Management of Benign and Aggressive Intracranial Meningiomas

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Meningioma is a prime example of a tumor requiring a multimodality approach. This tumor is usually benign and often grows slowly. Under many circumstances, such a benign tumor would never attract the attention of the oncologist or even require treatment at all. However, a meningioma is a benign tumor in a malignant location. In the closed space of the skull, there is no room for expansion of even a benign lesion; thus, effective treatment of this potentially neurologically devastating lesion is necessary. Neurosurgeons, neuroradiologists, radiotherapists, and medical oncologists are all directly involved in treatment decisions. Rapidly expanding knowledge concerning the etiology and natural history of meningiomas may now also involve epidemiologists, molecular geneticists, and endocrinologists. Despite this concentration of expertise, numerous questions remain unanswered or incompletely answered.

The epidemiology of meningiomas has always been of great interest. Observations that meningiomas are twice as common in women as in men, that they may wax and wane with pregnancy, and that they are positively associated with breast cancer opened the door to investigation of the role of sex hormone receptors in the growth of meningiomas and to a greater understanding of the pathways that control the expression and function of these receptors. However, other risk factors have also been identified. Trauma may be a factor in the induction of meningiomas; they may be the only tumors associated with participation in a competitive sport (head trauma from boxing). Radiation may also play a role in the induction of meningiomas, including either therapeutic radiation to the brain or scalp or possible risk from excessive dental x-rays. Description of deletions of chromosome 22 as a possible marker for meningiomas may help identify a common pathway of chromosomal damage for these various risk factors.

Treatment Options

Surgery remains the acknowledged mainstay for potentially curative treatment of meningiomas. Surgical results have improved both through technical advances and through the development of effective multispecialty surgical teams, particularly in the area of skull-base procedures. However, planning the extent of appropriate surgery depends upon appreciation of the malignant potential of the tumor in question, and this has been a special area of difficulty for meningioma.

Some meningiomas may be obviously histologically malignant or may present as malignant tumors by metastasizing to distant sites. However, the description of an aggressive meningioma is often based more on the clinical picture than on particular histologic or cytologic features. In addition, there is a propensity for meningiomas that intermittently recur over many years to demonstrate increasingly aggressive behavior. More extensive surgery is therefore finally needed at the time when previous interventions make such an approach more difficult. Improvement of techniques for early identification of malignant or aggressive potential through the definition of appropriate markers of proliferation or through metabolic imaging (such as the use of positron emission tomography) is thus a major requirement for improvement in long-term results.
A significant literature now supports the use of radiotherapy for the treatment of advanced meningiomas or for adjuvant treatment after tumor resection [4]. In much of neuro-oncology, the use of aggressive cranial radiotherapy with potential delayed toxicity can be justified, in part, by the poor expectations for long-term outcome. In the case of meningiomas, where survival for a decade or more can be expected in many cases, the question of persistent or late toxicity becomes more important. Further work to identify the subset of patients who may be at increased risk for deterioration in cognitive function after cranial radiotherapy is required. In addition, a greater appreciation of the possible delayed effects of cranial radiotherapy, such as hypothalamic-pituitary dysfunction resulting in hypothyroidism [5], is necessary for physicians involved in the long-term care of patients with meningiomas.

Although isolated reports of success with cytotoxic chemotherapy or embolization of meningiomas can be found, neither treatment has become a significant part of general care. In contrast, the role of various growth factors has been a fascinating area. The epidemiologic association of meningiomas with female gender led to the original description of female sex hormone receptors with potential proliferative function on meningioma cells. Since then, the realization that progesterone receptors on meningiomas may be expressed independently of estrogen receptor stimulation has led to potentially important insights into the regulation of these receptors (including the possibilities of either totally independent expression of progesterone receptors or expression induced by a constitutively activated modified estrogen receptor) [6].

The suggestive results of early trials of antiprogesterone manipulation of meningiomas (now being tested in larger phase III trials) have introduced a new form of hormonal manipulation to the antineoplastic armamentarium [7]. This line of research has advanced the idea that sex hormones and sex hormone receptors may function as growth factors and growth factor receptors, even in the absence of an obvious gender relationship of the organ in question. This concept may have far-reaching implications for the management of numerous medical conditions. Furthermore, the identification of additional hormone receptors that could potentially serve as growth factor receptors on meningiomas (including androgen and somatostatin receptors) may suggest an increasingly important role for biologics (rather than cytotoxics) in the medical management of meningiomas [1]. Although treatment of benign tumors should be simple (ie, resection), meningiomas, by virtue of their location and natural history, have turned this simple question into a multifaceted research and treatment challenge. In view of the expected long survival of patients with meningiomas, superb surgical and radiotherapeutic techniques for the avoidance of chronic and late toxicities are needed. Meningiomas also have provided the opportunity to gain greater insights into the role of hormonal and other growth factors, which may have widespread implications for the understanding and management of both malignant and nonmalignant conditions. Increased knowledge of these signalling pathways may be the most important contribution to emerge from the many ongoing avenues of meningioma research.

References:

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