



A Review of Meningioma : The Most Common Intracranial Benign Tumour in Adults

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ABSTRACT

Grossly term meningiomas describe group of tumours arising from meninges. It is a slow growing tumour. It can involve any age group and gender, however it is more common in elderly and in females. It is most common secondary malignancy attributed to radiation exposure. World Health Organization typically classifies it in three different grades. Grade I is benign, grade II atypical and grade III is considered malignant. Most of the meningiomas are benign. Surgery is the mainstay of treatment. Indication of adjuvant radiotherapy (RT) depends upon tumour grade and extent of resection. Both conventional fractionation and stereotactic radiosurgery are associated with good local control of disease. Role of Systemic treatment has not been yet established.

KEYWORDS

grade, surgery, radiation

EPIDEMIOLOGY

Meningioma term is given by Harvey Cushing to represent a group of tumours arising from meninges. Meningiomas constitute about 20% of all primary intracranial tumours and are considered most common benign intracranial tumour in adults [1]. They can present in any age group, however more commonly they occur in sixth and seventh decade of life. In adults, females are more frequently affected than males. In pediatric age group meningiomas are less common, comprising only 1-4% of all intracranial tumours and there is no female predisposition. Meningiomas are mostly unifocal but might be multifocal in 5-9% of cases [2]. Meningiomas seldom metastasize outside central nervous system [3]. Some common sites for meningiomas are cerebral convexities, falx cerebri, sphenoid ridge, cerebellar convexities and tentorium cerebelli.

ETIOLOGY

Several studies have shown development of intracranial meningioma in patients having previous history of scalp irradiation for tinea capitis disease, suggesting role of radiation exposure in pathogenesis of meningioma [4]. Radiation induced meningiomas are most common secondary malignancies. More common incidence in females, increase in meningioma related symptoms during pregnancy, progesterone receptor expression in 75% of meningiomas and more common occurrence in women on long acting hormonal contraceptives suggest important role of female sex hormones in etiology of meningioma [5,6]. The incidence of meningioma is also more common in some rare genetic diseases like neurofibromatosis type 2. Mutation in NF2 gene is most common associated genetic abnormality [7].

PATHOLOGY

Meningiomas are firm, well circumscribed lesions tan to grayish in appearance. Most of the meningiomas are benign but few are malignant also. According to 2007 World Health Organization (WHO) grading criteria, meningiomas are classified in to 3 different grades. Grade I meningiomas are benign, constitute about 80% of all meningiomas and associated with slow growth and lower risk of recurrence. Grade I meningiomas comprise any variant other than clear cell, choroid, papillary and rhabdoid and does not fulfill criteria for grades II and III.

Grade II or atypical meningioma constitute 20% of all and is characterized by - 4 or more mitoses per 10 high-power field or presence of minimum three of some certain features like sheeting architecture, focal or diffuse hypercellularity, prominent nucleoli, small cells with high nuclear- to- cytoplasmic

ratio, foci of spontaneous necrosis or presence of additional subtypes such as choroid meningioma, clear cell meningioma and brain invasion. Anaplastic/ Malignant are grade III meningiomas which comprise 3-5% of all and pathologically identified by features like 20 or more mitoses per 10 high-power field or focal /diffuse loss of meningotheial differentiation resembling sarcoma, carcinoma, melanoma or presence of additional subtypes such as papillary and rhabdoid meningioma.

CLINICAL FEATURES AND DIAGNOSIS

Meningiomas are slow growing tumours. Many patients do not show any clinical feature, diagnosed having meningioma on incidental imaging and remain asymptomatic for a long time. However, in the patients manifesting the disease, clinical features largely depends upon location of the lesion and associated oedema. Patient may present with any of these symptoms or in combination- headache, personality changes, paresis, focal or generalised seizures, visual impairment, ataxia, aphasia, diplopia, vertigo and many others.

Contrast-enhanced MRI is the imaging modality of choice. On MRI meningiomas show isointense appearance with intense contrast enhancement [8]. MRI also depicts inhomogeneities due to calcification, pseudocyst and central necrosis. The contrast enhancing lesion and associated oedema are better appreciated on MRI while osseous changes (like destruction) and calcifications are better visualised on computed tomography (CT) scans.

The diagnosis is confirmed on basis of post-operative histopathology report.

TREATMENT

Patients with asymptomatic disease could be observed with serial imaging. For symptomatic/ progressive disease active intervention is required. Surgery is primary treatment for meningioma. However depending upon tumour location, size of the tumour and proximity to critical structures complete resection is not always possible. Previous irradiation, vessel encasement, multiple fossa involvement, and cranial nerve palsies are other factors which decrease chances of complete resection. It has been observed that one out of three cases is not completely resectable.

For grade I meningioma, adjuvant radiotherapy (RT) after gross total resection is not recommended. RT is advised either after sub-total resection as adjuvant treatment or as definitive treatment for primary disease. Various studies have shown that adjuvant RT after sub-total resection is associ-

ated with better local control as compared to surgery alone [9]. For grade I tumours adjuvant RT dose varies from 50-54 Gy with conventional fractionation. However, Goldsmith et al have shown that in patients of benign meningioma after subtotal resection, progression free survival was significantly improved (93% vs. 65% at 10 years) with RT dose more than 52 Gy. The study also showed that CT- or MRI-based treatment planning was associated with better outcomes. For atypical (grade II) and malignant (grade III) meningioma, post-operative adjuvant RT is recommended even after complete surgical resection because of high recurrence rate [10]. Like grade I meningiomas, adjuvant RT (as compared to surgery alone) has shown to be associated with better local control and progression-free survival also in grade II and III meningiomas.

For delineating the proper treatment target volume, both pre-operative and post-operative MRI images as well as neurosurgeon's per-operative notes should be considered. If possible, treatment planning system capable of fusing CT and MRI images should be used. For benign gliomas Clinical Target Volume (CTV) is same as Gross Tumour Volume (GTV) and it consists of enhancing disease on post-operative MRI. For atypical and anaplastic meningiomas CTV consists of 1-1.5 cm margin to GTV (any enhancing lesion on post-operative MRI), post-operative bed, any dural thickening or hyperostotic bone. For anaplastic meningioma the perilesional oedema should also be included in CTV. The Planning Target Volume (PTV) typically consists of CTV + margin for setup errors in all cases. Adjuvant RT doses for grade I, grade II and grade III meningiomas with conventional fractionation are 50-54 Gy, 54 Gy and 60 Gy respectively.

Radiation therapy is also used as definitive treatment in meningiomas especially in optic nerve sheath meningiomas. Optic nerve sheath meningioma constitutes 1-4% of all meningiomas and owing to its closeness to optic nerve and optic chiasma, it is quite difficult to get good functional outcome (in terms of vision preservation) after surgery alone or surgery followed by adjuvant radiation. Therefore definitive RT is considered as standard of care in such cases. A study by Turbin et al including 64 patients compared surgery alone, surgery plus RT, RT alone or observation and showed that RT alone was associated with excellent tumour control with best vision preservation. RT dose of 45-54 Gy with conventional fractionation is considered standard.

Stereotactic Radiosurgery (SRS) is an alternative to fractionated RT in certain cases. Tumours having size less than 4 cm in maximum dimension with no associated oedema, having distinct margins and situated far away from normal critical structures are considered suitable for SRS. For SRS, CTV for all grades include enhancing tumour on post-operative MRI. SRS usual dose for grade-I, grade-II and grade-III are usually 12-14 Gy, 14 Gy and >14 Gy respectively. Many studies have shown excellent long-term control with SRS.

For unresectable and recurrent tumours (after surgery), various studies have shown excellent progression-free survival with RT. Various chemotherapeutic agents like doxorubicin, dacarbazine, ifosfamide, hydroxyurea have also been tried in recurrent cases. Apart from chemotherapy some hormonal agents have also found to be active against recurrent as well as de novo cases of meningioma. However, significant role of systemic therapy has not been established in meningiomas till date and it remains an area of future investigation.

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