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Craniopharyngioma: the pendulum of surgical management

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Abstract *Background:* For a long time, craniopharyngiomas have been considered surgically attractive tumours. The fact that they are rare, histologically benign, and located in a challenging (but considered accessible) area made them worthy surgical prizes. *Methods:* As we have saved vision and "cured" many of these tumours, the insidious and devastating effects on quality of life for these children has become evident. *Discussion:* The state-of-the-art in the surgical management of craniopharyngioma is now turning to multi-modality treatment strategies (combination surgery and radiotherapy) aiming to limit morbidity. Questions remain—what factors influence our surgical decision making? Do we understand the long-term effects of the radiotherapy now being employed? We review a series of craniopharyngiomas looking for variables that correlated with outcome as perceived in terms of quality of life and we review briefly the history of craniopharyngioma surgery and the relevant literature.

Keywords Craniopharyngioma · Child · Surgery · Radiotherapy · Hypothalamus · Quality of life

Introduction

The surgical history of craniopharyngioma management represents largely the history of microsurgery. We cannot speak of craniopharyngioma surgery without paying tribute to the pioneers of microsurgery such as Yasargil et al. [26]. These new microsurgical techniques allowed us to embrace a tumour previously feared for both its location—nestled between visual pathways, basal arteries, and the neuroendocrine nuclei—and for the characteristics of the tumour being frequently calcified and indigenous to the endocrine/hypothalamic structures, and made it the "ideal" case for microsurgery. Such became the enthusiasm for this challenging tumour that the next generation of neurosurgeons

embraced craniopharyngioma surgery as the emblem of their surgical success.

In the pre-MRI era, patients presenting with obvious clinical symptoms such as visual or endocrinological impairment underwent a plain X-ray, the characteristic calcification in the sellar or suprasellar region allowing craniopharyngiomas to be diagnosed relatively easily. As a cornerstone of craniopharyngioma symptomatology, it was logical that the treatment focus would be that of saving vision—a goal potentially achieved by microsurgery [5, 13, 24].

The 1990s represents the decade of peak enthusiasm for craniopharyngioma surgery. Leading figures such as Hoffman [14], Epstein [8], Choux [5], Hirsch [19] and Di Rocco [2] all published large surgical series revealing their surgical success in resecting these tumours. Interestingly, it is these same surgeons who are the founders of modern Paediatric Neurosurgery. As the leading lights of our specialty demonstrated mastery of these tumours, concurrent with technological advancements, the profile of craniopharyngioma surgery rose to be seen as a pinnacle of Neurosurgery.

The endocrine disorders accompanying radical craniopharyngioma resection were (and still are) considered both inevitable and acceptable [1, 15]. The acceptability of this morbidity was due to progress in Endocrinology allowing hormonal replacement compatible with "normal life". It is only recently that questions are starting to be raised about the "normality" achieved as more subtle issues such as fertility and adult growth hormone deficiency are critically reviewed [16, 21].

Following the heady enthusiasm for gross total resection, the first sense of disquiet came with the recognition of a high rate of recurrence despite apparent surgical clearance [12, 24, 26]. This heralded the beginning of a period of experimentation in craniopharyngioma management. Multiple re-operations as well as radiotherapy were obvious choices to employ, but help was also drawn from other specialty areas with the trials of intracavity therapy such as brachytherapy [25] and chemotherapy with bleomycin [23]. There was a sense of haste to find a solution for this vexing problem once held to represent neurosurgical success, correspondingly many of these therapies were tried without, seemingly, a solid empirical basis. Whilst none of these treatments have proven to be consistently efficacious, they add to our understanding of craniopharyngioma and give us a basis to build an effective multimodal therapeutic strategy.

Current surgical standards include the use of open resection/debulking via a variety of approaches, transphenoidal surgery (including cysto-sphenoidal drains) and cyst drainage procedures (reservoirs placed either stereotactically or endoscopically, shunts). All of these various approaches found their justification in the fact that we do not have a solution for craniopharyngioma in that beside endocrine and visual problems, a significant percentage of these patients will develop signs related to the treatment and incompatible with normal life. This recognition of hypothalamic dysfunction [3, 4, 7] (hyperphagia/obesity, behavioural disorders, memory problems and loss of neurovegetative homeostasis) yielded the second sense of unease and has led many groups to independently conclude that this level of morbidity is unacceptable. Whilst further review confirms that in a percentage of patients these hypothalamic effects are in part attributable to the tumour itself (dysfunction noted at presentation), radical surgery inevitably makes things worse especially for tumours associated with the hypothalamus.

The Necker experience

Noting this history, it is clear that over the past 20 years we have followed the same roaming path. Several studies have been conducted on, to date, 127 patients, each of the studies reflecting the surgical preoccupation of the time—Visual Salvage [20], Radical Surgery [19], Endocrine deficits [1], prospective trial of Neuro-psychological Outcome "2005 unpublished", and the effect of Hypothalamic involvement "2005 unpublished".

The general attitude in the service until the late 1990s was to attempt gross total resection in all cases. Following this we, like many others [6, 17, 18, 21, 24], became self-conscious of the long-term outcomes—other than that of vision and endocrinological status—and decided that it was unacceptable be left with a high proportion of disabled children. This stimulated us to critically review our craniopharyngioma series looking for a means to classify craniopharyngioma at presentation to allow rationalisation of multimodal therapy. Whilst the body of this work is beyond the scope of this paper, we present a summary of its findings to explain the conclusions we draw here.

We retrospectively reviewed all patients presenting with Craniopharyngioma to Necker from 1984 to 2003. Patients (n=37) who underwent part of their therapy elsewhere and patients for whom a pre-operative MRI was not available were excluded. In addition to neurological status, visual and endocrine function, the quality of life outcome [functional Health Utility Index (HUI)] and the body mass index (BMI) were recorded. The pre- and post-operative MRIs were independently scored for the degree of hypothalamic involvement (type 0, no visible involvement pre-operatively or no evidence of damage post-operatively; type 1, intermediate involvement/damage; and type 2, severe hypothalamic involvement/damage) (Fig. 1). Tumour volume, hydrocephalus and the relationship to the chiasm, ventricles and sellar were noted. Surgical experience was defined as more than 3 cases/year.

The series included 66 children (42 boys and 14 girls) with a mean age of 7.4 years at presentation and a mean follow-up of 7 years. At referral, whilst 44% presented with visual impairment (10% blind), raised intracranial pressure due either directly to the tumour volume and/or obstruction of CSF circulation was evident in 68%, with 58% of the series requiring emergency intervention. Clinical endocrine

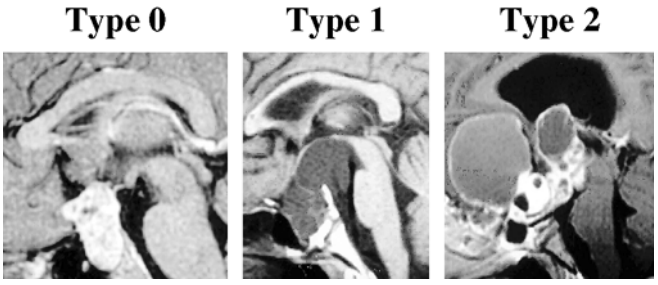

Fig. 1 MRI assessment of hypothalamic involvement. *Type 0*: no involvement of the hypothalamus; *type 1*: the hypothalamus is elevated/distorted but visible, *type 2*: the hypothalamus is involved and no longer visible

dysfunction was noted in one third of the cases (growth retardation 27%, diabetes insipidus 9%); however, endocrine disorders were biochemically present at diagnosis in 80% [1]. Additionally, hypothalamic dysfunction was also noted in a significant number of cases, hyperphagia 26%, and diencephalic syndrome 4.5%. The mean BMI was +1.15 standard deviation (SD) from the norm. The pre-operative hypothalamic involvement as noted on the MRI (type 0, 1 and 2) was 21, 37 and 42%, respectively.

Surgical management with the intention of gross total resection was undertaken in all cases; however, in many cases this goal was not achieved. Post-operative imaging confirmed total resection in 50%, subtotal in 36%, and partial/debulking in 14%. Of the 33 patients with residual tumour, 13 underwent a second operation and five a third. Six of these patients underwent radiotherapy after their first excision, and another six after their second or third operations.

In this series over an average follow-up of 7 years, we observed 36% recurrence rate after previously "confirmed gross total resection", and 54% tumour progression after incomplete resection, all of which were treated subsequently by surgery and/or irradiation.

The vast majority of the patients (90%) required post-operative hormonal replacement therapy. Post-operative visual function was improved in 68% but worse in 21%. The post-operative hypothalamic damage types (0, 1 and 2) were 32, 30 and 38%, respectively. A degree of hyperphagia was observed in 70% of the cases (18% severe leading to morbid obesity), and 15% of the children had an impaired neuropsychological evaluation post-operatively.

The BMI at the last follow-up (mean±2.5 SD) significantly correlated with the degree of hypothalamic involvement/damage both pre-operatively (p=0.007) and post-operatively (p=0.001). At follow-up the mean HUI, at 0.8, was notably lower than the age appropriate normal population. We found that the HUI was correlated with pre and post-operative hypothalamic types (p<0.001 and p=0.003, respectively), psychological disorders and hyperphagia. Moreover, psychological disorders were correlated with pre- and post-operative hypothalamic types (p=0.01 and p=0.002, respectively). Finally, the surgeons' experience (more than 3 cases/year) correlated with the post-operative BMI and HUI.

Reviewing our series, we see that in craniopharyngioma surgery, quality of life outcome correlates with the degree of hypothalamic damage evident on the post-operative MRI. Furthermore, the likelihood of hypothalamic damage may be predicted by the degree of pre-operative hypothalamic involvement, but is also influenced by the surgeons experience with these tumours. This indicates that the treatment strategy may be adapted according to the degree of hypothalamic involvement as shown by the pre-operative MRI (type 0, 1 and 2) in order to minimise the morbidity. It is likely that this classification could be refined by the addition of clinical factors suggesting hypothalamic dysfunction pre-operatively.

Our results suggest that when the tumour does not involve the hypothalamus (type 0), a total resection is suitable; when the tumour compresses but not invades the hypothalamus (type 1), a total resection still seems the best solution; however, the outcome depends on the surgical familiarity with craniopharyngiomas. Finally, when the tumour involves the hypothalamus (type 2), subtotal surgery respecting the invaded hypothalamus combined with local radiation therapy at present seems to be the best option.

Discussion

Like many other paediatric groups (St Judes [17], Great Ormond Street [11], Toronto Sick Children's [22], etc.), we have taken advantage of the progress in radiotherapy, such as conformal planning and proton beam therapy, and built these into treatment plans as combination surgery and radiotherapy [9]. The key to this approach, where we attend to the quality of life and psycho social outcomes, is in the ability to classify patient subgroups. Traditionally, classification systems have been based on anatomical features relating to the chiasm—reflecting the emphasis on vision and visual salvage as the main surgical goal. As our goals now shift to a more "holistic" view—preservation of quality of life—we need to redefine our classification to this end. Using the results of this recent review of our history with craniopharyngioma treatment, we have been able to further refine patient groups based on the degree of hypothalamic involvement. Whilst at this stage this is primarily based on the pre-operative MRI, for the future this should be refined by clinical indicators suggesting hypothalamic damage such as BMI, pre-operative neuropsychological evaluation, etc. We hope that by stratifying the therapeutic approach, we can both reduce the operative morbidity especially in relation to the devastating hypothalamic dysfunction and also identify the groups of patients in whom a judicious attempt at resection is possible. By using a reproducible scoring system, we will be able to take this retrospectively identified variable and assess its value in the future.

The motivation for attempting to tailor the treatment to the tumour lies in the nature of craniopharyngiomas. To date all current treatments still have a failure rate compelling us to apply treatment as safely but also as efficaciously as possible. Tailored treatment protocols such as this are becoming the state of art in the treatment of craniopharyngioma.However, we must be mindful that there remain a number of unknown factors. We do not yet have the data to tell us the long-term outcomes and effects of new protocols which include radiation [10] (such as the one proposed by Hayward [11] in this journal). How do we treat the post-radiotherapy recurrences, estimated in the order of 15–20% [10]—and with our current option of surgery, are the risks of surgery after irradiation higher than at first presentation? In assessing our outcomes will we see in the future that the morbidity of managing the recurrences overwhelms that which we are currently trying to avoid?

Endocrine deficiencies are still considered as inevitable and perceived as acceptable due to the ability to provide hormone replacement therapy. With more emphasis on quality of life in our decision making, it is now time to assess the more subtle endocrine effects such as fertility and adult growth hormone deficiency.

With the universal application of a more conservative approach, we cannot disregard those patients who present with an absolute surgical indication such as chiasmatic compression. This makes us all the more cognizant of the similarities to the concerns seen in aneurysm surgery—as less and less procedures are undertaken, how do we avoid the de-skilling of our surgeons in what is already a rare tumour? This concern is emphasised by our series showing a significant increase in morbidity with relative inexperience.

We must be able to evaluate these techniques and protocols on a significant series of patients. Clearly, it is an illusion to imagine that one may develop and maintain expertise in managing these rare tumours if one only sees a small number of cases. By consolidating these cases we hope to improve outcomes, but also it allows us with greater numbers to monitor the effects of these treatment strategies. As other modalities have a greater role in craniopharyngioma management, we need to assess not only our surgical limitations but also the limitations on the other required modalities a need which will also drive us to consolidation into specialised treatment units.

Conclusion

The history of the management of craniopharyngioma exemplifies the trend of Paediatric Neurosurgery and indeed in medicine in general. Firstly, we recognise the lesion. Secondly, we make them survive at any price. And finally, we must make them live well. So, what do we currently have in our armamentarium to achieve this? The ability with modern imaging to reasonably determine the location of the tumour and its relationship to the chiasm, hypophysis and hypothalamus and therefore predict the risks of intervention; the microsurgical and stereotactic techniques to allow both open surgery via a surgical approach customised to each particular case or a more conservative approach such as cyst drainage. We have modern techniques of irradiation focusing not solely on tumour treatment, but also on limitation of radiation to surrounding structures. We also have a wealth of knowledge regarding the relentless recurring nature of this tumour and morbidity both from our interventions and from tumour progression.

The challenge for us now lies in the way that we apply this knowledge and skill, to find for each patient the appropriate strategy to control their tumour without devastating their future potential.

The history of craniopharyngioma surgery may be thought of as a swinging pendulum from aggressive to conservative management. As we now appropriately swing away from radical resection, it is our duty to be mindful our pioneers' knowledge of the relentless nature of this tumour, to try and avoid dogmatism, and to balance the swing of the pendulum.

References

1. Brauner R, Malandry F, Rappaport R, Pierre-Kahn A, Hirsch JF (1987) Craniopharyngiomes de l'enfant, A propos de 37 cas. Arch Fr Pediatr 44:765–769
2. Caldarelli M, Di Rocco C, Papacci F, Colosimo C Jr (1998) Management of recurrent craniopharyngioma. Acta Neurochir 140:447–454
3. Carpentieri SC, Waber DP, Scott RM, Goumnerova LC, Kieran MW, Cohen LE, Kim F, Billett AL, Tarbell NJ, Pomeroy SL (2001) Memory deficits among children with craniopharyngiomas. Neurosurgery 49 (5): 1053–1058
4. Cavazzuti V, Fischer EG, Welch K, Belli JA, Winston KR (1983) Neurological and psychological sequelae following different treatments of craniopharyngioma in children. J Neurosurg 59:409–417
5. Choux M, Lena G, Genitori L (1991) Rapport de la société française de neurochirurgie, craniopharyngiomes de l'enfant. Neurochirurgie 37:Suppl 1
6. De Vile CJ, Grant DB, Kendall BE, Neville BGR, Stanhope R, Watkins KE, Hayward RD (1996) Management of childhood craniopharyngioma: can the morbidity of radical surgery be predicted? J Neurosurg 85:73–81
7. De Vile CJ, Grant DB, Hayward RD, Kendall BE, Neville BGR, Stanhope R (1996) Obesity in childhood craniopharyngioma: relation to post-operative hypothalamic damage shown by magnetic resonance imaging. J Clin Endocrinol 81:2734–2737

8. Epstein FJ, Handler MH (1994) Craniopharyngioma: the answer. Proc Symposium, New York, NY, December 17–19, 1993. Pediatr Neurosurg 21 (Suppl 1):1–132
9. Fischer EG, Welch K, Shillito J Jr, Winston KR, Tarbell NJ (1990) Craniopharyngiomas in children. Long term effects of conservative surgical procedures combined with radiation therapy. J Neurosurg 73:534–540
10. Habrand J-L, Ganry O, Couanet D, Rouxel V, Levy-Piedbois C, Pierre-Kahn A, Kalifa C (1999) The role of radiation therapy in the management of craniopharyngioma: a 25-year experience and review of the literature. Int J Radiat Oncol Biol Phys 44:255–263
11. Hayward R (1999) The present and future management of childhood craniopharygioma. Childs Nerv Syst 15:764–769
12. Hetelekidis S, Barnes PD, Tao ML, Fischer EG, Schneider L, Scott RM, Tarbell NJ (1993) 20-year experience in childhood craniopharyngioma. Int J Radiat Oncol Biol Phys 27(2):189–195
13. Hoffman HJ, Hendrick EB, Humphreys RP, Buncic JR, Amstrong DL, Jenkin RDT (1977) Management of craniopharyngioma in children. J Neurosurg 47:218–227
14. Hoffman HJ, De Silva M, Humphreys RP, Drake JM, Smith ML, Blaser SI (1992) Aggressive surgical management of craniopharyngiomas in children. J Neurosurg 76:47–52
15. Honegger J, Buchfelder M, Fahlbusch R (1999) Surgical treatment of craniopharyngiomas: endocrinological results. J Neurosurg 90:251–257
16. Islas Cruz G, Vite Vargas JA, Hernandez Marin I, Aguirre Ramirez A, Tovar Rodriguez JM, Ayala Ruiz AR (2004) Craniopharyngioma and its impact upon human reproduction: analysis of 15 cases at the Hospital Juarez de Mexico. Ginecol Obstet Mex 72:345–348
17. Merchant TE, Kiehna EN, Sanford RA, Mulhern RK, Thompson SJ, Wilson MW, Lustig RH, Kun LE (2002) Craniopharyngioma: the St Jude Children's Research Hospital experience. Int J Radiat Oncol Biol Phys 53:533–542
18. Muller HL, Gebhardt U, Etvard-Gorris N, Korenke E, Warmuth-Metz M, Kolb R, Sorensen N, Calaminus G (2004) Prognosis and sequela in patients with childhood craniopharyngioma—results of HIT-ENDO and update on KRANIOPHARYNGEOM 2000. Klin Padiatr 216(6):343–348
19. Pierre-Kahn A, Brauner R, Renier D, Sainte-Rose C, Gangemi MA, Rappaport R, Hirsch JF (1988) Traitement des craniopharyngiomes de l'enfant. Analyse rétrospectives de 50 observations. Arch Fr Pediatr 45:163–167
20. Pierre-Kahn A, Sainte-Rose C, Renier D (1994) Surgical approach to children with craniopharyngiomas and severely impaired vision: special considerations. Pediatr Neurosurg 21(Suppl 1):50–56
21. Poretti A, Grotzer MA, Ribi K, Schonle E, Boltshauser E (2004) Outcome of craniopharyngioma in children: long-term complications and quality of life. Dev Med Child Neurol 46 (4):220–229
22. Rutka JT (2002) Craniopharyngioma. J Neurosurg 97:1–2
23. Takahashi H, Nakazawa S, Shimura T (1985) Evaluation of postoperative intratumoral injection of Bleomycin for craniopharyngioma in children. J Neurosurg 62:120–127
24. Villani RM, Tomei G, Bello L, Sganzerla E, Ambrosi B, Re T, Barilari MG (1997) Long-term results of treatment for craniopharyngioma in children. Childs Nerv Syst 13:397–405
25. Voges J, Sturm V, Lehrke R, Treuer H, Gauss C, Berthold F (1997) Cystic craniopharyngioma: long-term results after intracavitary irradiation with stereotactically applied colloidal beta-emitting radioactive sources. Neurosurgery 40(2):263–270
26. Yasargil MG, Curcic M, Kis M, Siegenthaler G, Teddy PJ, Roth P (1990) Total removal of craniopharyngiomas. Approach and long-term results in 144 patients. J Neurosurg 73:3–11