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PINEAL GLAND CYSTS – AN OVERVIEW

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SUMMARY – Pineal cysts occur in all ages, predominantly in adults in the fourth decade of life. In series of magnetic resonance imaging (MRI) studies, the prevalence of pineal cysts ranged between 1.3% and 4.3% of patients examined for various neurologic reasons and up to 10.8% of asymptomatic healthy volunteers. The diagnosis of pineal cyst is usually established by MRI with defined radiological criteria to distinguish benign pineal cyst from tumors of this area. A recent study demonstrated the findings obtained by transcranial sonography to correspond to those obtained by MRI in the detection of both pineal gland cyst and pineal gland itself, and could be used in the future mainly as follow up examination. Pineal cysts usually have no clinical implications and remain asymptomatic for years. The most common symptoms include headache, vertigo, visual and oculomotor disturbances, and obstructive hydrocephalus. Less frequently, patients present with ataxia, motor and sensory impairment, mental and emotional disturbances, epilepsy, circadian rhythm disturbances, hypothalamic dysfunction of precocious puberty, and recently described occurrence of secondary parkinsonism. Symptomatic cysts vary in size from 7 mm to 45 mm, whereas asymptomatic cysts are usually less than 10 mm in diameter, although a relationship between the cyst size and the onset of symptoms has been proved to be irrelevant in many cases. There is agreement that surgical intervention should be undertaken in patients presenting with hydrocephalus, progression of neurologic symptoms, or cyst enlargement. Tissue sample of the pineal lesion can be obtained by open surgery, stereotaxy and neuroendoscopy.

Key words: *Brain neoplasms – diagnosis; Brain neoplasms – surgery; Cysts – diagnosis; Pineal gland; Brain pathology*

Pineal gland tumors account for 0.4%-1.0% of all intracranial tumors[1], and are 10 times more common in children than in adults. In adults, 60% of pineal tumors are benign, whereas in children 60% are malignant[2]. They can be divided into four main categories: 1) germ cell tumors, 2) pineal parenchymal tumors, 3) pineal interstitial cell tumors, and 4) cysts[3].

The pineal region includes the pineal gland itself, the posterior third ventricle and aqueduct, the supraclinoid cisterns (quadrigeminal plate, ambient cisterns, and the velum interpositum), brain (tectum and brainstem, thalami, corpus callosum splenium), dura (tentorial apex) and vessels (internal cerebral veins and vein of Galen, and posterior choroidal and posterior cerebral arteries)[4].

The pineal gland develops by the proliferation of walls of the third ventricle diverticulum in the diencephalic roof. A remnant of the pineal diverticulum or distension of its obliterated portion has been postulated as a possible source of pineal cyst[5]. Some studies suggest that they may evolve from necrotic and hemorrhagic lesions found in fetal pineal glands[6].

Non-neoplastic glial cysts of the pineal gland are relatively common findings on magnetic resonance imaging (MRI) studies of the brain[7], or in autopsy

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studies[8]. In series of MRI, the prevalence of asymptomatic intrapineal cysts ranged between 0.2%[9] and 10.8%[10] of healthy volunteers and between 1.3[11] and 4.3%[12] of patients examined for various neurologic reasons. On postmortem examinations, pineal cysts are found in 25%-41% of otherwise normal pineal glands[13]. Recently, the use of high resolution MRI demonstrated 23% of volunteers to have pineal cysts with a mean diameter of 4.3 mm (range 2-14 mm) and 13% showed smaller cystic lesions with the largest diameter less than 2 mm[14].

Pineal cysts occur in all ages, from fetal period to senility, with predominance in adults in the fourth decade of life, mainly in women. Symptomatic cysts are most common in young women.

The diagnosis of pineal cyst is usually established by MRI. There are radiological criteria that distinguish benign pineal cyst from tumors of this area. On MRI scan, benign pineal cyst is visualized as a round or ovoid area of signal abnormality in the pineal recess, unilocular, isointense or slightly hyperintense to the cerebrospinal fluid (CSF) signal on T1-weighted and FLAIR images, and isointense with CSF on T2-weighted images with the wall thickness of not more than 2 mm[15]. Sagittal scan on MRI is the most useful diagnostic test because it shows the anatomic relationship of the cyst to the aqueduct[16].

A recent study demonstrated the findings obtained by transcranial sonography (TCS) to correspond to those obtained by MRI in the detection of both pineal gland cyst and pineal gland itself. Pineal gland cyst is defined as any hypoechogenic area within the hyperechogenic gland matrix or hypoechogenic lesion with or without septum, surrounded by a thin echogenic wall. Using TCS, pineal gland can be visualized providing sufficient temporal bone window primarily visualizing hyperechogenic structures like falx cerebri, choroid plexus or mesencephalic brainstem. The diameter of pineal gland cyst as measured by TCS correlates with the diameter assessed by MRI. Ventricular enlargement on axial TCS can be reliably measured and can point to CSF obstruction. Due to fine resolution, portability and lack of invasiveness, assuming appropriate temporal bone window, TCS is a helpful tool in the detection of pineal lesions. Although its resolution cannot match the MRI resolution, its reproducibility and accuracy might add to its practical value mainly as a follow up examination[17,18].

Pineal cysts are most often mistaken for pineocytoma. The most important histologic feature to distinguish pineal cysts from pineocytomas is the absence of pineocytomatous rosettes[19,20].

Pineal cysts usually have no clinical implications and remain asymptomatic for years. The most common symptoms, resulting from compression of the surrounding structures, particularly the quadrigeminal plate and cerebral aqueduct, include headache of variable intensity, vertigo, visual and oculomotor disturbances, and obstructive hydrocephalus. Less frequently, patients present with ataxia, motor and sensory impairment, mental and emotional disturbances, epilepsy, circadian rhythm disturbances[2], and hypothalamic dysfunction of precocious puberty. During the last years, there are ever more publications on the occurrence of secondary parkinsonism as a symptom related to pineal cyst. Sudden death due to cystic lesion has also been reported[21-26].

The natural history of cyst development and the risk of its subsequent enlargement and clinical manifestation are not well understood[27]. MRI follow up of asymptomatic cysts demonstrated their size to remain stable for months or years[28]. In individual patients, the cysts exhibited enlargement or involution but small changes in their size were not associated with specific clinical symptoms. A relationship between the size of the cyst and the onset of symptoms is generally postulated; however, in many cases it may be irrelevant. Symptomatic cysts vary in size from 7 mm to 45 mm, whereas asymptomatic cysts are usually less than 10 mm in diameter, but may sometimes reach 20 mm. The onset of clinical symptoms is attributable to rapid enlargement of pineal cyst, rapid coalescence of the pre-existing smaller cavities, increase in the fluid pressure gradient between the third ventricle and the cyst cavity, or direct inflow of the CSF to the pineal cyst due to communication of the cyst with the third ventricle. Independently of the pathophysiologic aspects of pineal glial cysts, histopathologic findings in asymptomatic and symptomatic cysts are essentially the same[7].

There is still a controversy regarding the management of the pineal gland tumors in general, which is complicated by diversity of the histologic subtypes and their anatomical location close to critical vascular and functional structures[28]. There is agreement that surgical intervention should be undertaken in patients

presenting with hydrocephalus, progression of neurologic symptoms, or enlargement of the cyst. Tissue sample of the pineal lesion can be obtained by open surgery, stereotaxy and neuroendoscopy[29].

References

1. ENGEL U, GOTTSCHALK S, NIEHAUS L, LEHMANN R, MAY C, VOGEL S, JÄNISCH W. Cystic lesions of the pineal region – MRI and pathology. Neuroradiology 2000;42:399-402.
2. HERRMANN HD, WINKLER D, WESTPHAL M. Treatment of tumours of the pineal region and posterior part of the third ventricle. Acta Neurochir (Wien) 1992;116:137-46.
3. KUMAR P, TATKE M, SHARMA A, SINGH D. Histological analysis of lesions of the pineal region: a retrospective study of 12 years. Pathol Res Pract 2006;202:85-92.
4. KOROGI Y, TAKAHASHI M, USHIO Y. MRI of pineal region tumors. J Neurooncol 2001;54:251-61.
5. SAWAMURA Y, IKEDA J, OZAWA M, MINOSHIMA Y, SAITO H, ABE H. Magnetic resonance images reveal a high incidence of asymptomatic pineal cysts in young women. Neurosurgery 1995;37:11-5.
6. LAURE-KAMIONOWSKA M, MASLINSKA D, DEREGOWSKI K, CZICHOS E, RACZKOWSKA B. Morphology of pineal glands in human foetuses and infants with brain lesions. Folia Neuropathol 2003;41:209-15.
7. TARASZEWSKA A, MATYJA E, KOSZEWSKI W, ZACZYNSKI A, BARDADIN K, CZERNICKI Z. Asymptomatic and symptomatic glial cysts of the pineal gland. Folia Neuropathol 2008;46:186-95.
8. HASEGAWA A, OHTSUBO K, MORI W. Pineal gland in old age: quantitative and qualitative morphological study of 168 human autopsy cases. Brain Res 1987;409:343-9.
9. KATZMAN GL, DAGHER AP, PATRONAS NJ. Incidental findings on brain magnetic resonance imaging from 1000 asymptomatic volunteers. JAMA 1999;282:36-9.
10. JINKINS JR, XIONG L, REITER RJ. The midline pineal "eye": MR and CT characteristics of the pineal gland with and without benign cyst formation. J Pineal Res 1995;19:64-71.
11. PETITCOLIN V, GARCIER JM, MOHAMMEDI R, RAVEL A, MOFID R, VIALLET JF, VANNEUVILLE G, BOYER L. Prevalence and morphology of pineal cysts discovered at pituitary MRI: review of 1844 examinations. J Radiol 2002;83:141-5.
12. MAMOURIAN AC, TOWFIGHI J. Pineal cysts: MR imaging. AJNR Am J Neuroradiol 1986;7:1081-6.
13. TAPP E. The histology and pathology of the human pineal gland. In: KAPPERS JA, PEVET P, editors. The pineal gland of vertebrates including man. Amsterdam: Elsevier/North-Holland, 1979:481-500.
14. PU Y, MAHANKALI S, HOU J, LI J, LANCASTER JL, GAO J-H, APPELBAUM DE, FOX PT. High prevalence of pineal cysts in healthy adults demonstrated by high-resolution, noncontrast brain MR imaging. AJNR Am J Neuroradiol 2007;28:1706-9.
15. TAMAKI N, SHIRATAKI K, LIN TK, MASUMURA M, KATAYAMA S, MATSUMOTO S. Cysts of the pineal gland. A new clinical entity to be distinguished from tumors of the pineal region. Childs Nerv Syst 1989;5:172-6.
16. PERES MF, ZUKERMAN E, PORTO PP, BRANDT RA. Headaches and pineal cysts: a (more than) coincidential relationship? Headache 2004;44:929-30.
17. BUDIŠIĆ M, BOŠNJAK J, LOVRENČIĆ-HUZJAN A, MIKULA I, BEDEK D, DEMARIN V. Pineal gland cyst evaluated by transcranial sonography (TCS). Eur J Neurol 2008;15:229-33.
18. BUDIŠIĆ M, BOŠNJAK J, LOVRENČIĆ-HUZJAN A, STRINEKA M, BENE R, AŽMAN D, BEDEK D, TRKANJEC Z, DEMARIN V. Transcranial sonography in the evaluation of pineal lesions: two year follow up study. Acta Clin Croat 2008;47:205-10.
19. MENA H, ARMONDA RA, RIBAS JL, ONDRA SL, RUSHING EJ. Nonneoplastic pineal cyst: a clinicopathologic study of twenty-one cases. Ann Diagn Pathol 1997;1:11-18.
20. LOUIS DN, OHGAKI H, WIESTLER OD, CAVENEE WK, BURGER PC, JOUVET A, SCHEITHAUER BW, KLEIHUES P. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 2007;114:97-109.
21. MICHIELSEN G, BENOIT Y, BAERT E, MEIRE F, CAEMAERT J. Symptomatic pineal cysts: clinical manifestations and management. Acta Neurochir (Wien) 2002;144:233-42.
22. FAIN JS, TOMLINSON FH, SCHEITHAUER BW, PARISI JE, FLETCHER GP, KELLY PJ, MILLER GM. Symptomatic glial cysts of the pineal gland. J Neurosurg 1994;80:454-60.
23. MANDERA M, MARCOL W, BIERZYNSKA-MACYSZYN G, KLUCZEWSKA E. Pineal cysts in childhood. Childs Nerv Syst 2003;19:750-5.
24. DICKERMAN RD, STEVENS QE, STEIDE JA, SCHNEIDER SJ. Precocious puberty associated with pineal cyst: is it disinhibition of the hypothalamic-pituitary axis? Neuroendocrinol Lett 2004;25:173-5.
25. MORGAN JT, SCUMPIA AJ, WEBSTER TM, MITTLER MA, EDELMAN M, SCHNEIDER SJ. Resting tremor secondary to a pineal cyst: case report and review of the literature. Pediatr Neurosurg 2008;44:234-8.
26. MILROY CM, SMITH CL. Sudden death due to a glial cyst of the pineal gland. J Clin Pathol 1996;49:267-9.
27. BARBORIAK DP, LEE L, PROVENZALE JM. Serial MR imaging of pineal cyst: implications of natural history and follow-up. AJR Am J Radiol 2001;176:737-43.

28. REYNS N, HAYASHI M, CHINOT O, MANERA L, PÉRAGUT JC, BLOND S, RÉGIS J. The role of gamma knife radiosurgery in the treatment of pineal parenchymal tumours. Acta Neurochir (Wien) 2006;148:5-11.

CHERNOV MF, KAMIKAWA S, YAMANE S, ISHIHARA S, KUBO O, HORI T. Neurofiberoscopic biopsy of tumors of the pineal region and posterior third ventricle: indications, technique, complications and results. Neurosurgery 2006;59:267-77.

Sažetak

PINEALNE CISTE – PREGLEDNI OSVRT

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Pinealne ciste se pojavljuju u svim dobnim skupinama, a najviše kod odraslih u 4. desetljeću života. U nalazima magnetske rezonance (MR) mozga pojavljuju se kod 1,3% do 4,3% bolesnika s različitim neurološkim simptomima te kod 10,8% asimptomatskih zdravih dobrovoljaca. Dijagnoza ciste pinealne žlijezde se postavlja pomoću MR mozga s utvrđenim radiološkim kriterijima koji razlikuju benignu pinealnu cistu od ostalih tumora ove regije. Nedavne studije pomoću transkranijske sonografije (TCS) mozga su pokazale da TCS može prikazati pinealnu žlijezdu i cistu, a nalazi odgovaraju nalazima na MR mozga. TCS se u budućnosti može upotrebljavati u praćenju veličine ciste pinealne žlijezde. Pinealne ciste najčešće nemaju kliničkog značenja te ostaju asimptomatske godinama. Najznačajniji simptomi su glavobolja, vrtoglavica, vidni i okulomotorni simptomi te opstruktivni hidrocefalus. Rjeđe se opisuju ataksija, osjetna i motorička oštećenja, mentalne i emocionalne tegobe, epilepsija, poremećaj cirkadijanog ritma, hipotalamične disfunkcije te sekundarni parkinsonizam. Simptomatske ciste mogu biti promjera od 7 mm do 45 mm, dok su asimptomatske ciste promjera do 10 mm, iako dosadašnje studije pokazuju kako veličina ciste i pojava simptoma ne moraju biti povezane. Postoji suglasnost da se operacijski zahvat provodi kod bolesnika s hidrocefalusom, progresijom neuroloških simptoma ili kod povećanja ciste pinealne žlijezde. Uzorak tkiva može se dobiti otvorenom operacijom, stereotaksijom ili neuroendoskopijom.

Ključne riječi: *Novotvorine mozga – dijagnostika; Novotvorine mozga – kirurgija; Ciste – dijagnostika; Pinealna žlijezda; Patologija mozgae*