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Pathology of meningiomas

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Abstract

Because meningiomas arise from arachnoid cells present in the meninges, they can occur in any location where meninges or ectopic meninges exist, such as the nasal cavity, the paranasal sinuses, the middle ear, and even the mediastinum. Although the tumors may range in appearance from epithelial to mesenchymal, they are characterized by a uniform distribution of cells with shapes ranging from polygonal epithelial-like to spindled and fusiform. Historically, classification of meningiomas has been based upon cell shapes, cell patterns, cell products, or stroma, implying clinicopathologic differences among the types. Numerous observations have shown that certain conditions may indicate a predisposition for developing meningiomas, prompting extensive studies of meningiomas using cytogenetic techniques. Meningiomas are common neoplasms arising from the central nervous system meninges. They are important because of the morbidity they produce. Their critical intracranial and intraspinal locations make diagnosis and surgical removal difficult.

Introduction

The term "meningioma," coined by Cushing to describe tumors that arise from the central nervous system meninges [1], has been useful for unifying primary meningeal neoplasms that are characterized by a variety of morphologic features and variable behavior. Despite more recent data on meningiomas, traditional nomenclature consisting of histogenetically- and clinically-irrelevant terms continues to be used because of the extremely broad morphologic spectrum exhibited by meningiomas. The old term "angioblastic meningioma" that included hemangiopericytomas is a misnomer because hemangiopericytomas are derived not from meningothelial cells, but more likely from pericytes; hence, they are considered sarcomas. Today, the term "meningioma" refers strictly to tumors originating from meningothelial, or arachnoidal, cells, regardless of histology.

Meningiomas account for approximately 18% of all primary intracranial neoplasms and 25% of intraspinal neoplasms [2–4]. Because meningiomas arise from arachnoid cells present in the meninges, they can occur in any location where meninges or ectopic meninges exist, such as the nasal cavity, the paranasal sinuses, the middle ear, and even the mediastinum. They are tumors of adults that occur more frequently in women, showing a 3 : 2 female/male ratio in intracranial sites and an overwhelming predominance (10 : 1, female/male ratio) in intraspinal sites [2]. The occurrence of meningiomas in children is extremely rare, and when they do occur, they frequently have an uncharacteristic aggressive course.

Morphologically, meningiomas are composed of atypical arachnoid cells and vascular and fibrous tissue normally found in the meninges. Although the tumors may range in appearance from epithelial to mesenchymal, they are characterized by a uniform distribution of cells with shapes ranging from polygonal epithelial-like to spindled and fusiform.

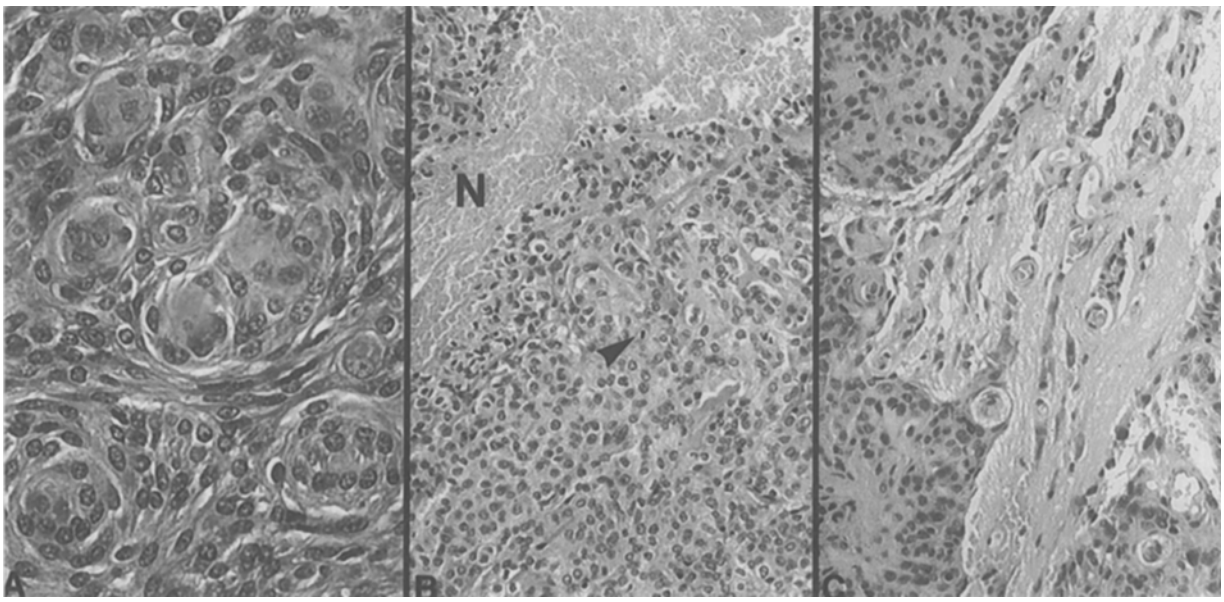

Fig. 1. A. Ordinary meningioma with regular nuclei and whorl formation. B. Atypical meningioma with increased mitotic activity (arrowhead) and focus of necrosis (N). C. Malignant meningioma with brain invasion. Hematoxylin and eosin stained. A, 400×. B, 200×. C, 200×.

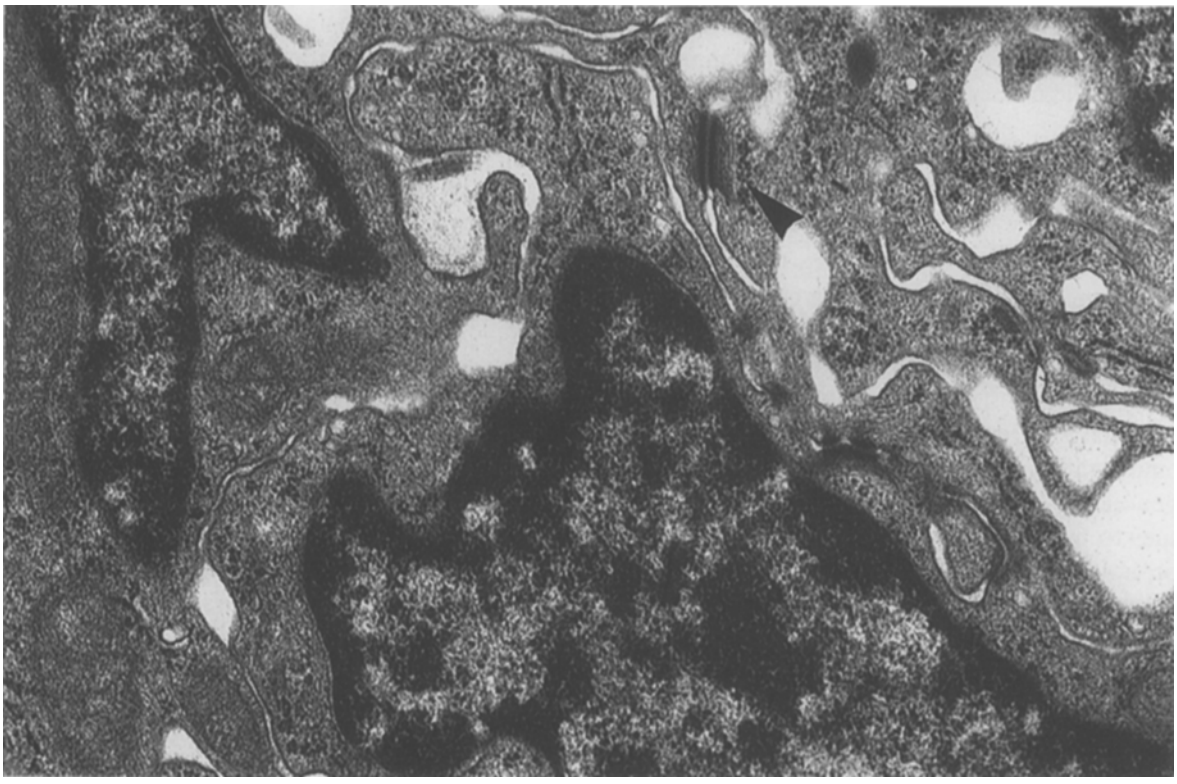

Fig. 2. Electron micrograph showing interdigitating cell processes and well-formed desmosomal attachments (arrow). 5000×.

Usually, the cells are arranged in elongated sheets or islands separated by connective tissue trabeculae. A faint whorling pattern can almost always be seen (Fig. 1A). The nuclei are characteristically abnormal with pseudonuclear inclusions or intranuclear intrusions of cytoplasm. Mineralizations or psammoma bodies may be present or absent in any tumor. Despite the variations in light microscopic appearances, meningiomas have, as shown by electron microscopic examination, similar features, including interdigitations of cell membranes, intracytoplasmic filaments, well-formed desmosomal attachments, and extracellular collagen fibers (Fig. 2).

Standard immunohistochemical procedures demonstrate that better than 95% of all meningiomas are immunopositive for antibodies to epithelial membrane antigen (EMA). Approximately 33% of meningiomas are immunopositive with antibodies to cytokeratins, and another third are immunoreactive with antibodies to S-100 protein. Occasionally, a meningioma will show immunopositivity to carcinoembryonic antigen (CEA).

Meningiomas are important because of the complications they produce (e.g., neurologic dysfunction and epilepsy) and the costs of diagnosis and treatment. The disabilities that meningiomas produce more often are related to their critical intracranial location than their malignant histologic features.

Classification schemes

Historically, classification of meningiomas has been based upon cell shapes, cell patterns, cell products, or stroma, implying clinicopathologic differences among the types. The biologic behavior of meningiomas is highly variable, and its correlation with histologic features is at best imprecise. The pathologist is frequently faced with the difficulty of reliably predicting the biologic behavior on the basis of clinical and morphological parameters. Some meningiomas are obviously benign or malignant, but many meningiomas fall into an intermediate or atypical category, in which cases accurate prognoses are not possible.

In an attempt to correlate biologic aggressiveness with histologic appearance, the updated World Health Organization (WHO) classification divides meningiomas into three broad categories: classic (clinically benign), atypical, and malignant [5]. Classic meningiomas have moderate cellularity, low mitotic activity, no necrosis, and no brain invasion (Fig. 1A). Invasion of bone, muscle, or dura mater by ordinary meningiomas is not a sign of malignancy, but, instead, is a characteristic behavior. Meningiomas in the atypical category have increased cellularity with sheeting and loss of cellular grouping, scattered mitotic figures, foci of necrosis, and absence of brain invasion (Fig. 1B). Malignant meningiomas usually have all of the features of atypical ones, but, in addition, have undisputed evidence of brain invasion (Fig. 1C); they account for fewer than 5% of all meningiomas.

Aggressiveness

Meningiomas typically exhibit variable growth rates and recurrence independent of ominous histopathologic features. Because of these tendencies, numerous studies have attempted to correlate morphologic features with aggressive behavior and rapid recurrence, but success in predicting either of these continues to be limited, partly because judging morphology is very subjective [6–8]. Determining the proliferation index, however, provides adjunct objective information about a neoplasm's behavior, and a direct correlation has been shown to exist between the proliferation rate and the biologic aggressiveness.

In a recent study, we demonstrated a statistically significant correlation between the MIB-1 (Ki-67 antigen) and bromodeoxyuridine (BUdR) proliferation indices in meningiomas and concluded that MIB-1 proliferation indices could be substituted for BUdR proliferation indices to determine the proliferative potential of meningiomas [9]. In the same study, we also showed that a high MIB-1 proliferative index corresponds to a more biologically aggressive neoplasm. The median MIB-1 proliferation indices were 3.4% in ordinary meningiomas, 6.6% in atypical meningiomas, and 11.8% in malignant meningiomas [9].

Molecular genetics

Numerous observations have shown that certain conditions may indicate a predisposition for developing meningiomas [10, 11], prompting extensive studies of meningiomas using cytogenetic techniques. The listed incidence of chromosomal abnormalities varies, but monosomy of chromosome 22 is the most characteristic aberration, occurring in 70–80% of the tumors studied [12]. Improved molecular genetic techniques have led to better definitions of the chromosomal abnormalities, thereby allowing sublocalization of the region of chromosome 22 involved in the tumorigenesis [13, 14]. The involvement of a tumor suppressor gene, particularly one associated with neurofibromatosis type 2, was suspected because meningiomas that occur sporadically or in patients with NF2 show loss of alleles on chromosome 22 [15–17]. The region containing the neurofibromatosis type 2 gene (NF2) has recently been mapped to 22q12 between the loci D22S212 and D22S32 [18, 19]. The candidate gene, named Merlin (moesin, ezrin, and radixin-like gene), encodes a 587-amino-acid protein that has a striking similarity to several members of a family of proteins proposed to link cytoskeletal components with proteins in the cell membrane [19]. The candidate meningioma gene (MEN) is now described in region 22q12.3-qter [20, 21].

Numerous etiologic risk factors, including ionizing radiation, head trauma, estrogens, progestins, cigarette smoking, nitrite consumption, and even elevated cholesterol levels, have been implicated [3]. At present, strong epidemiologic evidence links ionizing radiation and the occurrence of meningioma, the most convincing data coming from studies of radiation therapy for tinea capitis in childhood [22]. Head trauma has also been suspected of being a risk factor for meningioma, but the epidemiologic data is contradictory and not convincing.

Conclusion

Meningiomas are common neoplasms arising from the central nervous system meninges. They are important because of the morbidity they produce. Their critical intracranial and intraspinal locations make diagnosis and surgical removal difficult. Meningiomas may cause headaches, seizures, impairment of neurologic function, and the psychological burden of having a tumor. Approximately 15% of resected meningiomas will recur, necessitating additional surgical resection, and, perhaps, adjuvant therapy. Meningiomas typically exhibit variable growth rates and recurrence independent of histopathologic features, with the result that determining a correlation of morphologic characteristics with aggressive behavior and rapid recurrence is unsatisfyingly low. The primary treatment modality for meningiomas remains surgical resection, with the extent of resection being the primary factor influencing the recurrence rate. Other forms of therapy include adjuvant radiotherapy and chemotherapy. Analyses of cytogenetic and molecular properties of meningiomas show a close association between a postulated meningioma (MEN) locus and the neurofibromatosis type 2 gene on chromosome 22.

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