlation was found between age and cyst size, the very large (>19mm) cysts were all found in patients under the age of 55 years.

Cyst appearance on radiology

Pineal cysts typically are well circumscribed and homogenous in appearance with a thin smooth capsule.3,5,11,20,21,32,35 The lesion’s content is hyperechoic to isoechoic to CSF on T1WI, T2WI and FLAIR images, and contrast enhancement is typically incomplete.6,8,36,37

A number of authors have suggested that pineal cysts can be easily interpreted radiologically due to their characteristic pattern.4,37 Although two studies of histologically benign cysts have demonstrated 58% and 50% irregular rim enhancement on imaging suggesting difficulty in interpreting cystic pineal lesions.18,38 In addition, Al-Holou et al demonstrated 53% of cysts demonstrated atypical imaging characteristics in some way, such as septations or abnormal enhancement,1 this has since been echoed in a number of publications.2,39

To combat this uncertainty, in the present study we exclude those patients with enhancing components to their pineal cysts suggestive of non-benign lesions. Therefore the conclusions of the present study should not be applied to pineal cysts with abnormal imaging characteristics.

Cyst size and symptoms

Pineal cysts associated with symptoms are rare.5,24,38 However, there have been reports of complications attributable directly to pineal cysts including direct midbrain compression, aqueduct compression resulting in tri-ventricular hydrocephalus, vein of Galen blockage, compression of superior colliculus resulting in Parinaud syndrome, vertigo, hemiparesis, Parkinsonism, aseptic meningitis and pineal apoplexy resulting in sudden death.5,15–20,22–25,29,33,35,38,40–45

In the present study no patients had symptoms that were deemed attributable to pineal pathology. However, a case-control study has demonstrated that headache was twice as common in age and sex matched individuals with pineal cysts when compared to patients without cysts, although severity of headache was not associated with size of cyst.46 Furthermore, multiple publications have highlighted that larger cyst size is associated with increase in prevalence of symptoms; with an increase in symptoms frequency in patients with cysts greater 1cm.1,11,18,19,24,33 Consequently, clinicians should be reminded that if no other pathology can be demonstrated, symptom etiology could be considered to be due to a pineal cyst.

Change in size

The natural history of pineal cysts is poorly described and for this reason there is large variation in the surveillance strategies for these tumours. We have demonstrated that only 6% of pineal cysts changed in size, and no patients developed symptoms attributable to this. Therefore we cannot promote aggressive surveillance of these tumours. In addition to this, no cyst increased more than 2mm during the surveillance period. Although we are confident that our measurements are accurate, it is possible that the small increase in size may represent measurement error.

This tendancy for pineal cysts to remain stable has been repeatedly reflected in small cohorts of patients. Barboriak et al reported on 32 patients with pineal cysts over 3.7 years; finding that 5 cysts decreased in size, and 2 cysts increased in size and one patient developed a new pineal cyst, the remaining 75% of cysts remained stable over this time.28 Tamaki et al demonstrated that 2 of 31 patients with pineal cysts had reduction in size, the reminder underwent no change in size with follow up from 3 months to 4 years.30 Sawamura et al and Golzarian et al reviewed 20 and 12 patients respectively, and demonstrated no change in cyst size throughout their follow up.6,10 Therefore, coupled with the present evidence, there is an argument to be made for pineal cysts to be monitored clinically and perhaps interval scanning is not indicated as change in size and the development of symptoms is extremely rare.28

Complications and surgical intervention

Surgical approaches to pineal cysts include direct, via occipital trans-tentorial and supra-cerebellar infra-tentorial approach, or endoscopic techniques by cisternal supra-cerebellar and intraventricular approaches.19,29,41,47–49 However, operative management of clinically silent pineal cysts remains controversial, in light of the fact that many symptoms which result in the patient seeking medical help are often not attributable to the incidental pineal cyst.

We have demonstrated that no patients had symptoms or complications during the follow up period, and all patients with cyst growth remained asymptomatic. Therefore we cannot advocate operative management of incidental pineal cysts. To support this, Fetell et al demonstrated that headache was only relieved by operative management of pineal cysts if hydrocephalus was present. The authors also demonstrated that hydrocephalus only occurred only in patients with cysts greater than 2cm in AP diameter.17 Therefore clinicians should also be reassured when dealing with smaller cysts, that they are unlikely to cause complications.

However, a recent publication has suggested that pineal cysts may result in intermittent symptoms and demonstrated that 17 out of 18 patients with non-hydrocephalic, non-Parinaud symptoms, had resolution or improvement of symptoms following complete resection of their pineal cysts.50 However, given the risks of pineal surgery, this is highly debatable and most neurosurgeons would not consider this a reason to operate.

Furthermore, size alone should not be an indicator for surgical intervention, as we have seen with 5 patients with cysts greater than 19mm.2

Reason for growth

Reasons for pineal cyst growth have been postulated but there is little evidence for the following theories. It has been suggested that haemorrhage into cyst, may result in sudden increase in cyst size, which may be supported by heterogenous appearance on MRI.1,2,19,21,38 In addition, histological sections of pineal cysts can contain clear, haemorrhagic, or coagulated fluid.6,19,24,38

There has also been a suggestion of hormonal drive which causes the cysts to increase in size.1,6,19,24,38 This may account for the female predominance in this study and the literature.1,2,5,6,8,17,19,20,24,28 Further evidence in support of this hormonal theory, which may account for this sex distribution, is that pineal cysts have been implemented in the disturbance of the production of melatonin which is involved in regulation of sleep wake cycles.14 They have also been suggested to be responsible for precocious puberty, hypogonadism and diabetes insipidus.51,52

A third theory into why pineal cysts may increase in size is due to conjugation of smaller pineal cysts.1,19,24 However if this was the case, it would be likely that cyst prevalence would increase into older age. This does not corroborate the present findings or previously published data.1,6,9,19,24,30

Surveillance strategy

As the majority of patients with pineal cysts remain asymptomatic there is much debate as to the appropriateness of routine long term follow up. In the paediatric cohort, Marques and Rivero suggest a follow up MRI at 1 and 3 years, and if the cyst remains stable the patient is discharged; however should the cyst grow, the patient is monitored annually for 3 years after stabilisation. However, the authors agree that this is mainly to pacify parents who have received the news of “brain tumour.”53

We have not demonstrated any pineal cysts which have significantly increased in size resulting in symptomatic presentation. Therefore we cannot advocate that pineal cysts should be repeatedly interval scanned. We suggest a single follow up MRI scan at 12 months and if the cyst remains stable the patient should be discharged (See Figure 3). 5 of 7 patients with pineal cysts which increased in size did so within 12 months therefore we believe our suggested surveillance strategy will identify the majority of patients who are at risk of pineal cyst growth.

The surveillance MRI scan will also aid in confirmation of diagnosis. Ideally, this scan should be performed using the highest field strength machine available in order to best characterise the lesion. However, we do agree that this may not be practical given the current financial climate. Therefore surveillance using the same field strength MRI scanner would be sufficient to compare size.

The repeated MRI may not be necessary in the elderly (>60 years) population as we did not demonstrate a change in cyst size in any patient aged greater than 62, this would also exclude 10% of our patients from requiring follow up, again resulting in fewer neurosurgical and neuro-radiology appointments. Furthermore, a number of studies have suggested against interval imaging smaller cysts.28,29,54,55 This method could also be considered where resources are limited.

Al-Holou et al states that neurosurgical referral of patients with pineal cysts should be considered optional.2 However, given the small number of cases reported in the literature with complications attributable to pineal cysts we cannot advocate this. Moreover, literature suggests the diagnosis should be made by an experienced neurosurgeon or neuro-radiologist, as those diagnosed by general radiologists may result in misdiagnosis. Marques et al demonstrated that 5 of 113 cases of referred pineal cysts were misdiagnosed and were in fact; 3 pineal tumours, 1 suprasellar arachnoid cyst and 1 thalamic cyst.53

So as not to miss more aggressive pineal tumours, it has been suggested that patients with pineal cysts with unusual characteristics on imaging, young patients and patients with cysts greater than 1cm should be followed up more frequently than cysts without these characteristics, although there is little evidence to suggest that these patients are at more risk of becoming symptomatic.28,29,56 Importantly, Cauley et al reviewed indeterminate cystic pineal lesions with suspicious imaging characteristics and did not demonstrate any growth during surveillance of 26 patients.57 Readers should be reminded that in the present study we excluded pineal cysts with atypical appearance.

Limitations

There are a number of limitations to this present study. As patients were recruited from a large tertiary neurosciences centre there may be a selection bias where our population demonstrates a higher rate of intracranial pathology when compared to the general population. However, despite this possible bias our reported prevalence was lower than other studies.

Pineal cysts which were not commented upon in initial radiological reports will have been missed, this will have resulted in an under estimation of prevalence. However as all scans were initially reported by neuro-radiologists this number should be very low. Nonetheless, it was not possible for the authors to review greater than 42,000 MRI scans. Additionally, prevalence rates may be lowered by those patients who were scanned using low field strength MRI scans where the machine was not sensitive to small pineal cysts. However, due to the way in which data was stored we are unable to say what proportion of the 42,099 patients were scanned using low field strength MRI.

Of the few pineal cysts which increased in size the change was very small. Although our neuro-radiologists are confident that the change in size is accurate, this may reflect measurement error. Measurement error of cystic pineal lesions is typically quoted at less than 2mm.57 Therefore there is a possibility that we have overestimated the patients with pineal cyst growth.

It could be argued that the present cohort of patients have not been followed up for a sufficient period of time. However, given there was previously no surveillance protocol for patients with pineal cysts we have presented complete retrospective data of surveillance strategies employed by neurosurgical consultants in Liverpool. Furthermore, 3 out of 7 patients demonstrated and increase in cyst size in 6 months or less, therefore, we felt it prudent not to exclude patients with short surveillance periods.

As none of the patients in the present study underwent surgical intervention there is no histological evidence that all of the lesions were in fact pineal cysts. Although, as none of the patients developed serious complications or a significant change in cyst size, histological sub-typing may largely prove to be academic and not clinically important.

**Conclusions**:

Incidental pineal cysts are a common radiological finding. Serial MRI and long term neurosurgical follow up of adults with pineal cysts is not necessary as they have a tendency to remain stable or reduce in size. We therefore recommend a single repeated MRI scan with gadolinium at 12 months after diagnosis and discharge from routine follow up if the pineal cyst has not increased in size.

Figure 1 – Age and gender distribution of patient with incidental pineal cysts.

Table 1 – Demographics of patients who demonstrated an increase in pineal cyst size.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Sex | Age | Size of cyst at diagnosis (mm) | Increase in cyst size at surveillance scan (mm) | Scan interval (months) |
| female | 55 | 6 | 1 | 9 |
| female | 62 | 13 | 2 | 6 |
| female | 46 | 16 | 2 | 11 |
| female | 32 | 10 | 2 | 18 |
| female | 35 | 17 | 1 | 2 |
| male | 44 | 10 | 2 | 26 |
| male | 30 | 13 | 2 | 5 |

Figure 2 – Sagittal T1 images demonstrating a patient with a pineal cyst which decreased in size over a period of 14 months.

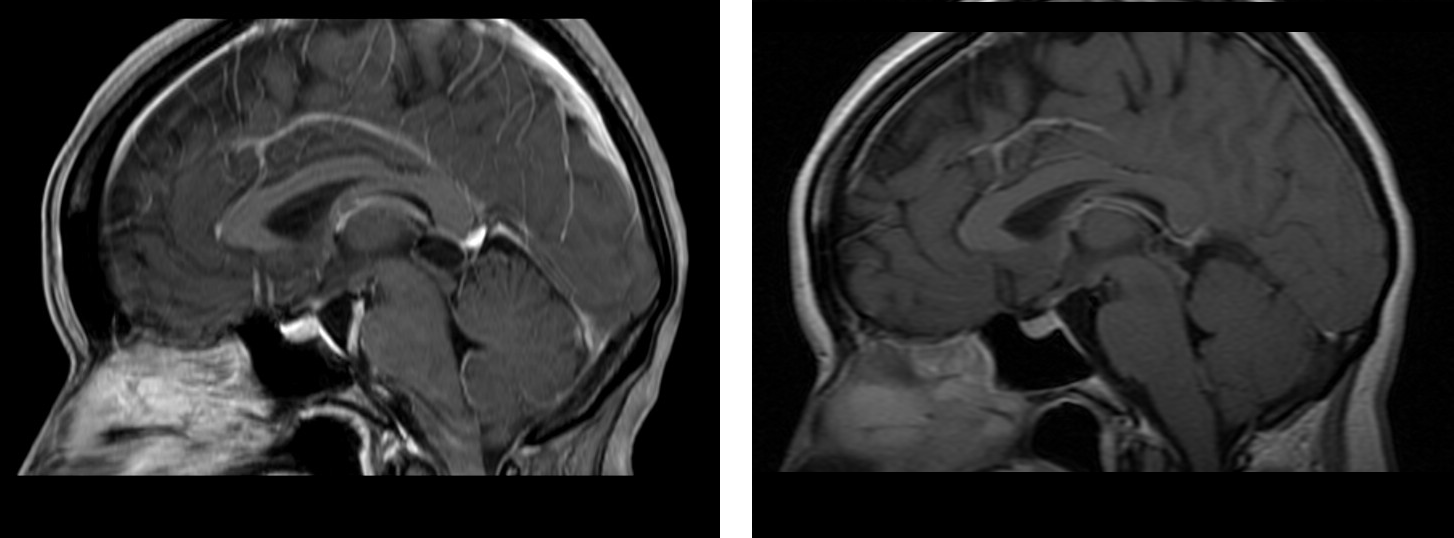
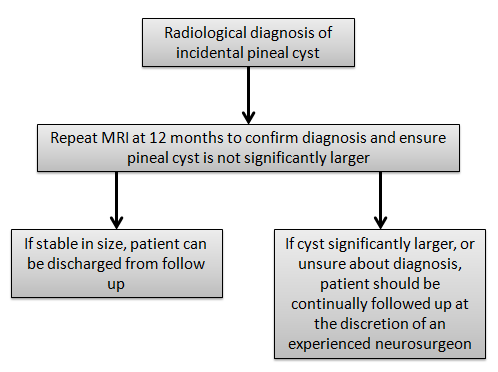
****\*Above left is the patient’s initial scan, above right demonstrates a smaller pineal cyst

Figure 3 – Proposed radiological surveillance strategy for patients with incidental pineal cysts.

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