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Occipito-cervical meningioma in pregnancy

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ABSTRACT

Meningiomas are tumors that are believed to be derived from the cells and vascular elements of the meninges, and grow intracranially or in the vertebral canal. They are most common in women. The growth of meningiomas is stimulated by female sex hormones and thus may progress more rapidly in pregnant women and in women with breast cancer. The patient was a pregnant 39-year old woman ($G_4P_3A_0$) of 8 months gestation. The clinical symptoms and signs were progressive upper motor neuron quadriparesis, diminished sensory functions from the level of C_2 downwards, and loss of bladder and rectal control. Brain and cervical computed tomography (CT) scans done 2 months before admission showed no abnormalities. Induced delivery was terminated by forceps extraction, resulting in a baby of 2,100 g with Apgar score 7/9. After delivery, postcontrast magnetic resonance imaging (MRI) showed a large contrast-enhancing tumor mass of intradural-extramedullary location in the right occipito-cervical region. The tumor had a meningeal tail, extended into the right posterior fossa and caudally to the level of C_3, with compression of the spinal cord. The patient underwent a nontotal resection to remove a tumor that microscopically had the features of a meningioma.

Keywords : Meningioma, pregnancy

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INTRODUCTION

A meningioma is a tumor that is derived from cellular or vascular elements of the meningeal membranes covering the brain and spinal cord. This type of tumor is the second most common of primary intracranial tumors. Around 15–30% of all brain tumors are meningiomas, which increase in frequency above the age of 40 years. The tumor is rarely found in children (in only 15% of all cases), and is more predominant in females than in males, in the ratio of 3 : 1. Meningiomas may be located intracranially or within the vertebral canal, in a ratio of 6 : 1. Around 90% of meningiomas occur in the head, on the cerebral hemispheres, at the base of the skull or the inferior aspect of the brain, such as the brain stem proximal to the spinal cord. Meningiomas may also occur on the meningeal coverings of the optic nerve or in the spinal cord.[1-5] The majority of meningiomas have an intradural-extramedullary

location.[6] High cervical, spinal, or intradural meningiomas are rare lesions, generating a gradual neurological decline, with severe deficits or acute loss of spinal function.[7] The incidence of meningioma in pregnant women is comparable with that in non-pregnant women of the same age group. The clinical presentation of headache, vomiting, or seizures could be misdiagnosed as hyperemesis gravidarum during early pregnancy or as eclampsia during late pregnancy. An abnormal fundoscopic examination, visual impairment, focal seizures, and lateralizing neurological deficits support the diagnosis of an intracranial mass lesion and should prompt further investigation with magnetic resonance imaging (MRI) to confirm the diagnosis.[8] In this paper, a case of meningioma in pregnancy and its diagnostic and therapeutic management is presented.

CASE DESCRIPTION

A 39-year-old women, $G_4P_3A_0$, of 8 months gestation, presented with paresis of all four extremities beginning two months before admission. The patient had already been admitted to another hospital, where brain and cervical computed tomography (CT) scans were performed with normal results. Subsequently the patient was treated by alternative medicine, but the symptoms became worse. There were no history of trauma, radiation therapy or a family history of a similar illness.

On physical examination there were upper motor neuron quadriparesis with power of 2, physiological reflexes -/-, pathological reflexes +/+, clonus +/+, hypesthesia from the C_2 dermatome downwards, and urinary and fecal incontinence. Neurofibromatosis was not found. Laboratory examination yielded a hemoglobin concentration of 10.7 g/dL, white cell count 8 x 10^9/L, red cell count 3.8 x 10^{12}/L, hematocrit 0.32 L/L, platelet count 256 x 10^9/L, blood group O Rh+, total protein 61 g/L, albumin 38 g/L, globulin 28 g/L, SGOT 27 iu/L, SGPT 30 iu/L, ureum 1.1 mmol/L, creatinine 90 mmol/L, sodium 133 mmol/L, potassium 34 mmol/L, chloride 109 mmol/L, random serum glucose 9.7 mmol/L. Delivery was initiated by induction; there was complete cervical dilatation, but the patient could not bear down adequately and the delivery was terminated by forceps extraction; the infant weighed 2100 g and had an Apgar score of 7/9.

Postcontrast magnetic resonance imaging (MRI) performed after delivery showed an extensive contrast-enhancing tumor mass, of intradural-extramedullary location in the right occipito-cervical region, having a meningeal tail, extending into the right posterior fossa and caudally to the level of C_3, accompanied by compression of the spinal cord (Figure 1, Figure 2). The patient underwent a nontotal resection with pathological diagnosis of meningioma.

DISCUSSION

Meningiomas are the most common primary intracranial neoplasms in the adult population, representing about 24% of all brain tumors.[9] They originate from the meningeal membranes covering the brain and spinal cord. Ninety percent of meningiomas are benign, whereas the remaining 10% are atypical or malignant. Although designated as 'benign', brain tumors may cause disability or even be life-threatening. In a number of cases, benign meningiomas grow slowly and may attain a large size (depending on their location) before causing symptoms or signs. Other meningiomas grow more rapidly. In most patients with meningioma, there is only one tumor, but occasionally several tumors are found at different locations in the brain and spinal cord.[1-5]

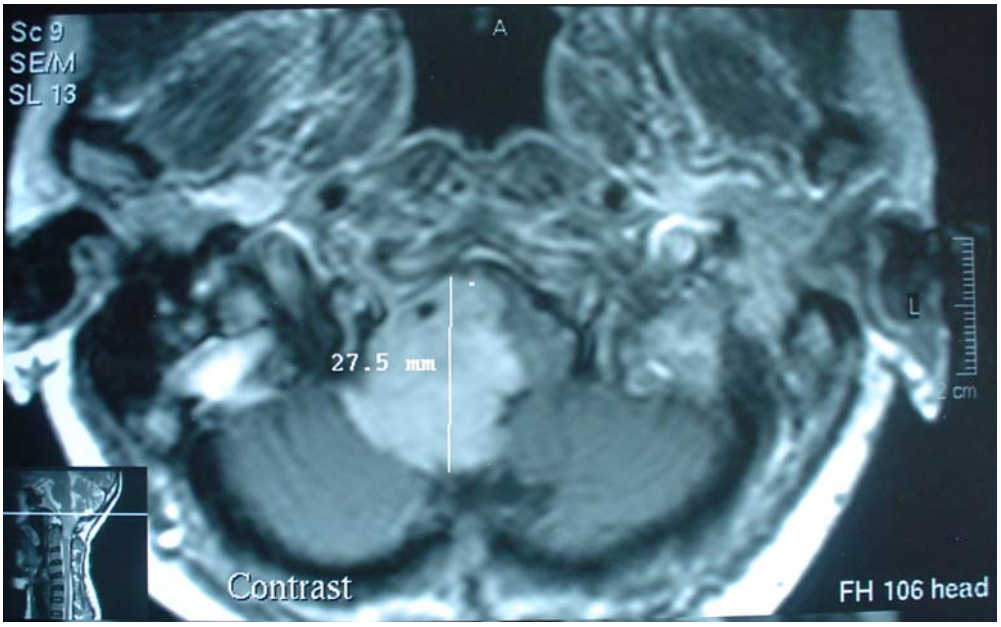

Figure 1. Axial MRI section showing extensive tumor mass, with intradural extramedullary location in right ocipito-cervical region, and compression of spinal cord

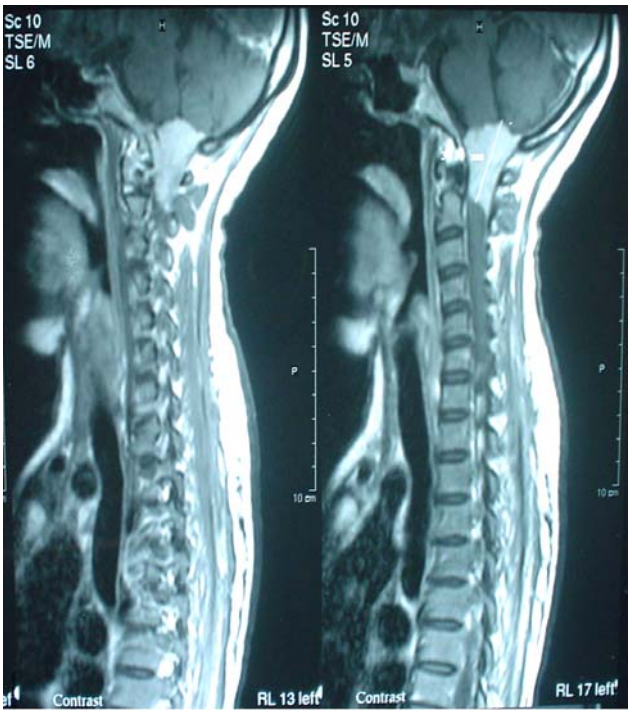

Figure 2. Sagittal MRI section showing tumor with meningeal tail, extending into posterior fossa and caudally to level of C3

Meningiomas may be graded according to the World Health Organization classification of tumors of the central nervous system, which uses histological grades to communicate a "stage of malignancy" that will predict biologic behavior. Grade I tumors are generally well circumscribed, slowly progressing, and can often be cured by resection; grade II lesions are typically infiltrative with low proliferation, but have a higher likelihood of recurrence; grade III tumors are histologically malignant and generally require more aggressive adjuvant therapy; and grade IV tumors are highly malignant and can be rapidly fatal.[16]

The current WHO grading of meningioma into three categories is as follows:[15,16]

i) grade I: benign meningioma does not fulfill criteria of grade II and III; comprises histologic variants other than clear cell, papillary and rhabdoid tumors. The most common histological subtypes are meningothelial, fibrous (fibroplastic), and transitional (mixed) meningiomas. Less common subtypes are psammomatous, angiomatous, microcystic, secretory, lymphoplasmacytic-rich, and metaplastic meningiomas. Grade I tumors account for the majority (90%) of all meningiomas.
ii) grade II: atypical meningioma mitotic index of 4 or more per 10 high-power fields; or at least 3 of the following parameters in an otherwise grade I tumor: sheeting architecture (loss of whorling and/or fascicles), small cells with high nuclear/cytoplasmic index, macronucleoli, hypercellularity, spontaneous necrosis; or brain invasion; or clear cell meningioma; or chordoid meningioma. Grade II tumors account for 5-7% of all meningiomas.
iii) grade III: anaplastic (or malignant) meningioma mitotic index of 20 or more per 10 high-power fields; or frank anaplasia (obviously malignant cytology, eg. resemblance to sarcoma, carcinoma, or melanoma); or papillary meningioma; or rhabdoid meningioma. Malignant meningiomas are rare, accounting for 3-5% of all meningiomas.

A high grade is associated with a poor prognosis. Patients with grade I meningioma usually have a good prognosis, with 80% or more patients experiencing no progressivity or recurrence of tumors after initial therapy. Patients with grade II or grade III tumors have a higher risk of recurrence; patients with grade II tumors will experience a recurrence within 5 years, and grade III patients will have a recurrence within 2 years.[1,3]

The etiology of meningioma is as yet not known with certainty, but possibly both genetic and environmental factors are of influence. Conditions associated with a higher risk of meningioma are the following: i) neurofibromatosis. In about 40–80% of these tumors there is a deletion in the long arm of chromosome 22, at the locus of the neurofibromatosis 2 (NF2) gene. NF2 is a tumor suppressor gene at 22Q12 that is inactive in 40% of sporadic meningiomas. Patients with NF2 and familial non-NF2 syndromes may develop multiple meningiomas, commonly at a young age; ii) radiation therapy. Patients receiving radiation therapy of the head have higher risk of meningiomas, particularly 10-20 years after therapy; iii) history of head trauma. Meningioma is found at the site of previous trauma; iv) female hormones and breast cancer. Meningiomas are more common in women, especially postmenopausal women on hormonal replacement therapy. Meningiomas may increase in size during pregnancy, and there is also an association between meningiomas and breast cancer.

The occurrence of a meningioma during pregnancy is extremely rare. The signs and symptoms of a meningioma may initially appear

during the second or third trimester of pregnancy and then subside in the postpartum period. The most frequent symptoms of a brain tumor such as headache, visual disturbance, nausea and vomiting are often attributed to pregnancy itself and hence the diagnosis may be delayed. It is believed that the presence of hormone receptors, mainly progesterone receptors, are responsible for the worsening symptoms of meningioma.[10,11] The fluctuations in the hormonal milieu of pregnancy as a result of increase in the blood volume, redistribution of body water between intracellular and extracellular fluid compartments and the influence of steroid hormones may increase the tumor size and peritumor edema.

Meningiomas have receptors for sex hormones and other ligands, including progesterones, estrogens, androgens, dopamines dan a receptors for platelet derived growth factor. Using specific immunohistochemical and molecular biological techniques it was found that estrogen receptors are only expressed in approximately 10% of meningiomas and only at very low levels. In contrast, progesterone and androgen receptors are present in approximately two thirds of meningiomas. In multiple meningiomas, the number of progesterone receptors is higher than that in solitary meningiomas. Progesterone receptors in meningiomas are identical to those found in mammary carcinomas.[1-4,12] The present case concerns a meningioma that occurred during pregnancy, without a history of previous trauma, radiation or the presence of neurofibromatosis, leading to the supposition that female hormonal factors in pregnancy had affected the progression of the tumor.

Meningiomas cause symptoms and signs by a number of mechanisms, namely irritation of the underlying cortex, pressure on the brain and cranial nerves, hyperostosis and/or invasion of the surrounding soft tissues, or induction of vascular injury in the brain. In general, the symptoms of meningioma consist of headache, vomiting, seizures and focal neurological deficits. The site of the lesion affects the clinical symptoms. Depending on the location of the lesion, a meningioma may cause visual disturbances, hearing loss, changes in mental state, paralysis of the limbs, or even cause hydrocephalus, when the tumor is blocking the flow of cerebrospinal fluid.[1-5,13]

In the case described here, the meningioma was located in the occipito-cervical region, with pressure on the motor pathways (corticospinal tracts) of the spinal cord, resulting in upper motor neuron quadriparesis. The tumor also exerted pressure on the sensory pathways (spinothalamic tract and dorsal column), causing hypesthesia from the C2 dermatome downwards and pressing on the autonomic pathways, giving rise to fecal and urinary incontinence. Extramedullary tumors of the occipito-cervical region may also include neoplasms of the occipital bone, which are in general rather infrequent when compared to other bones of the skull. These occipital bone tumors comprise such diverse entities as chondroblastoma, ossifying fibroma, atypical juvenile epidermoid tumor, giant cell tumor in the background of von Recklinghausen disease, and primary lymphoma.[13]

The diagnosis of meningioma is established by neurological examination, followed by ancillary procedures such as computerised tomography (CT), magnetic resonance imaging (MRI), angiography or biopsy. In the CT scan, the lesion may appear isodense or hyperdense, and hyperostosis or erosion of bones may be found and occasionally even intratumoral calcification. After administration of contrast, the tumor will be of higher intensity than the surrounding tissues. Cystic cavities may also be found, which may represent tumor necrosis, previous hemorrhage,

cystic degeneration, or entrapped cerebrospinal fluid. MRI of meningioma yields an isointense or hypointense image on T1-weighted sequence, and will appear isointense or hyperintense on T2. Enhancement occurs after administration of contrast, and occasionally a 'dural tail' appears. The presence of a heterogenous enhancement, irregular tumor boundaries, and edema are indicative of an anaplastic tumor. On magnetic resonance spectroscopy a choline/creatine ratio may be found illustrating the proliferative potential of the lesion; if there is a peak at 1.5 ppm, a meningioma should be suspected. On digital substraction angiography (DSA), pial vessels will be seen supplying the peripheral areas and dural vessels supplying the center of the lesion. In addition, a 'sunburst' appearance of enlarged 'dural feeders' and 'prolonged vascular stain' may be found. It is essential to perform endovascular angiography for visualizing the tumor vasculature and impairment of vital vascular structures. Preoperative endovascular embolization in 'vascular feeders' of the external circulation may be beneficial, because it reduces the risk of hemorrhage. Resection should be performed as soon as possible after embolization to reduce the likelihood of revascularization of the tumor.[1-5,12]

The management of meningioma includes surgical therapy, radiation therapy (stereotactic radiosurgery or stereotactic radiotherapy), or conservative management for small asymptomatic tumors, consisting of close observation without therapy. The choice of therapy is based on location of the tumor, tumor size, symptoms and signs, and age and medical condition of the patient. In a tumor indicated for operation, the therapeutic goal is total resection. However, for tumors in a virtually inaccessible location, the resection frequently cannot be performed maximally, and the patient will continue to have clinical symptoms. Recurrence and survival rate depend on extent of tumor resection and histological grade. Postoperative recurrence within 10 years may be estimated from the extent of resection according to the Simpson scale: i) grade 1: total resection, including dura and skull, recurrence 9%; ii) grade 2: total resection with coagulation of dural adhesions, recurrence 19%; iii) grade 3: total resection without coagulation of dural adhesions, recurrence 29%; iv) grade 4: subtotal resection, recurrence 29%; and v) grade 5: decompression, recurrence 40%.

Administration of corticosteroids before and after operation significantly reduces mortality and morbidity rates of surgical resection. Patients with supratentorial meningioma should receive anticonvulsant therapy. For medical management of meningioma, mifepristone and hydroxyurea may be given as antiprogesterones. Administration of COX-2 and 5-LO inhibitors is still under investigation, as is administration of temozolomide in patients with recurrent meningioma and incomplete resection. The use of interferon a as an angiostatic may also be considered. Indications for radiotherapy of meningiomas are tumors unsuitable for total resection, and recurrent, inoperable, or histologically malignant meningiomas.[1-5,14]

At 32 weeks of pregnancy a consensus was reached to terminate the pregnancy, considering that the fetus would be capable of survival outside the maternal environment. It was decided to perform induction of labor to initiate uterine contractions and opening of the uterine cervix. The delivery was terminated by forceps extraction, because of inability of the patient to bear down, due to impairment of voluntary nerves from the brain to the corresponding muscles. Cesarean section was not performed, due to financial considerations and the presence of quadriparesis and immobilization, leading to fears that postoperative recovery would be suboptimal.

The prognosis of patients undergoing total resection of meningioma is commonly quite good. However, incompletely excised malignant and multiple meningiomas tend to recur.[3] In the present case the tumor could not be totally resected due to the difficult location of the tumor, but as much as possible of the tumor was removed to relieve pressure on the brain stem and spinal cord, which could have fatal consequences.

CONCLUSIONS

The management of a pregnant patient with a brain tumor should be tailored to the individual according to the circumstances. In this patient with meningioma the pregnancy could continue to term and delivery without endangering the mother or the fetus.

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