

Craniopharyngioma. A Pathological Experience from Tertiary Medical Centre

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Abstract *Introduction:* Craniopharyngioma (CPs) are rare, nearly always benign epithelial tumors derived from cell remnants of Rathke's pouch. The overall incidence of CPs is 0.13 to 2 per 100,000 populations per year. Most frequently they are suprasellar in location and can be detected at any age. *Objectives:* To study clinicopathological features of craniopharyngioma in our region and compare the results with the reported literature. *Methods:* We retrospectively studied 18 patients with histological diagnosis of craniopharyngioma at King Faisal specialist Hospital Jeddah, Kingdom of Saudi Arabia in the last 10 years. Clinical and pre operative imaging data was obtained from computerized medical records of the patients. Histopathological material was obtained by craniotomy. Haematoxylin and Eosin (H&E) stained slides were examined through light microscope. Data was analyzed for age distribution, location, radiological appearance and pathological type. Data was expressed as mean (range) or percent as appropriate. *Results:* Of the 18 patients analyzed, 13 were males (72.2%) and 5 were females (27.8%) with ages ranging between 23 months and 75 years. Maximum (72.3%) of the cases were found in age groups < 25 year. On pre operative CT scan and MRI, the predominant location of CPs was suprasellar region in 12(80%) patients. The average size of tumour on imaging was 4.2 cm. Calcification was evident in 7 (77.7%) patients on CT scanning. MRI, revealed mixed solid and cystic nature of craniopharyngioma. The predominantly cystic were 46.2%, predominantly solid 30.8%, solid 7.7% and cystic 15.4%. Light microscopy revealed adamantinomatous type of histopathological pattern of CPs in 17 (94.4%) and papillary pattern in 1(5.5%) patient. *Conclusion:* Craniopharyngiomas were found as mixed solid and cystic calcified suprasellar tumors with an average size of 4 cm, occurring in young patients with male predominance. Most common pathological pattern was the adamantinomatous type.

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1- Introduction

Craniopharyngioma (CPs) are rare, nearly always benign epithelial tumors of the sellar and suprasellar region [1]. The first description of craniopharyngioma was in 1857 by Zenker [2, 3] who identified masses of cells resembling squamous epithelium along the pars distalis and pars tuberalis of the pituitary gland. The significance of these findings remained overlooked for many decades. In 1902 Saxer reported a tumor consisting of these cells. During the following years, different terminologies were used for them (including hypophyseal duct or craniopharyngeal duct or Rathke's pouch tumors, interpeduncular or dysontogenetic or suprasellar or craniobuccal cysts, suprasellar epitheliomas and adamantinomas), until 1932, when the name "craniopharyngioma" was introduced by Cushing [2, 3].

Craniopharyngiomas are derived from cell remnants of Rathke's pouch along a line from the nasopharynx to the diencephalon. The Rathke's pouch is an ectodermal out pouching of stomodeum (primitive

oral cavity lined by ectoderm) which forms the different structures of the adenohypophysis. Finally, this pouch involutes into a mere cleft and may disappear completely. The craniopharyngeal duct is the neck of the pouch, connecting to the stomodeum, which involutes and separates the pouch from the primitive oral cavity by the end of the second month of gestation. The Rathke cleft, together with remnants of the involuted craniopharyngeal duct, can be the site of origin of craniopharyngiomas [4].

The incidence of newly diagnosed craniopharyngiomas ranges from 0.13 to 2 per 100,000 populations per year, with a point prevalence of 1 to 3 per 100,000 populations. They account for 5-10% of all pediatric brain tumors and 1.2-4% of adult brain tumors. Distribution by age is bimodal with the peak incidence in children at 5-14 years and in adults at 65-74 years of age. There is no variance by gender or race [5, 6, 7].

Craniopharyngiomas may arise anywhere along the craniopharyngeal canal, but most of them are

located in the sellar/parasellar region [2, 3, 8, 9]. The close relationship of craniopharyngioma to the vital structures of the brain predisposes the patient to multiple clinical manifestations, the severity of which depends upon the location, size, and the growth potential of the tumour [3, 7, 8]. The common symptoms at presentation include signs of increased intracranial pressure, including head ache, vomiting, visual and endocrine dysfunction [1, 3, 7, 8].

Imaging is part of neuroradiological evaluation of a patient with a probable craniopharyngioma and consists of cranial computed tomography (CT) and/or magnetic resonance imaging (MRI) with and without contrast enhancement. Calcifications and bony structures are best evaluated on CT, while the delineation of tumour size and the extension of tumour to the neighboring structures can be assessed most accurately by MRI [2, 3, 8].

The characteristic imaging findings of craniopharyngioma are described as calcified, solid, and /or cystic lesions typically with lobular shape and diameter of 2-4 cm. Craniopharyngiomas occasionally extend into the anterior, middle, or posterior fossa and may invade the floor or walls of the third ventricle. Hydrocephalus is observed in up to 38% of cases and is a more common finding in children [10, 11].

There are two distinctive pathological subtypes of craniopharyngioma; 'adamantinomatous' and 'squamous papillary', but mixed types also have been reported. These 2 generalized subtypes vary in age at presentation, tumor location, consistency, imaging characteristics, and histopathological features [12]. The adamantinomatous type may develop at all ages, whereas the papillary type almost exclusively occurs in adults comprising about 14–50% of the tumors in this age group [3, 8].

Objectives

The objectives were to study the clinicopathological features of craniopharyngioma in this region and compare the results with the reported literature.

2. Material and Methods

A retrospective study was carried out on 18 patients with histological diagnosis of craniopharyngioma, diagnosed between Jan 2002 to Dec 2011. Data was collected through a computerized search of the Anatomical Pathology Archives at King Faisal Specialist Hospital Jeddah, Kingdom of Saudi Arabia.

Male and female patients of all age groups were included in this study. Data regarding the age, sex, and imaging reports was obtained from the patients' computerized records. Preoperative imaging data was available for 15 out of 18 cases: computed tomography

(CT) scanning for 2; magnetic resonance imaging (MRI) for 6 and CT + MRI for 7. Tumor calcification was evaluated on CT scanning. The tumour size was calculated on CT + MRI by observing number of cases with 2-4 cm, < 2 cm and > 4 cm with average size. Imaging features including tumour characteristics and post contrast enhancement were evaluated on MRI and were classified as solid, mixed solid and cystic, including predominantly solid and predominantly cystic, and/or cystic. Post contrast enhancement patterns were classified as homogeneous or heterogeneous enhancement.

Material for histopathological examination was obtained through craniotomy and was first routinely fixed in 10% formalin, and then 5 micron meter sections prepared from paraffin embedded tissue and were stained with haematoxylin and eosin (H & E). All the cases were examined through light microscope to identify the two principle patterns of craniopharyngioma: the adamantinomatous craniopharyngioma and papillary craniopharyngioma. Slides were examined to observe characteristic features of tumour including superficial keratinizing layer, mid zone of loose stallete cells and basal palisaded columnar layer associated with keratin nodules, and calcification in cases of adamantinomatous pattern, fronds of squamous epithelial cells with fibro vascular cores, absence of palisaded layer, keratinization and calcification in cases of papillary pattern. In three recurrent cases, slides were examined to observe atypia and mitotic activity.

3. Results

Clinical findings

The age of the patients ranged from 23 months to 75 years. The maximum clustering of cases (72.3%) was observed in the age groups < 25 years and rest of the cases (27.7%) was observed in the age groups > 40 years. There were 13 male (72.2%) and 5 female (27.8%) patients (Fig.1).

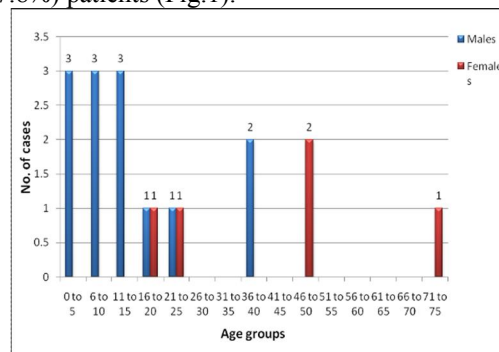


Figure 1: Age and sex of 18 patients of craniopharyngioma

Location

Anatomical localization of craniopharyngioma in 15 out of 18 cases was confirmed by computed tomography (CT) scans and magnetic resonance imaging (MRI). The predominant location was suprasellar region in 12 out of 15 cases (80%), followed by seller/ suprasellar region in 2 out of 15 cases (13.3%), and 1 out of 15 cases (6.7%) was found in the third ventricle. (Fig.2)

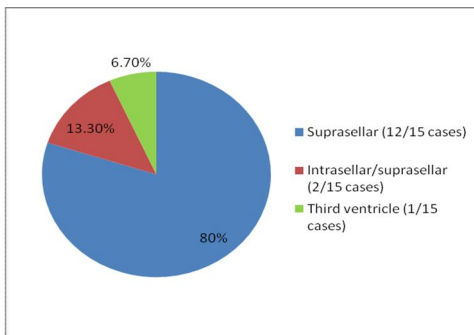


Figure 2 : Locations of craniopharyngioma in 15 patients

Neuro-imaging

The average size of tumour on imaging was 4.2 cm. 8 out of 15 cases (53.3%) were between 2-4 cm, 6 out of 15 (40%) were >4 cm, and 1 out of 15 (6.6%) cases were <2cm.

Pre operative CT scan revealed calcification in 7 out of 9 (77.7%) cases. Pre operative MRI, in 13 out of 15 (77%) cases, revealed mixed solid and cystic nature of craniopharyngioma. The predominantly cystic were 6/13 cases (46.2%), predominantly solid

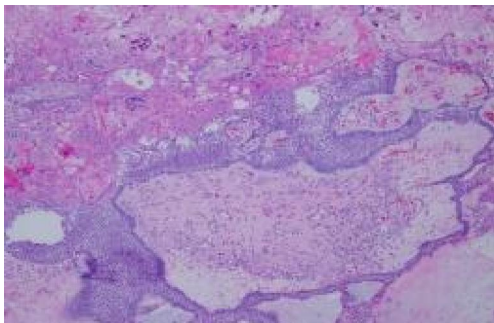


Figure 3: Adamantinomatous craniopharyngioma composed of squamous epithelium arranged in sheets, lobules, and anastomosing trabeculae lined by palisaded columnar epithelium. (H & E × 100)

The microscopic features found were typical adamantinomatous epithelium with peripheral palisading of a single basal cell layer of columnar

4/13 cases (30.8%), solid 1/13 cases (7.7%) and cystic 2/13 cases (15.4%). In terms of signal intensity of tumour, T1-weighted images revealed craniopharyngioma as hypo-intense, iso-intense or hyper-intense lesion and T2-weighted images revealed hyper-intense lesion. Post contrast study revealed heterogeneous enhancement in all 13 cases. The neuro-imaging data is summarized in table 1.

Table 1: Neuro-imaging data of 15 cases of craniopharyngioma:-

	No. of cases evaluated on CT or MRI (% age)
CT findings:-	
Calcification	7/9 cases (77.7%)
CT + MRI findings:-	
Tumour size:	
Average size = 4.2 cm	
2 to 4 cm	8/15 cases (53.3%)
< 2 cm	1/15 cases (6.7%)
> 4 cm	6/15 cases (40%)
MRI findings:-	
Component characteristics:	
Solid	1/13 cases (7.7%)
Predominantly solid	4/13 cases (30.8%)
Predominantly cystic	6/13 cases (46.2%)
Cystic	2/13 cases (15.4%)
Post contrast enhancement	
Heterogeneous	13/13 cases (100%)
Homogenous	0%

Pathology

Light microscopy revealed adamantinomatous type of histopathological pattern of craniopharyngioma in 17 out of 18 (94.4%) cases.

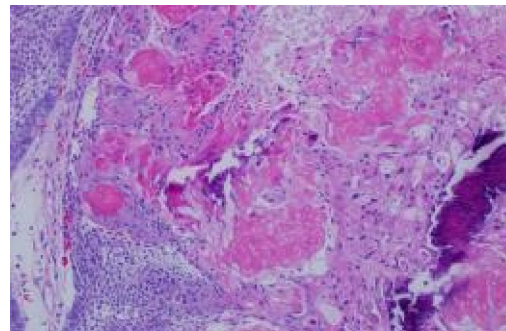


Figure 4: Adamantinomatous craniopharyngioma. Nodules of "wet" keratin and calcification (H & E x 200).

epithelium, surrounding nests of loose stellate cells in association with abundant amounts of compact wet keratin (figures3&4). Additional findings were cysts,

cholesterol, mixed inflammatory cells, chronic hemorrhages, giant cell reaction and calcification. One case (5.5%), with third ventricular location, revealed papillary pattern composed of solid sheets of squamous epithelial cells forming papillary fronds with fibro vascular cores. No calcification was found in papillary pattern. In three recurrent cases, in addition to characteristic microscopic features of adamantinomatous pattern, reactive gliosis was found, but there was no evidence of cellular atypia or increased mitotic activity.

4. Discussion

Although craniopharyngiomas are the commonest lesions to involve the hypothalamopituitary region in childhood populations, almost 50% of the total cases are diagnosed in adults. They may be detected at any age, even in the prenatal and neonatal periods [13, 14]. In the present study we observed the maximum number of cases in age groups 0-25 years, which is slightly different from other reports which have mentioned a bimodal age distribution with peak incidence rates in children of ages 5–14 years [3], 5-9 years [15], 6-15 years [16] and < 16 years [7]. Sherif *et al.*, in a study of 18 patients, reported that 44% of the tumour cases occurred in children < 18 years [17]. The second peak observed in the present study is from 40-73 years. The peak incidence rates in adults are reported from ages 50–74 years [3], 40-44 years [15] and older than 65 years [4]. Barbosa *et al.*, in a study of 32 cases, reported maximum cases (15/32) in the middle age group, between 15-49 years [18].

There is controversy about gender variation of craniopharyngioma. The present study showed a clear sex predilection of craniopharyngioma. Analysis of our series has resulted in the general conclusion that there is a preponderance of males over females (72 to 28%) which is in agreement with the results of studies from South India and Iran [16, 19], but in contrast to the report of Sherif *et al.*, in which preponderance of females is observed [17] and studies from the west that reported no gender variation [5, 6]. However multi-institutional and population based studies may exactly define sex predilection.

Location

Craniopharyngioma may arise anywhere along the craniopharyngeal duct, but most of them are located in the sellar/parasellar region. The majority has a suprasellar component (94-95%), both suprasellar and intrasellar (53-75%), whereas the purely intrasellar are the least common ones (5-6%) [3].

Other rare locations include the nasopharynx [3, 20], the Para nasal area, the sphenoid bone, the ethmoid sinus, chiasma [3], the temporal lobe [21] the pineal gland, the posterior cranial fossa, the mid portion of the midbrain, [3], the cerebellopontine angle [3, 22], or completely within the third ventricle [3, 7].

In the present study, we found that vast majority of craniopharyngioma (80%) were located in the suprasellar region, as reported in literature. We found one case within the third ventricle, which is a rare location [3, 7].

Neuro-imaging

The size of craniopharyngiomas, on CT or MRI evaluation, has been reported to be larger than 4 cm in 14-20% of the cases, 2-4 cm in 58-76%, and smaller than 2 cm in 4-8%. Rare cases of giant tumors with diameter up to 12 cm have been also described [3].

In the present study, the average size of craniopharyngioma was 4.2 cm and most of the cases (53%) were found with the size in the range between 2-4 cm and less frequent were smaller than 2 cm (6%). The results are in agreement with the mentioned reports.

Based on computed tomography (CT) and/or magnetic resonance imaging (MRI), appearance of craniopharyngiomas is typically described as calcified, solid, and or/cystic lesion with size of 2-4 cm [12]. Calcifications and bony structures are best evaluated on CT, while MRI is useful for delineation of tumor size, and for more accurate topographic and structural evaluation of the tumor [2, 3]. According to a recent study, there are no significant differences in neuroradiological characteristics of craniopharyngiomas between children and adults, with the exception of lower rates of tumor calcification in adult patients [8].

In the present study, calcification was evident in 72% of cases evaluated on CT and all cases were < 18 years. The range of calcifications evaluated on CT is between 45-57% of the subjects and is probably more common in childhood ranging between 78-100% [3, 10, 12, 23, 24].

In terms of tumor characteristics on MRI, craniopharyngiomas are mainly mixed solid and cystic tumors; purely solid type is the least common variety. Barbosa *et al.*, [18] reported 62.5 % mixed solid-cystic lesions. Karavitiki [7] reported predominantly cystic CPs to be 46% and Choi *et al.*, [11] observed 46.2% of CPs as predominantly cystic, 30.1% as predominantly solid, 23.1% as cystic and solid as 0%. Other studies reported range of solid CPs between 8% and 27 % [7]. In the present study, CPs

appeared as mixed solid-cystic lesions in 79.9% of cases; predominantly cystic tumors were 46.6%. Solid tumors were less frequent, 6.6% in our series and all appeared with heterogeneous post contrast enhancement, which compares to the mentioned reports.

We did not find any differences in radiological appearance of craniopharyngioma between children and adults, except calcification, which was more evident in children. There was no difference in imaging findings in the cases of recurrence.

Pathology

Despite their sellar location, CPs are not glial or neuronal lesions; rather, they are epithelial neoplasms [1]. By light microscopy, 2 principle patterns of CPs are recognized: adamantinomatous craniopharyngioma and papillary craniopharyngioma.

Adamantinomatous craniopharyngiomas (commonly encountered) are most often diagnosed in childhood and young adults and as a general rule, are both solid and cystic lesions. The second type is papillary CPs, solid (less commonly encountered) found most often in older adults [1]. Barbosa [7] found adamantinomatous type CPs in 92.6% of the cases and papillary type in 7.4 %, (all men in the middle age group). In other study of 80 patients, adamantinomatous type of craniopharyngioma was found in 86.2% and papillary type in 11.2% of the cases [25]. In our series we diagnosed adamantinomatous craniopharyngioma in 94.4% of the cases and we found classic light microscopic features of adamantinomatous CPs with presence of lobules of adamantinomatous epithelial cells with peripheral palisading of a single cell layer bordering clusters of loose stellate cells. The other associated features were wet keratin, cysts, cholesterol, inflammatory cells, giant cell reaction, and calcification [1, 4]. One case, located in third ventricle, was diagnosed in older age and was a solid tumor composed of solid sheets of squamous epithelial cells forming papillary fronds with fibrovascular cores. The papillary craniopharyngioma is more often solid and generally lack the peripheral palisading of epithelial cells, the cystic changes, calcification, and the cholesterol deposition typically seen in adamantinomatous type of craniopharyngioma [1, 4, 10].

Although both types of craniopharyngioma are benign lesions, but they may recur locally if incompletely excised. There are exceedingly rare lesions that satisfy the conventional criteria for a malignant lesion by light microscopic examination [1]. In the present study three cases with recurrence did not demonstrated any features of malignancy.

Conclusion

In general, the maximum cases of craniopharyngioma were of the adamantinomatous type and were found in young age with male preponderance. The common location was the suprasellar region. On imaging, craniopharyngioma was found as mixed solid and cystic calcified lesion with an average size of 4.2 cm. Our results are comparable with the reported literature.

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