Headache
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ISSN 0017-8748
doi: 10.1111/j.1526-4610.2010.01652.x
Published by Wiley Periodicals, Inc.

Expert Opinion

Headaches and Pineal Cysts

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Pineal cysts are common incidental imaging findings that may be associated with primary headaches.

CASE

This is a 27-year-old man with migraines without aura for about 15 years that have increased in frequency to about twice a week in the last 1 year. The headaches are relieved within 1 hour by a triptan. Neurological examination was normal. Family history reveals that both parents, his brother, and sister are all migraineurs. A magnetic resonance imaging (MRI) of the brain obtained at the patient's request revealed a 6-7 mm pineal cyst without mass effect.

Questions: What is the natural history of pineal cysts? When are follow-up MRI scans indicated? Are pineal cysts associated with migraines?

EXPERT COMMENTARY

Pineal cysts are benign lesions found in up to 2.6% of adults.[1] Asymptomatic pineal cysts are usually an incidental neuroimaging finding. Their main importance is in their differentiation from a normal cystic component of the gland, from a true pineal cyst (5 mm or larger in diameter) or cystic tumors such as germ cell tumors (GCTs), pineal parenchymal tumors (PPTs), low-grade astrocytomas, and teratomas.[2]

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The natural history of pineal cysts is typically benign. The majority of pineal cysts are silent, and remain so for years; some may even spontaneously collapse. In 1 report of 32 patients with pineal cysts who underwent serial MRIs, 75% of cysts remained stable over time, while 16% decreased in size or regressed completely; only 8% increased in size.[3] In another study of 26 patients with incidentally found indeterminate pineal lesions ranging from probable benign cysts to pineal masses with follow-up MRI imaging from 7 months to 8 years, all lesions were stable over time.[4] In a third study of 106 children and young adults with pineal cysts followed for a mean interval of 3.0 years, 98 had no increase in size and no change in imaging appearance, 6 increased in size, and 2 others had a change in imaging characteristics without associated growth. The mean age of patients with cysts that changed or grew was 5.5 years.[5] The authors of both studies suggest that pineal cysts can be followed clinically rather than with serial imaging. However, the preference for follow-up imaging of individual clinicians and patients may vary.

Three principal histologic types account for most tumors arising within the pineal gland: GCTs (38-69% of pineal tumors), PPTs (pineocytomas and pineoblastomas, 14-27%), and astrocytomas (12-27%).[6] Meningiomas, teratomas, and lipomas may also occur.

RADIOLOGIC FEATURES

On MRI, pineal cysts are typically sharply delineated ovoid-shaped lesions, without intracystic trabeculations. They have low signal intensity on both T1 and T2, and contrast enhancement is usually nodular

and irregular. Like pineal cysts, pineocytomas may be isointense with cerebrospinal fluid (CSF), but they usually have intratumoral trabeculations.[7] On computerized tomography, pineal cysts are hypodense with respect to CSF, and occasionally there is evidence of recent intra-cyst hemorrhage. Cyst walls may or may not show contrast enhancement, and calcifications within the wall are found in about one-half of cases.

Radiologic differential diagnosis with other pineal gland masses is made more commonly by MRI. GCTs and malignant gliomas characteristically invade through the third ventricle wall, but expansive compressions are more common with PPTs, low-grade astrocytomas, and meningiomas. Imaging alone is not reliable enough to predict histology. In suspected cases, a biopsy should be performed.

Cysts and calcifications are present in up to one-half of PPT cases, with peripheral calcifications more suggestive of pineocytoma than germinoma. Benign pineal cysts may present similarly.

Cystic areas are common, and may be multiple in GCTs. Calcifications can be identified in two-thirds of pineal gliomas. Low-grade pilocytic astrocytomas may be cystic, and unlike other low-grade gliomas, they enhance with contrast.[7]

CLINICAL FEATURES

Pineal cysts are benign and asymptomatic lesions. Symptomatic pineal cysts are usually larger than those found incidentally. The incidence of symptomatic pineal cysts is highest in young women between 21 and 30 years of age, leading to the hypothesis that hormonal influences contribute to their etiology.[1] Symptoms may be caused by aqueductal compression resulting in hydrocephalus, obstruction of the vein of Galen, or compression of the collicular plate leading to Parinaud's syndrome.

Peres et al described 5 cases of primary headaches associated with pineal cysts and suggested that pineal cysts could be related to headache disorders not because of compression but abnormal secretion of the pineal hormone melatonin.[8] Seifert et al[9] studied 51 pineal cysts patients compared with 51 controls. Pineal cyst patients had 2-fold more headaches than controls (51% vs 25%). The most common diagnosis in pineal cysts patients was migraine in 26% including the 14% with migraine with aura. One patient had hemicrania continua.

The authors suggest pineal cysts may be related to headaches, particularly migraine. Interestingly, cyst diameter was not different in patients with headache as compared with those without headache. This finding supports the idea of Peres et al[8] that melatonin dysfunction may be the main mechanism related to the headache. Melatonin has been linked extensively to headache disorders with experimental and clinical evidence.[10-15] Unfortunately, to date, no measures of melatonin secretion have been performed in pineal cysts patients.

It is important to look for clinical symptoms related to pineal and melatonin secretion dysfunction such as insomnia, delayed sleep phase syndrome, and desynchronoses in pineal cysts patients. If those signs are present, a melatonin dysfunction is probably occurring.

TREATMENT

Small, asymptomatic pineal cysts require no therapy. If they become symptomatic from hydrocephalus, surgical options can be considered.

Melatonin has been studied as a treatment for headache disorders. Migraine, cluster headache, headaches secondary to delayed sleep phase syndrome, and hypnic headache have all shown to benefit from melatonin supplementation with minimal side effects. The patient with a headache disorder and a pineal cyst may be treated preventively with melatonin starting with 3 mg at bedtime and increasing to 15 mg.[10] Melatonin analogs including ramelteon and agomelatin may also be helpful but further studies are needed to confirm their role in headache patients. Sleep hygiene, sun, daylight exposure, or light therapy may also be used.

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