Benign symptomatic glial cysts of the pineal gland: a report of seven cases and review of the literature

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SUMMARY Seven cases of clinically symptomatic benign glial cyst of the pineal gland are reported. The cysts' size ranged from 1-0–4-5 cm in diameter. They were characterised by a golden or, less frequently, brown-reddish proteinaceous or haemorrhagic fluid content. The cyst wall, up to 2 mm thick, consisted of clusters of normal pineal parenchymal cells, often compressed and distorted, surrounded by reactive gliotic tissue which sometimes contained Rosenthal fibres. The presenting clinical features included headache (6/7), signs of raised intracranial pressure, partial or complete Parinaud’s syndrome (5/7), cerebellar deficits (2/7), corticospinal and corticopontine fibre (2/7) or sensory (1/7) deficits, and emotional disturbances (2/7). CT and MRI (in 2/7 cases) scans showed a hypodense or nonhomogeneous lesion in the region of the pineal gland, with or without contrast enhancement. Surgical excision resulted in complete clearance of the symptoms in 5/7 patients. The previous literature is reviewed and the clinicopathological correlations and the possible pathogenetic mechanisms are discussed. The need to distinguish this benign lesion from other mass lesions of the pineal region, in particular from pinealocytoma, is stressed.

Lesions of the pineal region comprise germinomas, teratomas, tumours arising from the pineal parenchyma such as pineocytomas and pineoblastomas, gliomas, and cysts, including epidermoid, dermoid, arachnoid and glial cysts. Small benign glial cysts of the pineal gland are a common incidental finding in adults, discovered on CT scanning and on post-mortem examination; they are usually less than 0-5 cm in diameter and, unlike the other lesions mentioned above, do not give rise to symptoms. Large, symptomatic pineal cysts of the same nature have been described only rarely. We have studied seven such cases over the last five years. Their clinical and pathological features are presented in this report.

Materials and methods

The cases described in this report were referred by other pathologists to one of us (LJR) for consultation on histological diagnosis. They are seven out of about 1500 consultation cases seen consecutively at the Division of Neuropathology of the University of Virginia School of Medicine between 1982–1987. The referring physicians were contacted for clinical information, including post-operative follow-up information.

Case reports

Brief case summaries are given below.

Patient 1 (Case No. C5863) A 54 year old man suffered worsening headache of several months' duration, with paralysis of upward gaze on examination. Computer tomographic (CT) and magnetic resonance imaging (MRI) scans demonstrated a cystic calcified mass in the pineal region, 2 cm in size (figs 1 and 2). The cyst was excised. Histological examination disclosed portions of pineal gland with irregularly arranged pineocytes. The pineal tissue showed areas of compression with focal cystic changes, microcalcifications, and the accumulation of granular amorphous material. Within and contiguous to the pineal tissue there was glial proliferation which contained Rosenthal fibres. Numerous haemosiderin-laden macrophages were present, chiefly perivascularly. The perivascular spaces also contained infiltrates of chronic inflammatory cells. Post-operatively the patient has remained symptom-free.

Patient 2 (Case No. C5816) A 27 year old female with a three months' history of positional headaches and "slight visual disturbance". Examination was normal. CT and MRI scans showed a cystic lesion in the pineal region. There was no associated hydrocephalus or mass effect. At operation, a 1-5 cm-large, thin-walled cyst was found. There was a focal area of thickening in the cyst membrane anteriorly, up to 1 mm thick, which was vascular and contained yellowish tissue.
The cyst was filled with clear fluid which clotted into a gel-like substance upon aspiration. The initial diagnosis was pinealocytoma. However, on review, microscopical examination showed clusters of normal pineal cells surrounded by gliotic and, in a few places, connective tissue. Corpora arenacea were seen at the pineal-glial border. The thickened area of the wall contained normal pineal cells, representing the original pineal gland which had become a mural nodule. No cellular atypism was seen. The patient's symptoms resolved with the operation and she was asymptomatic 10 months later.

Patient 3 (Case No. C5725) A 30 year old female had morning headaches of several months' duration. CT showed a well-circumscribed lesion in the pineal region, 2.0 cm in diameter. At operation, a 2 × 1.5 cm multilobulated cystic mass was found which contained dark brown haemorrhagic fluid and, within the cyst wall, calcification granules. The initial histological diagnosis was pinealocytoma with previous haemorrhage. On review, histological examination showed the cyst wall to consist of gliotic tissue with nests of normal pineal cells segregated by thin strands of glial tissue (fig 3). The cyst wall contained scattered haemosiderin-laden macrophages, frequent Rosenthal fibres and scattered corpora arenacea. This patient was lost to follow-up.

Patient 4 (Case No. C4966) A 12 year old boy developed acute headache, photophobia, fatigue and malaise, slurring of speech, right sided facial weakness, clumsiness of the left hand, and impairment of gait. On examination, his speech was slurred, he was unable to sustain upward gaze but had normal response to light, and had left-sided upper motor neuron facial weakness, right-sided spastic hemiparesis, and cerebellar ataxia. CT showed a non-homogeneous mass in the pineal region, 1 cm in diameter, containing low and high attenuation areas, the latter enhancing with contrast medium. At operation, the mass was removed. The initial histological diagnosis was pineocytoma. The patient's headache, gaze paresis, dysarthria, facial weakness and limb...
ataxia cleared within two weeks of the operation. He then underwent whole central neuraxis radiation. Subsequent histological review of the surgical specimen showed it to contain normal pineal tissue with central cystic change, the cyst being lined with glial fibres.

**Patient 5 (Case No. C4877)**  A 22 year old woman had a 1 year's history of severe headaches, nausea, vomiting, fatigue and irritability. On examination, she had bilateral papilloedema and impairment of ocular convergence. CT showed a cystic lesion involving the third ventricle, with obstructive hydrocephalus. At operation, a 4.5 x 3.2 cm cyst was found. It was tan in colour, had a wall 0.5-2 mm thick, and contained clear yellow fluid. Post-operatively, the patient's symptoms receded. Histological examination showed the cyst wall to contain glial tissue flanked on either side by compressed normal pineal gland. The patient was lost to follow up.

**Patient 6 (Case No. C4458)**  A 31 year old woman had a seven months' history of severe headaches, nausea, vomiting, fatigue and irritability. On examination, she had bilateral papilloedema and impairment of ocular convergence. CT showed a cystic lesion involving the third ventricle, with obstructive hydrocephalus. At operation, a 4.5 x 3.2 cm cyst was found. It was tan in colour, had a wall 0.5-2 mm thick, and contained clear yellow fluid. Post-operatively, the patient's symptoms receded. Histological examination showed the cyst to contain foci of residual pineal parenchymal cells, distorted by the pressure of the cyst. The lining of the cyst was composed of dense fibrillary astrocytes with associated Rosenthal fibres (fig 4).

**Patient 7 (Case No. C4222)**  A 25 year old woman developed slowly progressive diplopia and difficulty with upward gaze affecting her left eye followed two years later by right-sided hemiparesis, hemiparaesthesia and ataxia, and over the next year by left-sided facial weakness, tinnitus and deafness, and by vertigo. CT disclosed a cystic lesion in the pons anterior to the fourth ventricle with displacement of the pineal gland. At operation, two independent cysts were discovered: one in the dorsolateral mesencephalon, and the other in the pons, ventral to the fourth ventricle. The mesencephalic cyst lay caudal to the pineal gland and separate from it, and filled the left side of the quadrigeminal cistern; the cyst's membrane extended along the wall of the third ventricle as far as the foramen of Monro. The surrounding arachnoid was thickened. Postoperatively, the patient improved. At follow up two years after the operation, she had residual diplopia and right hemiparesis and ataxia, which had improved. At the time of the initial histological examination the diagnosis of pineocytoma or germinoma had been entertained. On review, examination showed the cyst to originate from the pineal gland; the gland itself was compressed by the cyst wall, which was gliotic.

**Discussion**

Large benign cysts of the pineal were first described as a histological entity probably in 1899. The first craniotomy was performed for the condition in 1914. In 1937, Liber had reviewed 28 cases which had appeared in the literature up to that time. Carr reported in 1944 on six cases (see table). The cysts ranged from 1.0-2.5 cm in size, and were symptomatic in three patients. In other large series of pineal examinations, large cysts have occurred either as isolated examples (1/150 and 1/74) or have not been found at all (eg 0/50 and 0/168). Since Carr's series only eight histologically documented cases have been reported. Six of these were symptomatic. The symptoms included headache, raised intracranial pressure, Parinaud's syndrome, cerebellar, corticospinal and sensory deficits, and loss of consciousness (see table). Recently, two series reported respectively 15 and 14 cases of large pineal cyst among 1000 routinely reviewed MRI scans of the brain: four patients were asymptomatic, all with cysts of 0.7 cm or larger; one suffered from headache, another from weight gain, and one each from "body jerks" and "stumbling".

Thus, symptomatic large benign cysts of the pineal gland are not common. Nevertheless, the fact that seven cases were seen in the last five years our of some 1500 cases of brain tumour referred to us for consultation suggests that they may be more frequent than is currently appreciated, a suggestion which is supported by the MRI figures quoted above.

On gross inspection, the cysts are tan-yellow or opaque, and have a smooth capsule. Those that have bled may be chocolate brown. The cyst wall may be up to 2 mm thick. The fluid content is clear yellow or yellow-white, and may gel upon standing; it may be brown if haemorrhage into the cyst has occurred. Microscopically, the appearance of the cyst wall is characteristic. The wall consists of three layers which may be more or less clearly recognisable. The outer layer consists of a fibrous capsule. The fibroblasts are sometimes arranged in a thin layer, but more commonly are densely packed. Inner to the capsule is a
layer of pineal cells. These may be many layers deep or consist of a few sheets of cells only. They may form a continuous layer or be clustered in isolated islands. Corpora arenacea may be present alongside the pineal cells (4/7 of our cases, 6/9 of the other reported cases with detailed histological description). The inner layer is formed by a thin lining of glial cells. In some cases, there may be a further lining of ependymal cells adjacent to the cyst cavity (0/7 in our series, but 4/9 amongst the other reported cases). Histologically, the cyst is most often mistaken for a pineocytoma. This occurred in four of our patients, to one of whom whole-central neuraxis radiation was administered. The features that distinguish a cyst from a pineocytoma include the presence of the external fibrous capsule, of a modest number of normal pineocytes arranged in clusters usually modified by compression, and of conspicuous adjacent reactive fibrillar gliosis.

The aetiology and pathogenesis of the larger cysts are still disputed. Small (0-2 cm) cysts of the pineal occur with a frequency of 25% to 40% of the normal adult population.7 They appear most commonly after the onset of puberty and are thought to be related to involution of the pineal gland. Cooper18 suggested that they arise as a result of the failure of growing pineal cells to obliterate completely the cavum pineale during embryonic development. Others19 believed them to originate secondarily to ischaemic glial degeneration; ependymal invasion of glial lacunae; or invagination of the pineal gland.

In regard to the larger cysts, Carr4 suggested that they formed by coalescence of the smaller ones in most
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cases, and, occasionally, as a result of the intrapineal inclusion of ependymal cells. Both suggestions seem, however, unlikely. The first explanation does not account for the rarity of the larger cysts in contrast to the frequency of the smaller ones: thus, not a single large cyst was found in Hasegawa's series of 168 autopsied cases, 40% of which were found to contain a small pineal cyst. Nor does it account for the fact that the majority of the large cysts occur in young patients—6/7 of our patients were under 31 years. One would expect that, were large cysts to arise from smaller ones, their incidence would be higher in the elderly. As to the second hypothesis, ependymal cells are found only in a minority of cases (none among our series). It is therefore unlikely to explain the genesis of most of the large cysts. Recent or old haemorrhage has been propounded in three instances to result in an expansion of a previously extant cyst. Two of our own cases had histological evidence of old haemorrhage. Previous head injury has also been suggested. Sevitt and Schorstein's patient and one of our patients first became symptomatic during pregnancy. Most of the patients (5/7 in our series) have been young women. It is conceivable that hormonal influences, associated with pregnancy or with the menstrual cycle, may play a role, perhaps by causing enlargement of previously existing small cysts.

Patients may present with symptoms and signs of raised intracranial pressure, or with focal signs and symptoms due to compression and oedema of neighbouring structures. The commonest symptom, headache (6/7 of our cases), may arise from obstructive hydrocephalus caused by compression by the cyst of the anterior portion of the aqueduct of Sylvius. Focal deficits include Parinaud's syndrome, cerebellar and long tract (motor and sensory) signs, and are indistinguishable from those of other mass lesions in the pineal region. No endocrine disturbances have been described in patients with simple glial cysts, except for one patient with excessive weight gain. One of our patients and three of Carr's patients suffered from emotional disturbances such as depression and emotional lability. The pathogenesis of these symptoms is unclear.

The radiological features have been well described. On CT the cyst may be homogeneously hypodense with Hounsfield count approaching that of the CSF, or it may be non-uniform. It may contain blood or calcified areas. Its rim may or may not be contrast-enhancing, and frequently contains calcified areas, representing the corpora arenacea within the capsule wall. There may be associated obstructive hydrocephalus. On MRI, the cystic lesions have a signal characteristic of cerebrospinal fluid, as opposed to dermoid cysts, which have signal characteristics similar to fat, and to primary pineal tumours, in which the T1 signal is similar to that of grey matter.

In conclusion, benign glial cysts are important in the differential diagnosis of mass lesions of the pineal region. The treatment, surgical excision, is curative. The histological distinction between these benign cysts and true tumours of the pineal, especially pineocytoma, is crucial both for prognostic and therapeutic reasons.

References

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