ORIGINAL ARTICLE

Age-related Cyst Formation in Human Pineal Gland

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ABSTRACT

Aim: To determine age-related incidence of human pineal cyst using cadaveric material.
Methods: The present study was carried out in Department of Anatomy, University of Health Sciences, Lahore for two years. The study design was analytical cross-sectional. Thirty pineal glands from human cadavers ranging from 16-80 years of age were collected from the mortuary of King Edward Medical University Lahore using purposive, non-probability sampling. These were divided in three different age groups: I, II and III each between 16 to 30, 31 to 45 and 46 to 80 years of age respectively. Each bisected specimen of pineal gland was observed for presence of macroscopic cyst. Microscopic cysts were noted using 4 µm thick sections, stained with H & E and PAS. The percentages were given for qualitative variables such as presence of cyst and gliosis. Fisher exact test was applied to observe associations between qualitative variables.
Results: Cyst formation was observed in 26.7% of cases but no statistically significant association was observed between age groups and cyst formation (p-value=0.509).
Conclusion: Human pineal cyst is a common finding on autopsy but its incidence is not age-related.
Key words: Human pineal gland; Cyst; Autopsy; Incidence.

INTRODUCTION

Cysts in the pineal gland had been observed in 25-40% of autopsy series[1,2]. It is found to be an incidental finding on MRI[3] and there is difficulty in differentiating these cysts from neoplasms of this region[4]. Pineal cysts may be missed on CT scan if their resolution is less than that of imaging technique or it may be confused with quadrigeminal cistern[3].

Cysts measuring 2-15mm are usually asymptomatic but may enlarge the pineal gland, compressing the adjacent structures[5]. Symptomatic cysts are usually larger and their size ranges from 1-4cm[6], these may be associated with headache, vomiting[7] visual disturbances, gait instability, dizziness, episodic loss of consciousness, and sleep disturbances[8]. Midbrain tectum may be compressed leading to Parinaud syndrome, however, hydrocephalus may be produced if cerebral aqueduct is compressed[4]. Spontaneous intracystic hemorrhage may occur[9] and can lead to sudden death[10]. On MRI, asymptomatic pineal cysts had been reported in patients diagnosed with central precocious puberty[7]. The degree of displacement of pineal from midline on radiological examination had been correlated with the severity of neurological symptoms[11].

Histologically, the pineal cyst may be mistaken for a pineocytoma. However, the pineal cyst can be distinguished from pineocytoma due to presence of the external fibrous capsule, clusters of compressed normal pinealocytes and adjacent gliosis[6]. Successful treatment of pineal cysts can be undertaken[12] using infra-tentorial and supra-cerebellar surgical approaches[13].

In view of above mentioned importance of cyst formation in the human pineal gland, its symptoms and possible treatment, it was decided to investigate the effects of advancing age on pineal gland cyst formation in local population, using cadaveric material.

METHODOLOGY

The present study was carried out in Department of Anatomy, University of Health Sciences, Lahore, from January 2008 to January 2009. A total of thirty specimens of pineal glands were obtained from the cadavers of different age groups from the mortuary of King Edward Medical University Lahore using purposive, non-probability sampling. The cadavers were brought to cold storage within 3 hours after death and kept at a temperature of 4°C; pineal glands were removed within 24 to 48 hours after death. The study was carried out in three groups I, II and III according to their age: 16 to 30, 31 to 45 and 46 to 80 years respectively. The cadavers with history of accidental brain damage, diabetes mellitus, hypertension, disease of central nervous system or drug intake were excluded. Pineal gland was identified and removed along with superior colliculi to include the pineal recess in the sample and was fixed in 10% formal-saline for 6 to 8 days. Then each pineal gland was bisected and was observed for

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presence of any cyst; the size of a macroscopically visible cyst was noted.

Each half of sample was processed for sectioning and the specimens were properly oriented in the paraffin blocks. Four µm thick sections were obtained and stained with Hematoxylin and Eosin (H and E) and Per-iodic Acid Schiff (PAS) for examining them under light microscope (Leica DM 1000).

The size of the microscopically visible cyst was measured with the help of an ocular micrometer calibrated with the stage micrometer at X1000 in a usual way: 10 eyepiece divisions= one stage division; and 1 stage division = 10µm; accordingly one division of eyepiece micrometer = 10/10=1.0µm.

The scale of the eyepiece micrometer was superimposed on the pineal cyst and the number of divisions covering it at the cross sectional diameter multiplied by 1.0 was taken as actual size of the cyst in µm.

The data was entered and analyzed using SPSS version 17.0. The percentages were given for qualitative variables such as presence of cyst and gliosis. Fisher exact test was applied to observe associations between qualitative variables. A p-value of 0.05 was considered as statistically significant.

RESULTS

No statistically significant association was observed between age groups and cyst formation (p-value=0.509). Cyst formation was seen in 8 out of 30 cases (26.7%) (Table I).

On light microscopic examination, three layers were recognized in the wall of cyst; the outer layer consisted of a fibrous capsule; inner to which was compressed pineal parenchyma and gliosis in the innermost layer (Fig. 2) with small blood vessels in its wall (Fig. 3)**.** One cyst from group I was filled with homogenous eosinophilic material. Acervuli (Corpora arenacea) were also observed in the wall of the cyst (Fig. 2).

The size of the pineal cysts was noted. All the cysts were less than 2 mm in size, however, cysts larger than 2 mm were observed in groups I and III. Two cysts measuring 3.5×1.5 mm and 1.5×1.5 mm (Fig. 1) were observed in a specimen of group I; two specimens from group III showed a cyst measuring 3×1.5 mm and 3.5×1.5 mm respectively.

Gliosis was observed around the cyst but its distribution varied within the gland; small plaques to large sheets of astrocytes were found replacing the gland parenchyma (Fig. 2 and 3). However, no significant association was observed between age groups and gliosis (p-value=0.198) (Table II).

Fig. 1: Photograph of cut section of pineal gland showing two cysts; cyst (A) is situated at apex (arrowhead) whereas (B) is in the centre of pineal gland, the stalk of the gland is indicated by an arrow.

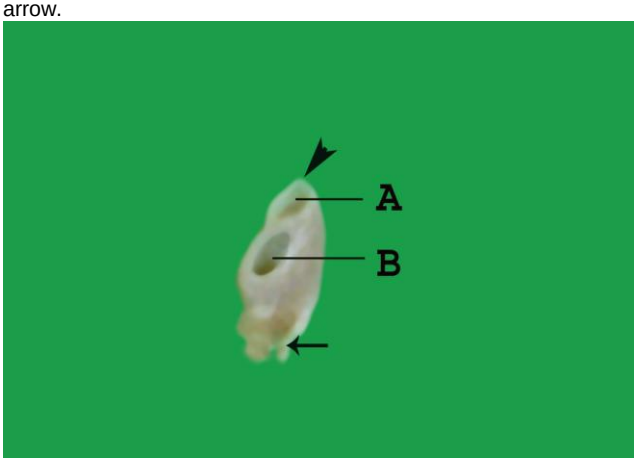

Fig. 2: Photomicrograph of pineal gland (Group I) showing cyst filled with homogenous eosinophilic material (asterisk) and surrounded by glial tissue (G). Parenchyma (thick arrow) is compressed between glial tissue (G) and gland capsule (arrowhead). Intrapineal acervuli (thin arrows) are also evident in the vicinity of cyst. PAS. X 50.

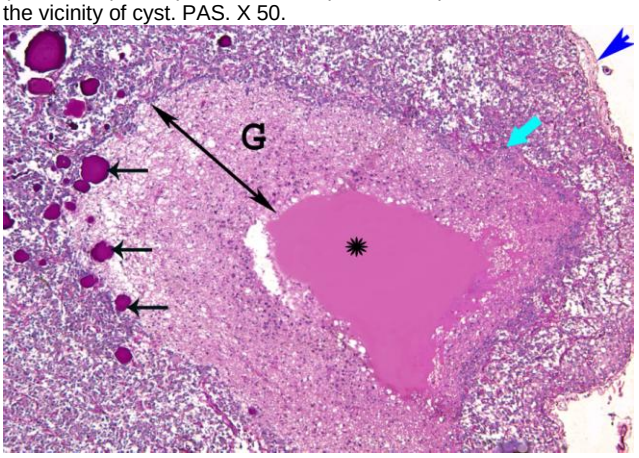

Fig. 3: Photomicrograph of pineal gland (Group II) showing cyst surrounded by glial tissue (G); small blood vessels (arrows) are also observed within glial tissue. Parenchyma (P) is compressed between glial tissue(G) and gland capsule (arrowhead). PAS. X 50.

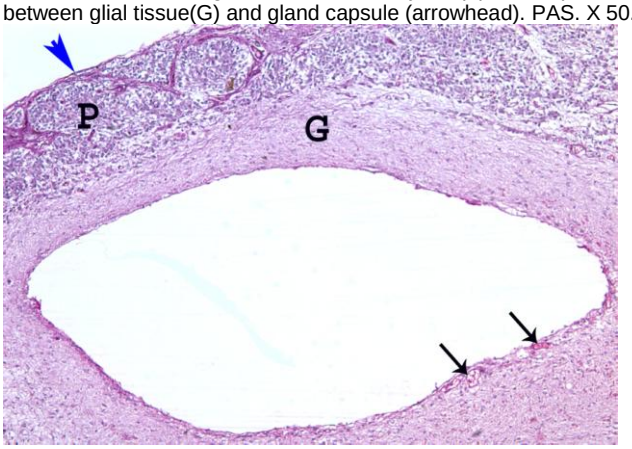

Table I: Distribution of cyst formation in different groups.

Groups (years)	Cyst		Total
	Present	Absent	
I (16-30)	3(10%)	9(30%)	12(40%)
II (31-45)	2(6.7%)	9(30%)	11(36.7%)
III (≥46)	3(10%)	4(13.3%)	7(23.3%)
Total	8(26.7%)	22(73.3%)	30(100%)
Fisher's Exact Test= 1.413; p-value=0.509.			
p value □ 0.05 is statistically significant.			

Table II: Distribution of gliosis in different groups.

Groups (years)	Gliosis		Total
	Present	Absent	
I (16-30)	2(6.7%)	10(33.3%)	12(40%)
II (31-45)	4(13.3%)	7(23.3%)	11(36.7%)
III (≥46)	4(13.3%)	3(10%)	7(23.3%)
Total	10(33.3%)	20(66.7%)	30(100%)
Fisher's Exact Test= 3.253; p-value=0.198.			
p value □ 0.05 is statistically significant.			

DISCUSSION

Cyst formation was observed in eight out of thirty cases (26.7%), both macroscopic and microscopic cysts were noted. They were seen in all age groups, however, our data was statistically insignificant when differences were compared among groups (p-value=0.509). Our findings support the previous observation in which incidence of human pineal cyst was reported to be 27.7%, which was not statistically significant in different age groups[14]; most of the cysts were localized in areas of gliosis and were lined by glial tissue[14]. In another cadaveric study pineal cysts were observed in 25% of cases, the finding corroborates our observations[1]. Similar findings were reported in a study on histopathology of pineal gland by Tapp;[15] he found cysts in pineal glands of all age groups and proposed that cyst formation resulted from cavitation in areas of gliosis secondary to degeneration[15]. Our findings were in conformity with the observations of Hasegawa et al. who could not find any association between cyst formation and advancing age[2]. Furthermore, he pointed out that cyst formation represented pineal involution or atherosclerosis or involution process per se in young adults.[2]

Our findings, however, did not agree with the findings of Koshy and Vettivel who associated cyst formation with progressing age.[16] According to another study, human pineal cysts are found in all age groups but there is an increase in their number and size with advancing age[17]. However, in the present study, there was no increase in size of the pineal cyst as the age advanced.

On high-resolution MRI, the incidence of pineal cyst had been reported to be 23% in healthy subjects, which is consistent with our findings and those reported by Pu.[5] However, other studies showed a higher incidence (35-40%) on MRI[18].

There is a linear correlation between pineal parenchymal volume and concentration of plasma melatonin[19]. Therefore, pineal cysts compressing the pineal parenchyma, lead to a reduction in melatonin secretion[19] due to a decrease in the active pineal volume[20, 21].

Pineal cysts can be differentiated from pineal parenchymal tumors on immunochemistry[22] pineal cysts show high expression of neurofilament protein (NFP) with no expression of Ki-67[22].

On MRI, pineal cysts should be differentiated from the arachnoid cysts; both show MRI signal characteristics similar to CSF; however, pineal cysts do not demonstrate signal suppression on FLAIR (fluid-attenuated inversion-recovery).[23] For accurate diagnosis, knowledge of the imaging characteristics and clinical features of pineal cyst should be kept in mind by the neurophysicians which will help in planning the treatment of the patient.

Serial neuro imaging is recommended for cases of large asymptomatic pineal cysts[7] and that with atypical imaging features[4] because pineal apoplexy may cause sudden death due to intracystic hemorrhage[10]. In symptomatic cases with hydrocephalus or Parinaud's syndrome[8], cyst should be removed completely; however, radical subtotal resection is appropriate if the cyst cannot be easily separated from the tectal plate[24]. Symptomatic improvement has been reported in 94% of patients[8]. Ventricular shunting should be reserved for patients who develop persistent hydrocephalus after cyst resection[24].

CONCLUSION

Human pineal cyst is not an uncommon autopsy finding but its incidence is not age-related.

REFERENCES

1. Tapp E and Huxley M. The histological appearance of the human pineal gland from puberty to old age. *J Pathol* 1972; 108:137-44.
2. Hasegawa A, Ohtsubo K and Mori W. Pineal gland in old age; quantitative and qualitative morphological study of 168 human autopsy cases. *Brain Res* 1987; 409:343-9.
3. Di Costanzo A, Tedeschi G, Golia F, Morrone R and Bonavita V. Pineal cysts: an incidental finding? *J Neurol Neurosurg Psychiatry* 1993; 56:207-8.
4. Steven DA, McGinn GJ and McClarty BM. A choroid plexus papilloma arising from an incidental pineal cyst. *Am J Neuroradiol* 1996; 7:939–42.
5. Pu Y, Mahankali S, Hou J, Li J, Lancaster JL, Gao JH, Appelbaum DE and Fox PT. High prevalence of pineal cysts in healthy adults demonstrated by high-

resolution, non-contrast brain MR imaging. *Am J Neuroradiol* 2007; 28:1706–9.
6. Klein P and Rubenstein U. Benign symptomatic glial cysts of the pineal gland: a report of seven cases and review of the literature. *J Neurol Neurosurg Psychiatry* 1989; 52:991-5.
7. Kumar KV, Verma A, Modi KD and Rayudu BR. Precocious puberty and pineal cyst—an uncommon association. *Indian Pediatr* 2009; 47:193-4.
8. Kalani MYS, Wilson DA, Koechlin NO, Abuhusain HJ, Dlouhy BJ, Gunawardena MP, Nozue-Okada K and Teo C. Pineal cyst resection in the absence of ventriculomegaly or Parinaud's syndrome: clinical outcomes and implications for patient selection. *J Neurosurg* 2015; 123(2):352-6.
9. Mattogno PP, Frassanito P, Massimi L, Tamburrini G, Novello M, Lauriola L and Caldarelli M. Spontaneous regression of pineal lesions: Ghost tumor or pineal apoplexy? *Neurosurg* 2016; 88:64–9.
10. Milroy CM and Smith CL. Sudden death due to a glial cyst of the pineal gland. *J Clin Pathol* 1996; 49:267–9.
11. Antic S, Jovanovic I, Stefanovic N, Pavlovic S, Rancic G and Ugrenovic S. Morphological and histochemical characteristics of human pineal gland acervuli during the aging. *Med Biol* 2004; 11:63-8.
12. Miyatake S, Kikuchi H, Yamasaki T, Asahi M, Asato R, Higuchi K and Nakashima Y. Glial cyst of the pineal gland with characteristic computed tomography, magnetic resonance imaging, and pathological findings: report of two cases. *Surg Neurol* 1992; 37(4):293-9.
13. Fain JS, Tomlinson FH, Scheithauer BW, Fletcher GP, Kelly PJ and Miller GM. Symptomatic glial cysts of the pineal gland. *J Neurosurg* 1994; 80:454-60.
14. Dokov V and Dokov W. Pineal gland morphology in relation to age and sex. Proceedings of IMAB-NATO ARW Conference “Risc infections and bioterrorism” 2003; Varna-Bulgaria.
15. Tapp E. The histology and pathology of the human pineal gland. *Prog Brain Res* 1979; 52:481-500.
16. Koshy S and Vettivel S. Varying appearances of calcification in human pineal gland: A light microscopic study. *J Anat Soc India* 2001; 50:17-8.
17. Singh R, Ghosh S, Joshi A and Haldar C. Human pineal gland: Histomorphological study in different age groups and different causes of death. *J Anat Soc India* 2014; 63(2):98–102.
18. Nölte I, Lütkhoff AT, Stuck BA, Lemmer B, Schredl M, Findeisen P and Groden C. Pineal volume and circadian melatonin profile in healthy volunteers: an interdisciplinary approach. *J Magn Reson Imaging* 2009; 30(3):499–505.
19. Nolte I, Brockmann MA, Gerigk L, Groden C and Scharf J. True FISP imaging of the pineal gland: more cysts and more abnormalities. *Clin Neurol Neurosurg* 2010; 112(3): 204–8.
20. Bumb JM, Brockmann MA, Groden C and Nolte I. Microstructural analysis of pineal volume using true FISP imaging. *World J Radiol* 2013; 5(4):166-72.
21. Beker-Acay M, Turamanlar O, Horata E, Unlu E, Fidan N and Oruc S. Assessment of pineal gland volume and calcification in healthy subjects: is it related to aging? *J Belgian Soc Radiol* 2016; 100(1):1–7.
22. Jouvet A, Vasiljevic A, Champier J, Fèvre MM. Tumors of the pineal region. Pineal parenchymal tumours and pineal cysts. *Neurochirurgie* 2015; 61(2-3):123–9.
23. Smith AB, Rushing EJ and Smirniotopoulos JG. From the Archives of the AFIP: Lesions of the Pineal Region: Radiologic-Pathologic Correlation. *Radiographics* 2010; 30:2001–20.
24. Wisoff JH and Epstein F. Surgical management of symptomatic pineal cysts. *J Neurosurg* 1992; 7(6):896-900.