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Retrospective Analysis of Cysts of Central Nervous System and Review of Literature

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Abstract: Diverse variety of non-neoplastic central nervous system (CNS) cystic lesions occurs in both adults and children. Basic understanding of the histopathological features of these cysts is necessary. This is a retrospective study of true CNS cystic lesions that were received over a period of 6 years. A total of thirty five cysts were reviewed. The clinical details and histological features were noted and compared in all cases. Epidermoid cysts are the most common accounting for 62.8% cases. The rest others are colloid cyst (14.3%), arachnoid cyst (11.4%), dermoid cyst (8.6%) and neuromeric cyst (2.9%). There is limited comprehensive data on the true cysts of CNS from India. In this paper we have reviewed the clinical and histopathological features of cysts of CNS and discussed the possible pathogenesis.
Keywords: arachnoid, cysts, CNS, colloid cyst, dermoid, neurenteric.

INTRODUCTION

True cysts of central nervous system (CNS) are rare lesions. Various cystic CNS lesions are either secondarily acquired or are because of maldevelopment. Only some qualify as true cysts (epithelium lined).They are usually benign and sometimes detected incidentally at autopsy. They become symptomatic either because of pressure (ventricular out flow obstruction), rupture or secondary inflammation. Advances in diagnostic radiology have facilitated diagnosis and surgical intervention in many patients with CNS cysts. However, a fundamental understanding of the pathological features of these lesions is clinically vital. Hirano broadly classified CNS cysts into two categories [1].

The first group includes cysts derived from the CNS, for example, arachnoid and ependymal cysts. The second category consists of intracranial or intraspinal lesions that are derived from non-CNS tissues such as endoderm or ectoderm. Histomorphology of cyst wall and at times immunohistochemistry (IHC) is required to characterize these cysts better. Limited studies on cysts of CNS are available from India. We are reporting our data and pathogenesis of these cysts.

MATERIALS AND METHODS

This is a retrospective study which was carried out in the Department of Pathology, Bhopal Memorial Hospital and Research Centre (BMHRC), Bhopal, Madhya Pradesh, India.

All the benign cystic lesions of CNS diagnosed in the department between the periods of January 2010 to December 2016 were reviewed. The study was approved by the Institutional ethics committee. From the medical record section, the patient's files were retrieved to record the age, sex, presenting complaints and location of tumour. The gross and microscopic features of the specimens were recorded from signed out reports. Histopathology slides [Haematoxylin and Eosin (H&E) stained slides, special histochemical stained slides like Periodic acid-schiff (PAS), Alcian blue, verhoff's elastic stain and immunohistochemistry (IHC)] of all the cases were reviewed. Wherever required the faded slides were restained. Cystic degeneration in tumours, inflammatory and parasitic lesions was excluded from the study.

RESULTS

There were thirty five true cysts in the study period of six years. The details about age, sex and

location of different types of CNS cysts are given in the table. Signs of raised intracranial pressure were noted in majority of intracranial cysts. In addition some patients had cerebellar signs, visual disturbances, deafness, seizures and increased head circumference. The spinal cysts of all types presented with cord compression.

Epidermoid cyst

It was the most commonly encountered cyst in our study 62.8% (22/35).It was predominant in males with average age of presentation of 38.2 years. All the epidermoid cysts were intracranial. The most common location of epidermoid cyst was cerebello-pontine (CP) angle (41%) (9/22). Histology showed cyst wall lined by keratinizing stratified squamous epithelium with no adnexal structure. The cyst content was composed of lamellated keratinous flakes (Fig.1a and1b). Focal foreign body giant cell reaction due to rupture and leak of the cystic content was seen in four cases. Calcification was observed in one case. Recurrence was noted in none.

Dermoid Cysts

Three cases of dermoid cysts were observed (8.6%) (3/35). All the dermoid cysts were located in the lumbosacral region and had symptoms of cord compression. Histologically, these were lined by keratinizing stratified squamous epithelium and filled with keratin rich debris. Hair shafts were seen in two cases while in one case pilosebaceous adnexa were present (Fig.1c). Glandular component, muscle or cartilage was not found in any of the case.

Colloid cysts

Total five colloid cysts were noted in our study (14.3%) (5/35). Male predominance with average age of 27 years was observed. All were located in third ventricle. Patients had symptoms of raised intracranial pressure. The cysts were lined by cuboidal to columnar epithelium with or without cilia, supported by delicate collagenous stroma (Fig.1d).In one case dense neutrophilic infiltration was observed (Fig.1e). Focal areas of haemorrhage were noted in two cases. Cyst contents were mucoid or thin gelatinous. Epithelial lining was positive for PAS stain (Fig.1f) and showed immunoreactivity for Pan-CK, EMA (Inset of Fig.1d and Fig.1e respectively) and negative for GFAP.

Arachnoid cysts

11.4% cases were of arachnoid cyst (4/35).Two cysts were found in the sellar suprasellar region while the other two were in posterior fossa. M: F ratio was 3:1 and average age was 39 years. Most patients presented with pressure symptoms. Cyst content was CSF like clear fluid. Microscopically, cyst wall was lined by flattened to cuboidal cells (meningothelial cells) supported by collagen (Fig.1g). The lining epithelial cells were positive for EMA (Fig.1g inset) and negative for GFAP, S100 and CEA.

Neurenteric cyst: Only one case of neurenteric cyst group B type (based on Wilkens and Odom) [2] was found in an 11 year old male patient with clinical features of cord compression. It accounted for 2.85% (1/35) of all the cases. The cyst was intradural extramedullary and located in the cervico-thoracic region. It was associated with split cord malformation and subcutaneous neurofibroma. Cyst was lined by ciliated pseudostratified columnar epithelium with presence of focal goblet cells (PAS positive) (Fig.1h and 1i). Subepithelial area revealed few small mucous glands, lymphoid aggregates and islands of mature cartilage. Focal areas of haemorrhage and mixed inflammation were seen. Neoplastic transformation or recurrence was not observed in any of the cases till date.

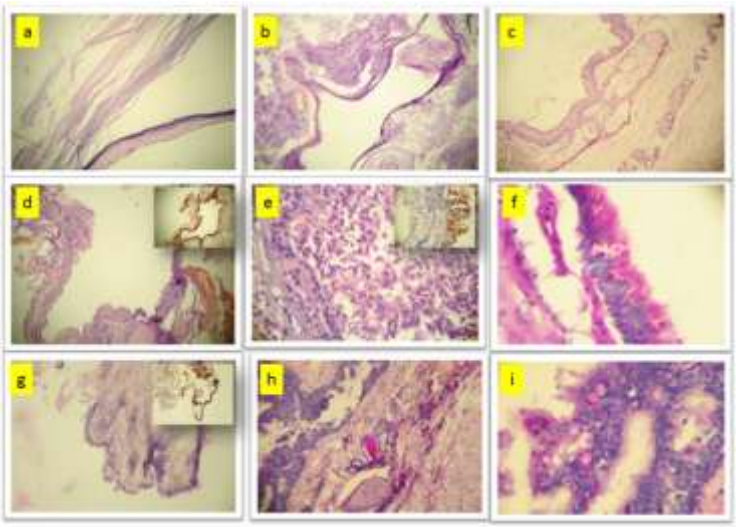

Fig-1: Showing microphotographs of various CNS cysts. 1a and 1b.Epidermoid cyst, 1c.Dermoid cyst,1d,e-colloid cyst, 1f-colloid cyst with PAS positive epithelium, 1g-Arachnoid cyst, 1h,i-neurenteric cyst

Table-1: Distribution of different Cysts of CNS

S.No.	Age in years	Sex	Type of cyst	Location
1.	16	M	Arachnoid cyst	Posterior fossa
2.	30	M	Arachnoid cyst	Sellar- suprasellar
3.	67	M	Arachnoid cyst	Suprasellar
4.	45	F	Arachnoid cyst	Posterior fossa
5.	20	M	Colloid cyst	Third ventricle
6.	25	M	Colloid cyst	Third ventricle
7.	35	F	Colloid cyst	Third ventricle
8.	12	M	Colloid cyst	Third ventricle
9.	43	M	Colloid cyst	Third ventricle
10.	36	F	Dermoid cyst	Spine-conus
11.	40	F	Dermoid cyst	Spine D12-L1
12.	30	F	Dermoid cyst	Spine L2-L3
13.	20	F	Epidermoid cyst	CP angle left
14.	45	F	Epidermoid cyst	Temporal lobe
15.	69	M	Epidermoid cyst	Frontal region
16.	37	M	Epidermoid cyst	CP angle right
17.	26	M	Epidermoid cyst	Temporal lobe left
18.	43	M	Epidermoid cyst	Medial Temporal
19.	35	M	Epidermoid cyst	CP angle left
20.	35	F	Epidermoid cyst	CP angle left
21.	25	M	Epidermoid cyst	Interhemisphere region.
22.	51	M	Epidermoid cyst	Pineal region
23.	14	F	Epidermoid cyst	CP angle right
24.	21	M	Epidermoid cyst	Pineal region
25.	35	M	Epidermoid cyst	CP angle right
26.	36	M	Epidermoid cyst	CP angle right
27.	70	F	Epidermoid cyst	Frontoparietal
28.	49	M	Epidermoid cyst	Ant.cranial fossa
29.	59	M	Epidermoid cyst	CP angle right
30.	11	F	Epidermoid cyst	Suprasellar
31.	31	M	Epidermoid cyst	Interhemispheric region
32.	52	M	Epidermoid cyst.	Middle cranial Fossa& left CP angle
33.	24	M	Epidermoid cysts.	Pineal region
34.	54	M	Epidermoid cysts.	CP angle right
35.	11	M	Neurenteric cyst	Cervicothoracic region

DISCUSSION

Mostly, cysts of CNS are due to maldevelopment and rests are acquired. The recognition of these cysts radiologically and confirmation by pathology is essential for prognostic purposes. Epidermoid cysts account for 0.2 to 1.8% of all intracranial tumours and less than 1% of all intra spinal tumours. Cranial sites outweigh spinal sites by 14:1 [3]. Similar findings were seen in our study, as all cases of epidermoid cysts were intracranial. Apart from the sellar region, the CP angle is the most common site for epidermoid cyst. Less frequently it may occur in the cerebral hemisphere, the lateral ventricles, and other major CSF cistern, at the base of brain and in the orbit [4]. In present study, CP angle is most common site (10/22). Epidermoid cysts and dermoid cysts are the variants of ectodermally derived neuraxis cysts, both lined by keratinizing squamous epithelium. Former is devoid of cutaneous type adnexal structures while latter contain skin appendages including pilosebaceous units, apocrine glands and mature adipose tissue. These present either due to mass effect of the slowly enlarging lesion or because of the immunological response to the rupture of cyst contents [5]. In our study,04 out of 22 epidermoid cysts and 01 out of 03 dermoid cysts presented with rupture, foreign body giant cell reaction and abscess formation. Dermoids typically become symptomatic during the first two decades of life and epidermoid because of their slow production of compact keratin tend to present between the ages of 20 and 50 years [5]. In this study the average age of presentation of dermoids is 35.3years and of epidermoid is 38.2 years.

Epidermoid and dermoid cysts represent nests of cutaneous tissues misplaced during embryogenesis and are found along lines of ontogenic neurocutaneous differentiation. These ectodermal inclusions occur between 3rd and 5th weeks of embryonic life. This inclusion can result in heterotopia of these elements. The median location of these tumours can be explained by the separation of neuroectoderm and its cutaneous counterpart which occurs dorsally along the midline. Laterally situated lesions may result from inclusion of ectoderm at a later stage of embryogenesis, especially during the formation of secondary otic and optic cerebral vesicles [3]. Acquired epidermoid cysts in the lumbar area are due to repeated lumbar punctures or incidental formation of a skin pocket by suturing [3].

Epidermoid cysts of suprasellar region should be differentiated from Rathke's cleft cyst and craniopharyngioma. Rathke's cleft cyst harbours mucicarminophilic cells of cuboidal/low columnar epithelium along with squamous element. Epidermoid cysts do not contain 'ghost cell' keratinocytes, machinery oil like contents and do not show basaloid element as well as stellate reticulum of craniopharyngioma. Sellar dermoids should be distinguished from mature cystic teratoma by the absence of glandular component, muscle or cartilage [6].

Colloid cysts of the third ventricle represents only 0.5%-1% of all intracranial neoplasms, although they account for 18% of tumour in third ventricular region [4]. Location is the key feature of colloid cyst, its location in the third ventricle, usually near the choroid plexus and foramen of monro helps distinguish it from other cysts that superficially resemble it (enterogenous, ependymal and Rathke's cleft cysts) but occur in different locations [7]. These generally present in the third through fifth decade of life with manifestation of ventricular outflow obstruction, a consequence of their intimate relation to the foramen of monro[6]. With the advent of CT and MRI, it is more readily diagnosed and the characteristic radiologic appearance is due to its high cholesterol content [8]. Histologically, this cyst is lined by simple or pseudostratified layers of cuboidal or low to high columnar cells, with scattered goblet cells, resting on thin capsule composed of collagen fibers, fibroblasts, and occasional arachnoid cells [9]. Cyst contents are PAS positive and commonly include hyphae- like aggregates of degenerate nucleoproteins as characteristic of this entity as to be diagnostic in the absence of identifiable epithelium [6]. In this study the average age of presentation of colloid cysts was 27 years. All patients presented with symptoms of hydrocephalous. These were located in the third ventricle and were lined by single layer of cuboidal to columnar epithelium which showed immunoreactivity for CK, EMA, but negative for GFAP.

Arachnoid cysts are mostly considered to begin as maldevelopmental cleft in the arachnoid membrane that subsequently undergoes cystic dilatation. Arachnoid cavity is completely surrounded by transparent arachnoid membrane and severely flattened cerebral cortex [10]. Lesions of this type are lined by attenuated meningothelium resting on a layer of supporting fibrous tissue so thin as to be transparent at operation [6]. These cysts most commonly occupy sylvian fissures, followed by cistern magna and CP angle but may also occur in the supra-sellar region and along the spinal neural axis. In present study, two cysts were located in posterior fossa, while two involved sellar-suprasellar region. These were filled with CSF like clear, colourless fluid. Despite several studies, the mechanism of formation of these cysts is not completely understood [11].

Neurenteric cyst is also known as enterogenous, foregut or teratomatous cyst. These are relatively rare developmental malformations located predominantly in the spinal canal at lower cervical and upper thoracic levels, more rarely in the lumbosacral region. The vast majority are intradural extramedullary and anterior to spinal cord, consisted with the posited developmental relationship with the foregut analage[9]. These cysts are usually associated with complex malformations in neonates. Neurenteric cysts are believed to originate from embryonal dysgenesis. Normal development in the 3rd week of embryonal life involves closure of the neurenteric canal and notochordal separation from the primitive gut. Disruption of this process may lead to the inclusion of endodermal tissue and cystic formation.

Microscopically, the cyst wall lining ranges from a simple cuboidal to columnar to pseudostratified epithelial layer resting on a thin layer of fibrous connective tissue. Mucous producing goblet cells and ciliated cells are commonly observed, producing an appearance similar to gastrointestinal epithelium, or when ciliated cell predominate, respiratory epithelium [9]. Wilkins and Odom [2] classified these cysts into three groups according to histological features. The simplest type of enterogenous cyst, group A is lined by a layer of single cuboidal or columnar epithelial cells with or without cilia. The more complex type, group B, has additional elements found along the course of the gastrointestinal tract or tracheobronchial tree, including the mucous glands, smooth muscle, cartilaginous rings and ganglion cells. Group C has ependymal or glial tissue in addition to the feature of group B. We have found one case of type B neurenteric cyst of cervico-thoracic region. It was intradural extramedullary and associated with split cord malformation and subcutaneous neurofibroma. Goblet cell bearing ciliated pseudostratified epithelium was also seen in colloid and Rathke's cyst which we can exclude by correlating with their location and IHC markers.

Cases of Rathke's cleft cyst, ependymal cyst and glial cyst of brain were not found in this study however review is incomplete without discussing these cysts.

Rathke's cleft cysts are small and asymptomatic and are found in 2-26% of routine autopsy series [12]. These cysts are thought to originate from remnants of Rathke's pouch. With the modern neuroimaging technology, they are being diagnosed much more frequently. Local compressive effects are the basis for presentation in most symptomatic cases, with headache, hypopituitarism, hyperprolactinemia, visual disturbance and rarely diabetes insipidus being the principal clinical features [9]. Histologically the lining epithelium usually consists of columnar or cuboidal cells, which may be stratified in places and bear apical cilia or have a goblet cell appearance [4]. Desmosome connection between the cells of superficial layer of respiratory type epithelium and the underlying cell of squamous epithelium were observed by Hirano *et al*.[10] Immunohistochemically studies confirm the foregut derivation of Rathke's cleft cysts similar to colloid cysts and enteric cysts.

Ependymal cysts are intraparenchymal cysts lined by ependymal cells. These may be ciliated but do not exhibit goblet cell differentiation and do not rest on basal lamina. These are situated in the paraventricular white matter of frontal and parietal lobes, cerebellum, brain stem and spinal cord [6]. These probably arise embryologically by budding or cell displacement from the forming ventricular system [13].

The etiology and pathogenesis of intraparenchymal glial cysts of the cerebellum are not clear. Probably such cysts are formed by budding from the ventricular system like ependymal cysts with subsequent loss of ependymal cells by stretching or pressure effects [14]. It has been postulated that these cysts represent burnt out pilocytic astrocytomas[6].

CONCLUSION

Cysts of CNS are clinically important and often need surgical intervention. Although CT and MRI provide insight into brain lesions, proper microscopic identification of cysts is necessary to know the prognosis and for optimal treatment. Complete resection of the cysts is must to prevent recurrence or neoplastic transformation.

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