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Historical note

Craniopharyngiomas. Historical aspects of their management

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ABSTRACT

The history of the management of craniopharyngiomas offers a comprehensive review of the exciting progress in neurosurgery, neuroimaging, neuroendocrinology and radiation oncology during the last century. In this historical note, we present the evolution in management of these most challenging of brain tumours, which, despite the substantial knowledge and expertise gained since the first attempt of surgical removal, remains a subject of considerable debate.

Key words: Craniopharyngiomas, Neuroendocrinology, Neurosurgery

INTRODUCTION

In 1910,[1] a thirty-nine year-old man presented to a Chicago hospital with failing eyesight and frontal headaches. A perforated nasal septum and aortic regurgitation suggested the diagnosis of cerebral syphilis and treatment was commenced, yet no clinical improvement was seen. Since the patient had been impotent for eighteen months, when his visual defect evolved into a bitemporal hemianopia and bilateral optic atrophy, the possibility of a hypophyseal tumour was raised; yet he never exhibited signs of "feminization, acromegaly or adiposity". Nevertheless, the possibility was investigated and radiologically confirmed; a tumour resection was performed by A.E. Halstead in the same year. Lewis, the receiving pathologist, reported that the tissue "corresponds more closely to those arising from cranio-pharyngeal epithelium than to any other". Thus, the first successful resection of a craniopharyngioma took place and the patient returned to his work as an express coach driver.

Although histologically benign, these rare brain tumours are locally invasive and difficult to eradicate. While the optimal management has been subject to more than one hundred years of debate, this has been a century encompassing significant advances in neurosurgery and radiotherapy, as well as increasingly sophisticated endocrinological support. We here review the developments made since this first case report.

SURGERY

Early hypothalamic surgery was a risky undertaking, associated with almost universal mortality from collateral damage and lack of exogenous corticosteroid

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support. By 1905 there was only one documented success in the literature. Surgeons of the early 20th century experimented with a range of intracranial and transsphenoidal techniques. Horsley,[1] using a lateral intracranial approach advocated by Liverpool surgeons R. Caton and F.T. Paul,[1] entered the middle cranial fossa to access the hypophysis by elevation of the temporosphenoidal lobe. Halstead employed a different technique in 1910, when he performed the first successful resection of a craniopharyngioma. He used an infranasal route, which, whilst technically less challenging, appeared to carry a greater risk of infection.[1] Both techniques continued to be used with varying degrees of success and, as Frazier observed in 1912, the route of access should be decided based on the specific characteristics of each individual case.[2] No technique seemed appropriate to all cases of these large, irregular tumours that are so hazardously related to critical intracranial structures.[3] Moreover, much of the research had been done on cadaveric specimens and Halstead himself observed that many "have yet to be tried in the operating theatre before their merits and defects can be properly estimated".[4] By the end of the 1920s, the intracranial frontal approach had gained favour over the transsphenoidal route, Heurer reporting that it could best address the tumour's upward growth into the intracranial chamber. In 1923, Cushing operated on the longest recorded survivor of craniopharyngioma – described by him as "the most forbidding of the intracranial tumours"[5] – by frontal craniotomy with cyst drainage and partial excision of the capsule; his patient lived for a further fifty years. Craniotomy was generally performed on the side of poorest vision in order to expose the region of the chiasm intradurally and enable drainage and biopsy of the cyst as well as resection of those parts of the tumour that were accessible.

Opinion varied as to the relative merits of complete tumour excision and partial resection. Love et al advocated radical surgical removal in 1939, offering the patient "his only ray of hope",[6] but in practice, radical removal was rarely achieved. Usually, cystic tumours were aspirated and total clearance of the capsule was attempted. This gave an acceptable initial outcome, but frequently resulted in an early recurrence. So did simple cyst aspiration, which was considered to be of little value.

Post-operative complications remained common and in 1948 Grant identified three surgical issues to be addressed for improvement of the prognosis of these patients: avoidance of hyperthermic crises from damage to the hypothalamus, prevention of post-operative glandular collapse and avoidance of damage to the carotid arteries.[7] Adrenal gland extracts were being introduced into post-operative care and in 1946 Ingraham and Scott were the first to describe the value of adrenal substitution therapy as "a useful adjunct in the surgical treatment of craniopharyngiomas in children".[8] Techniques were refined to avoid hyperthermic crises and achieve a stable post-operative course at the same time that 'roentgen therapy' was proving effective in reducing the risk of recurrence in subtotal resections. Further advances followed after 1950, with improvements in the field of neurosurgery (resulting from the experiences of the 2nd World War) and the introduction of pneumoencephalography, ventriculography and cerebral angiography.

In 1969, Matson and Crigler observed that there remained a lack of "good pre-operative or intra-operative criteria to determine in each case whether the advantages of radical tumour excision are possible without producing hypothalamic damage or whether one must accept partial excision with its unsatisfactory prognosis".[9] However, the introduction of computed tomography scanning in the 1970s, followed by magnetic resonance imaging, offered "the closest thing to absolute diagnostic precision ever known for the craniopharyngiomas".[10] In combination with the introduction of microsurgical techniques, this led to significant improvements in peri-operative morbidity and mortality.[11] Radical resection was generally advocated as the treatment of choice for intrasellar and prechiasmatic tumours, with microsurgery offering "an expectation of cure, prevention of recurrence and avoidance of the side effects of radiotherapy".[12] This opinion was supported by the work in the 1970s of Sweet and others, who reported that the dense gliotic capsule between the tumour and brain constituted a margin of safety which justified radical excision as a first-line treatment. Raimondi et al proposed subtotal resection for retrochiasmatic and giant tumours to reduce morbidity and mortality to acceptable levels, although this incurred a 75% symptomatic recur-

rence.[13] Yet opinion on the optimal management of these tumours remained divergent, with, for example, Mori et al in 1980 asserting that a craniopharyngioma "should be considered as malignant...therefore, no forceful attempt should be made to totally extirpate it and the operation should, as a rule, be palliative".[14] Endocrine and radiological support continued to improve, but there were inadequate data to favour any one of the various evolving surgical treatment options.

Recently, endoscopic surgery has been introduced into the management of craniopharyngiomas;[15] its value remains to be assessed.

EXTERNAL BEAM IRRADIATION

The radiosensitivity of craniopharyngiomas first came under scrutiny in 1937, when Carpenter's group successfully treated four cases by cyst aspiration and irradiation.[16] Although previously thought to be radioresistant, studies showed that the progression and symptom severity of these tumours could be relieved by external beam irradiation; however, no effect was seen on patient longevity.[17] More than two decades passed before a definitive role for radiotherapy was established. In 1961, Kramer and colleagues published promising results of high-dose supervoltage irradiation following subtotal resection of solid tumours. They concluded that "the combined approach to the problem by neurosurgery and radiation therapy is likely to produce the best results".[18]

During the 1970s, advances in computed tomography brought the role of radiotherapy into question, as it raised the real possibility of radical excision.[19] Debate ensued, with advocates of radiation therapy asserting that "radical removal, even if technically feasible, is unnecessary in patients harbouring craniopharyngiomas because we have found that radiation therapy administered after initial biopsy and cyst decompression is curative in most of these patients".[20]

By the 1980s, radiotherapy was integral to the management of small primary tumours and recurrent tumours, as well as the post-operative management of subtotal resections. The evidence arising in subsequent decades clearly displayed a reduction in disease progression and recurrence.[11] Advanced radiotherapy techniques (including stereotactic radiosurgery and stereotactic radiotherapy) have been applied over recent years and their impact on the management algorithm remains to be established.[11]

OTHER ADVANCES

In 1952, Leksell and Liden reported the effects of intracavitary irradiation (brachytherapy).[21] This was a minimally invasive management strategy involving stereotactically guided instillation of beta-emitting isotopes (mainly ^{32}phosphate, ^{90}yttrium, ^{186}rhenium, ^{198}gold) into cystic craniopharyngiomas, delivering higher radiation doses to the cyst lining than those offered by conventional external beam radiotherapy. The beneficial effect is achieved through destruction of the secretory epithelial lining, causing elimination of fluid production and cyst shrinkage.[11] In view of the low reported surgical morbidity and mortality, this became an attractive management option for predominantly cystic (and particularly monocystic) tumours.[11]

In 1985, Takahashi's group was the first to describe the intracystic instillation of bleomycin.[22] The drug is administered through an Ommaya reservoir connected to a catheter (placed in the cyst stereotactically or through craniotomy).[11] The value of this technique in arresting or delaying tumour growth (and thus the need for potentially harmful resection and/or radiotherapy, especially in young children) remains to be established.

Finally, both systemic chemotherapy and interferon-alpha have been used in the last two decades to treat a very limited number of recurrent or progressive tumours.[23-25] This option has not received wide acceptance, largely because of the significant cytotoxic burden.

CONCLUSION

The history of the treatment of any disease is undoubtedly fascinating and didactic. In the case of craniopharyngiomas, the early years of despair have been followed over the last century by relative optimism due to advances in neurosurgery, neuroimaging, neuroendocrinology and radiation oncology. However, the optimal treatment of these challenging

tumours remains controversial to the present day. Continuing developments offer a very real possibility of exciting future chapters in the history of their management.

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