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Craniopharyngioma and Oil Machinery Fluid: Review

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Abstracts

Craniopharyngiomas are non-glial epithelial tumors arising from the sellar/suprasellar region. They account for less to 4% of all intracranial neoplasms and for 5-10% of intracranial tumours in children. Are considered as benign tumors however, despite having a benign histologic appearance can turn to, invade, spread and have malignant transformation. Are tumors that may have a variety of histological findings, including; ghost cells, dystrophic calcifications, wet keratins, granulomas and cleft cholesterol, digitiform invasion, reticulum stellate hyper density or hipercellularity, whorl-like arrays formations etc. Little is known about these latest findings but studies have shown that this in association with β-catenin mutation. Too little is known about the oil machinery fluid of the cyst content. In this review we bet on the oil machinery fluid, to cause damage to brain tissue who for various unknown mechanism it is breaking the cyst wall or goes out the content towards the outside and in this process and output of neoplastic cells are implanted and may be the cause of recurrence, dissemination and cell growth. This theory could be very controversial and contradictory to what was written, described by the great master of neuropathology. However only intend to express a theory based on observation of some cases, which considered that many studies must confirm this one further studies are needed.

Keywords: Craniopharyngioma; Histological findings; Oil machinery fluid; Brain invasion

Introduction

Craniopharyngioma (CP) is one of the most common non-glial intracranial tumors of childhood. The term "craniopharyngioma" was coined in 1931 by Charles Frazier and further popularized by Harvey Cushing who described craniopharyngiomas as "the most formidable of intracranial tumours" [1]. In 1857, Zenker was the first describing pathological findings of clusters cells similar to squamous epithelium in the hypothalamic-pituitary area [2].

CPs are benign tumors that occur as two histological subtypes. The adamantinomatous type (aCP) and the papillary type (pCP) according WHO [3] and account for 1.2-4.6% of all intracranial tumor and are the most common non neuroepithelial brain neoplasms in children, and no sex predilection [3]. The annual incidence is 0.5-2.0 cases/million per year and approximately 60% of CP is seen in adulthood. Approximately 30-50% of all cases represent childhood CP. The aCP type usually occurs during childhood and pCP in middle-aged adults [3]. Clinical features are non-specific and basically the symptoms depend on the age and tumor size. Typical initial manifestations in children are symptoms of elevated intracranial pressure, visual disturbances and hypopituitarism [3-5]. The most common manifestations at diagnosis are headache, visual impairment, polyuria/polydypsia, growth retardation, puberty development disturbances, and significant weight gain [4,5].

Radiographic imaging provides a tumor with solid and cyst portions, with calcifications and irregular capsule [3]. Yasargil et al. [4] described CPs into 6 subtypes: 1) purely intrasellar-infradiaphragmatic; 2) intra- and suprasellar, infra- and supradiaphragmatic; 3) supradiaphragmatic parachiasmatic, extraventricular; 4) intra- and extraventricular; 5) paraventricular; and 6) pure Intraventricular Craiopharyngioma (IVC).

The treatment of CP remains a significant challenge. Gross total resection or subtotal resection in combination with adjuvant conventional radiotherapy are currently the treatment options for the management of craniopharyngiomas, but complete resection of these tumors is not always possible due to their large size, calcification and adherence to crucial surrounding neurovascular structures [5,6].

Talk about the pathogenesis very is controversial, several observations indicates arise from ectodermal derived epithelial remants of Rathke's pouch and the craniopharyngeal duct [7]. However, CP is also considered as an embryonic malformation of the sellar and parasellar region [8]. Their pathogenesis is still unclear and it is not known if they are collision tumors derived from independent stem cells or if they are originated from a single stem cell undergoing divergent differentiation [8].

The pathogenesis of pCP is less understood but these tumour may arise from metaplastic transformation of anterior pituitary epithelial cells. Metaplasis derived from the tooth promordia arise aCP type and from buccal mucosa promordia gives to pCP subtype [3]. Further support with ameloblastic tooth bud and adenohipophyseal primordial components [3].

Despite recent advances, the molecular mechanism that leads to ACP formation as well as markers of their development and progression are poorly understood. Multiple chromosomal abnormalities and genetic mutation have been reported in the two histological subtypes. It is well known that both have abnormalities on chromosome 2 and 12 [3]. aCPs often contain mutations in CTNNB1, encoding β-catenin, a component of the adherens junction and a

mediator of Wnt signalling [9-12]. Dysregulation of the Wnt signalling pathway contributes to develop abnormalities and carcinogenesis of solid tumors [13]. β-catenin mutations and/or nuclear accumulation are used as diagnostic hallmarks of the adamantinomatous variant, setting it apart from the papillary variant of craniopharyngioma [9-13].

The Wingless (Wnt)/β-catenin signaling pathway plays a critical role in the control of cellular proliferation and differentiation during embryonic development and organogenesis (is a critical regulator of stem cells, and has been associated with cancer in many tissues), the effect of these mutations are restricted to a small number of tumor cells, mostly forming clusters [13]. It also demonstrated the genetic expression of a degradation-resistant mutant form of β-catenin in early Rathke's Pouch (RP) progenitors; this leads to pituitary hyperplasia and severe disruption of the pituitary-specific transcription factor 1-lineage differentiation resulting in extreme growth retardation and hypopituitarism. Mutant mice mostly die perinatally, but those that survive weaning develop lethal pituitary tumors [9].

ACP contains cells with phenotypic characteristics of progenitor/stem cells: They are slow-dividing, undifferentiated, and express markers such as SOX2, SOX9, Cyclin D1, Cyclin D2, and p27Kip1, which have been associated with cell stemness in the pituitary gland and other tissues [14]. Recently, the existence of a small population of $SOX2^{+}$; $SOX9^{-}$ cells has been suggested to correspond to progenitor/stem cells located around the lumen of the postnatal pituitary [14]. A novel and unexpected role for pituitary stem cells has been proposed, which is fundamentally distinct from the cancer stem cell paradigm. Nevertheless, recent studies determine chromosomal imbalances are a rare event in both adamantinomatous and papillary craniopharyngiomas [15].

Histologically, two principal patterns of craniopharyngioma are recognized: papillary and adamantinomatous [3]. This latter pattern is made up by nests and cords of stratified squamous epithelium which are replaced by a layer of columnar cells on the outskirts, and it is characterized by the presence of dystrophic calcifications and cysts containing "motor-oil-like" or oil machinery fluid (brown-yellow cholesterol-rich fluid) [3]. The papillary pattern is made up by papillary squamous epithelium, and it is generally without calcifications or cysts [3]. Other histological components shortly described but are present in craniopharyngioma are the ghosts cells, the wet keratin, dystrophic calcifications, inflammatory infiltrate, macrophages, Hemosiderophages and Rosenthal fibers. But neither is known the mechanisms of formation of each one of the oil machinery fluid components that make it aggressive.

Rosenthal Fibers (RFs) have been described in the periphery or boundary of craniopharyngioma but little is known about it. As each of these components formed, is not known so far. RFs or piloide gliosis are inclusions within astrocytes, they are granular deposits, intimately associated with intermediate filaments, presented not only in Alexander's disease, also in astrocytic tumors, glial scar tissue and Rosenthal Fibers encephalopathy [16,17].

The inflammatory response, the cleft cholesterol and granulomas formation, probably are related to the immune response or as a consequence of the rupture of cystic structure in craniopharyngioma. 18 Spontaneous rupture may be presented with or without meningitis [17-19]. Chemical Meningitis (CM) may occurs due to an increased pressure of tumor or content of lipids, cholesterol crystals and proteins within in cyst fluid and the cyst wall weakness. It is caused by cyst expansion that conditions cyst wall degeneration [18].

Cystic forms of CPs are studied biochemically regarding lactate, pH, total protein, albumin, immunoglobulin's G and M contents. The CPs pathogenesis seems to be more similar to the other brain tumors than it was believed earlier [18].

Rathke's cleft cyst content includes more mucopolysaccharides or hemosiderin degradation products than CPs [17].

Ameloblastomas and Adenomatoid Odontogenic Tumors (AOTs) are common epithelial tumors of odontogenic origin. Craniopharyngiomas, derived from the remnants of Rathke's pouch or a misplaced enamel organ, are also comparable to the odontogenic tumors [20]. The dystrophic calcifications, the wet keratin and the ghost cells have been described in jaw tumors. Paulus W et al. [20] suggested to separate craniopharyngiomas as odontogenic tumors, though this theory wasn't validated in later studies.

Also, Paulus W et al. [21] and Vajtai et al. [22] suggested the granuloma in craniopharyngiomas can correspond to another type of lesion, as a clinicopathologically distinctive lesion of uncertain origin. They invited a probable inflammatory response due to the likely breakdown of cystic structures.

In our studies in process of publication we have suggested the oil machinery has a very important role in CP. The epithelial cells as reticulum stellate cells can produce lipids which causes the cyst structures growing. The output of this element by a mechanism we ignore occasions a toxicity conditioning a great inflammatory response, probably by the granulomas and cholesterol crystals formation, cytokines induction it conducts to a vicious cycle. The macrophages are incompetent because they try to digest the liquid leading them to dell death.

By the other side, the oil machinery fluid has neoplastic cells which cause their spread and reproduction. That's how we can explain multiples implants of the tumor with more reproductive capability than the first ones. Recurrence is a well-known characteristic of these tumors.

Recently, we have observed, in a rat models, oil machinery is capable to induce damage by reactive species of lipids peroxidation [23].

Histological features that signify transitional entities beyond simple benign Rathke cleft cysts include squamous metaplasia, stratified squamous epithelium, and ciliated or mucinous goblet cells in squamous-papillary CPs [17]. Several studies have identified key clinical, imaging, and histopathological features that can be used in the differentiation of these lesions [24]. Subsequent inflammatory, metaplastic, and neoplastic processes may promote further progression along the pathological continuum, ranging from benign epithelial cysts to aggressive neoplastic cystic CPs. Selected clinical, imaging, and histopathological features can be used collectively to help differentiate these lesions and assign a formal diagnosis.

To date no definitive predictive factors for rapid CP grow and recurrence have been identified as well as third ventricle involvement, large tumor size, tight adherence to surrounding structures, and presence of whorl-like arrays might also foster recurrence.

Ki67 concerned in the peripherally palisaded cells basically in ACP type and indices ranged from case to case, higher index has been observed in recurrence and malignant transformation. P53 expression,

and an intense reactive gliosis might point to rapid tumor growth [22], however the most important factor associated a recurrence is the extent of surgical resection. Prieto e et al. [25] suggested that third ventricle involvement, large tumor size, tight adherence to surrounding structures, and presence of whorl-like arrays might also foster recurrence. High Ki-67 levels, p53 expression, and an intense reactive gliosis might point to rapid tumor growth.

On the other hand, we considerate reactive gliosis and the presence of Rosenthal Fibers might point to a rapid tumor growth. Also we can explain it as a product of the oil machinery fluid output to the normal brain causing an interruption on macrophages activity. We also suggest that the output of the oil machinery fluid participates in the recurrence. Facilitating the exit to tumor cells to brain tissue and activating its capacity for growth.

We observed that reticulum stellate hyper density or hipercellularity, whorl-like arrays formations could be a factor of worse prognostic, those findings are observed by nuclear β-catenin immunoreactivity, how has been described in some cases with malignant transformation (basaloid type carcinoma). These mutations stabilise β-catenin, which evades destruction and accumulates in the nucleus to constitutive activation of the Wnt signaling pathway [10-13]. Activation of β-catenin has been suggested to activate expression of a variety of target genes including Lef1, Axin1 and CyclinD1. Cani et al. [11] and Buslei et al. [12] also demonstrated nuclear and cytoplasmic expression of β-catenin in the majority of human ACP tissue samples, mainly concentrated in epithelial cells within the whorl-like arrays. Those mechanism have been associated to tumor growth, recurrence survival or differentiation.

Immunohistochemical studies revealed that the p53 protein over-expressed in the malignant component, whereas its expression was much lower in the benign component [26,27]. The MIB-1 labeling index was markedly increased in the malignant component in comparison with the low-grade precursor [3] as well as β-catenin nuclear translocation [28] ErbB2 protein, expression and mutations in CTNNB1, could be to estimate whether these tumors could be candidates for anti-ErbB2 therapy [29].

Histologic Malignancy or Malignant Transformation (MT) is extremely rare; the literature shows mostly isolated few case reports. Malignant CP transformation has been associated with a poor prognosis [30,31]. MT occur years after the initial benign craniopharyngioma diagnosis and are associated with multiple benign craniopharyngioma recurrence [30,31]. Rodriguez F et al. [31] described a basaloid carcinoma, squamous cell carcinoma and low-grade myoepithelial carcinoma, and other histologically variants of malignant transformation is odontogenic ghost cell carcinoma [32]. Furthermore, malignant transformation in craniopharyngioma is reported after radiation therapy [33].

Therapy of choice in children with favorable tumor localization is complete resection with optic nerve and hypothalamic-pituitary functions preservation. In children with unfavorable tumor localization (hypothalamic involvement), a limited resection followed by local irradiation is recommended; in patients with favorable tumor localization, is needed an extreme care taken to preserve hypothalamic-pituitary and optical nerve functions. When tumor localization is unfavorable, and are involved the hypothalamic or optic structures, a limited resection followed by local irradiation is recommended [34].

Radiation therapy is a part of multidisciplinary management of several childhood neoplasm. Proton therapy is a new method of irradiation, which uses protons instead of photons [32-35]. Also, Intracystic bleomycin in the treatment of cystic craniopharyngiomas in children has been used having good responses [35].

However, Quality of Life (QoL) is substantially reduced in many survivors due to sequelae such as extreme obesity caused by hypothalamic lesions. Although overall surgical survival rates are high (92%), recurrence after complete resection and progression after incomplete resection are typical post-surgical events. Long-term sequelae substantially reduce the quality of life of approximately 50% of long-term survivors, notably extreme obesity owing to hypothalamic involvement and/or surgical- or radiation-induced lesions [30,33]. Quality of life is substantially reduced in approximately 50% of long-term survivors due to sequelae, impaired due to proximity to optical, pituitary, and hypothalamic structures, notably morbid hypothalamic obesity [35]. CPs have the highest mortality of all pituitary tumours [30]. High recurrence rates after complete resection and high progression rates after incomplete resection have been observed, although the risk of recurrence or progression is less after complete resection than partial resection [35]. CP should be recognized as a chronic disease requiring constant monitoring of the early life as well as post-pubescent consequences and appropriate medical resources for treatment in order to provide optimal quality of survival for patients [33-35].

The long-term morbidity is substantial with hypopituitarism, increased cardiovascular risk, hypothalamic damage, visual and neurological deficits, reduced bone health and reduction in quality of life and cognitive function [35].

Conclusion

We considered and hypothesize the damage caused to the hypothalamus is not always because a surgical procedure, but also it is made by the output and spread of the oil machinery fluid, which causes neuronal damage and the clinical neurological manifestations and obesity. This theory must be proved and studied in a deepest way to establish if the oily fluid is causing all the secondary damage in patients with craniopharyngioma. Further studies are needed.

References

1. Barkhoudarian G Laws ER (2013) Craniopharyngioma: history. Pituitary 16: 1-8.
2. Zenker FA (1857) Enorme Cystenbildung im Gehirn, vom Hirnanhang ausgehend, Archiv für Pathologische Anatomie und Physiologie und für Klinische Medicin 1: 454-466.
3. Perry A, Louis DN, Scheithauer BW, Budka H, Von Diemling A (2007) Meningiomas. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (eds.) WHO Classification of Tumours of the Central Nervous System. Lyon, France: IARC Press 164-172.
4. YaÅŸargil MG Curcic M, Kis M, Siegenthaler G, Teddy PJ, et al. (1990) Total removal of craniopharyngiomas. Approaches and long-term results in 144 patients. J Neurosurg 73: 3-11.
5. Müller HL (2011) Consequences of craniopharyngioma surgery in children. J Clin Endocrinol Metab 96: 1981-1991.
6. Rombi B, Vennarini S, Vinante L, Ravanelli D, Amichetti M (2014) Proton radiotherapy for pediatric tumors: review of first clinical results. Ital J Pediatr 40: 74.
7. Tanaka T Oka H, Kawano N, Kobayashi I, Saegusa H, et al. (1998) Juvenile symptomatic Rathke's cleft cyst--case report. Neurol Med Chir (Tokyo) 38: 578-581.

8. Alomari AK Kelley BJ, Damisah E, Marks A, Hui P, et al. (2015) Craniopharyngioma arising in a Rathke's cleft cyst: case report. J Neurosurg Pediatr .
9. Buslei R Hölsken A, Hofmann B, Kreutzer J, Siebzehnrubl F, et al. (2007) Nuclear beta-catenin accumulation associates with epithelial morphogenesis in craniopharyngiomas. Acta Neuropathol 113: 585-590.
10. Camper SA (2011) Beta-catenin stimulates pituitary stem cells to form aggressive tumors. Proc Natl Acad Sci U S A 108: 11303-11304.
11. Cani CM Matushita H, Carvalho LR, Soares IC, Brito LP, et al. (2011) PROP1 and CTNNB1 expression in adamantinomatous craniopharyngiomas with or without Î²-catenin mutations. Clinics (Sao Paulo) 66: 1849-1854.
12. Buslei R Nolde M, Hofmann B, Meissner S, Eyupoglu IY, et al. (2005) Common mutations of beta-catenin in adamantinomatous craniopharyngiomas but not in other tumours originating from the sellar region. Acta Neuropathol 109: 589-597.
13. Gaston-Massuet C Andoniadou CL, Signore M, Jayakody SA, Charolidi N, et al. (2011) Increased Wingless (Wnt) signaling in pituitary progenitor/stem cells gives rise to pituitary tumors in mice and humans. Proc Natl Acad Sci U S A 108: 11482-11487.
14. Fauquier T Rizzoti K, Dattani M, Lovell-Badge R, Robinson IC (2008) SOX2-expressing progenitor cells generate all of the major cell types in the adult mouse pituitary gland. Proc Natl Acad Sci U S A 105: 2907-2912.
15. Rickert CH Paulus W (2003) Lack of chromosomal imbalances in adamantinomatous and papillary craniopharyngiomas. J Neurol Neurosurg Psychiatry 74: 260-261.
16. Wilson SP Al-Sarraj S, Bridges LR (1996) Rosenthal fiber encephalopathy presenting with demyelination and Rosenthal fibers in a solvent abuser: adult Alexander's disease? Clin Neuropathol 15: 13-16.
17. Stendel R Pietilä TA, Lehmann K, Kurth R, Suess O, et al. (2002) Ruptured intracranial dermoid cysts. Surg Neurol 57: 391-398.
18. Shida N Nakasato N, Mizoi K, Kanaki M, Yoshimoto T (1998) Symptomatic vessel narrowing caused by spontaneous rupture of craniopharyngioma cyst--case report. Neurol Med Chir (Tokyo) 38: 666-668.
19. Arefyeva IA Semenova JB, Zubairaev MS, Kondrasheva EA, Moshkin AV (2002) Analysis of fluid in craniopharyngioma-related cysts in children: proteins, lactate and pH. Acta Neurochir (Wien) 144: 551-554.
20. Paulus W Stöckel C, Krauss J, Sörensen N, Roggendorf W (1997) Odontogenic classification of craniopharyngiomas: a clinicopathological study of 54 cases. Histopathology 30: 172-176.
21. Paulus W Honegger J, Keyvani K, Fahlbusch R (1999) Xanthogranuloma of the sellar region: a clinicopathological entity different from adamantinomatous craniopharyngioma. Acta Neuropathol 97: 377-382.
22. Vajtai I Kopniczky Z, Buza Z, Kovács J, Kovács Z, et al. (2001) [Cholesterol granuloma at the sella region: a new method of the differential diagnosis of craniopharyngioma]. Orv Hetil 142: 451-457.
23. Tena-Suck ML, Hernández-Campos ME, Ortiz-Plata A, Salinas-Lara C, Colín-González AL, et al. (2014) Intracerebral injection of oil cyst content of human craniopharyngioma (oil machinery fluid) as a toxic model in the rat brain. Acta Histochem 116: 448-456.
24. Zada G Lin N, Ojerholm E, Ramkissoon S, Laws ER (2010) Craniopharyngioma and other cystic epithelial lesions of the sellar region: a review of clinical, imaging, and histopathological relationships. Neurosurg Focus 28: E4.
25. Prieto R Pascual JM, Subhi-Issa I, Jorquera M, Yus M, et al. (2013) Predictive factors for craniopharyngioma recurrence: a systematic review and illustrative case report of a rapid recurrence. World Neurosurg 79: 733-749.
26. Sofela AA Hettige S, Curran O, Bassi S (2014) Malignant transformation in craniopharyngiomas. Neurosurgery 75: 306-314.
27. Rodriguez FJ Scheithauer BW, Tsunoda S, Kovacs K, Vidal S, et al. (2007) The spectrum of malignancy in craniopharyngioma. Am J Surg Pathol 31: 1020-1028.
28. Hölsken A Stache C, Schlaffer SM, Flitsch J, Fahlbusch R, et al. (2014) Adamantinomatous craniopharyngiomas express tumor stem cell markers in cells with activated Wnt signaling: further evidence for the existence of a tumor stem cell niche? Pituitary 17: 546-556.
29. Zuhur SS Tanik C, Erol RS, Musluman AM, Kabukcuoglu F, et al. (2013) Immunohistochemical expression of ErbB2 in adamantinomatous craniopharyngiomas: a possible target for immunotherapy. Turk Neurosurg 23: 55-60.
30. Lee SK Kim YS (2013) Current concepts and occurrence of epithelial odontogenic tumors: I. Ameloblastoma and adenomatoid odontogenic tumor. Korean J Pathol 47: 191-202.
31. Ishida M Hotta M, Tsukamura A, Taga T, Kato H, et al. (2010) Malignant transformation in craniopharyngioma after radiation therapy: a case report and review of the literature. Clin Neuropathol 29: 2-8.
32. Zheng J, Fang Y, Cai BW, Zhang H, Liu W, et al. (2014) Intracystic bleomycin for cystic craniopharyngiomas in children. Cochrane Database Syst Rev.
33. Müller HL (2010) Childhood craniopharyngioma--current concepts in diagnosis, therapy and follow-up. Nat Rev Endocrinol 6: 609-618.
34. Müller HL (2013) Childhood craniopharyngioma. Pituitary 16: 56-67.
35. Erfurth EM (2015) Endocrine aspects and sequel in patients with craniopharyngioma. J Pediatr Endocrinol Metab 28: 19-26.