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Meningioma in Pregnancy

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Background: Brain tumors in general are rare in pregnancy, however it is unquestionable that there is a hormonal relationship in the appearance of some tumors, particularly meningiomas.

Objective: The higher incidence of meningioma in women especially during pregnancy and the hormonal influence in the development and growth of these tumors will be discussed. Our aim is to present cases with intracranial meningioma in pregnant ladies presenting with signs and symptoms of increased intracranial pressure and neurodeficit.

Methods: Retrospective review of five patients who presented with intracranial meningioma during pregnancy.

Results: Four patients had surgical resection of the tumor. All operated patients were negative for estrogen receptors, while three were positive for progesterone receptors. The patient with negative progesterone and estrogen receptors had tumor recurrence during her subsequent pregnancy in spite of a tumor resection and radiotherapy. All the operated patients did well except the one with tumor recurrence who died.

Conclusion: Meningiomas have the tendency to grow and increase in size during pregnancy. The acute presentation during pregnancy adds to the difficulty of management.

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The occurrence of brain tumors during pregnancy is uncommon. Isla A, et al[1] reported 7 patients with brain tumors in a series of 126,413 pregnancies over 12 years, two of whom had meningioma. Many studies suggest that female hormones play a role in the etiology and growth of meningioma[2]. The incidence of meningioma is twice as high in females as in males[3]. In women, the growth of meningioma appears to be accelerated during the luteal phase of the menstrual cycle and during pregnancy[4]. There is also an association between meningioma and breast cancer[5].

METHODS

This is a retrospective study. The medical files of five pregnant patients with intracranial meningioma were reviewed for biological data age, sex, signs and symptoms, radiological diagnosis, medical and surgical management, outcome, and follow up during the period 1993 to 2001. Part of the follow up was done by telephone contact.

RESULTS

There were five pregnant patients with intracranial meningioma in this study. They were treated at King Fahad hospital of the university, Alkhobar, Saudi Arabia, during the period 1993 to 2001. Their mean age was 41 years, and the mean gestational age at presentation was 27.6 months. Most of the patients had chronic headache on presentation. All of them had brain MRI visualizing the sites as: two tentorial, one each of suprasellar, sphenoid wing and convexity meningioma. Four patients were operated on, three had total excision of the tumor, the fourth, with suprasellar meningioma, had subtotal resection. The fifth patient a 42 years woman with tentorial meningioma refused surgery and was lost to follow up. The histological diagnosis was meningiothelimatous meningioma in two patients, one fibroblastic and the fourth patient had atypical meningioma. Progesterone receptors were positive in three.

The operated patient with tentorial meningioma had radiotherapy due to presence of few mitosis in the tumor. She presented 4 years later in her 16^{th} week of gestation with a large recurrence, subtotal resection of the tumor was performed, and the histopathology was consistant with rhabdoid meningioma[6]. The tumor was negative for both progesterone and estrogen receptors. She deteriorated and expired 6 months later. The other three patients are alive and are in good health.

ILLUSTRATIVE CASES

CASE 1

Forty one years old Saudi lady at 24 weeks of gestation was admitted on 15 November 1998. Her main complaint was progressive generalized headache. The headache was associated with double vision, nausea and vomiting. The patient had similar symptoms three years earlier, when she was pregnant in her second month . Her symptoms subsided following abortion at that time. Examination revealed bilateral papillodema. MRI of the brain showed a large left Sphenoid wing meningioma (Fig1). Craniotomy with total excision of the tumor was performed and she had a smooth postoperative period. Histologic study was consistent with fibroblastic meningioma; the tumor was negative for estrogen and positive for progesterone receptors.

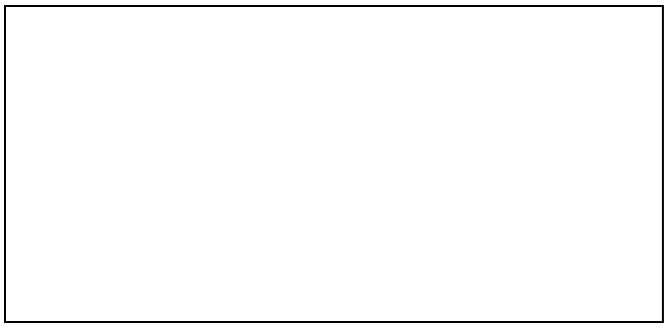

Figure 1. T1weighted image MRI, saggital view, post gadolinium shows dense homogenous enhancement of a large left sphenoid wing meningioma which is extending superiorly, anteriorly, and medially compressing the frontal lobe

CASE 2

Forty one years old right handed Saudi lady presented on 28 May 2001 at 28 weeks of gestation with one month history of headache and fatigability. Her concentration and memory started to deteriorate, therefore, she was seen by her obstetrician. She was found to have bilateral papilloedema, left sixth and seventh cranial nerves palsy, and up going planter reflex. Brain CT scan showed a large left frontotemporal convexity meningioma with midline shift (Fig 2). She was operated and total tumor excision was performed. Histologic study was consistent with atypical meningioma with positive progesterone receptors. The patient had a smooth postoperative recovery. She completed her pregnancy.

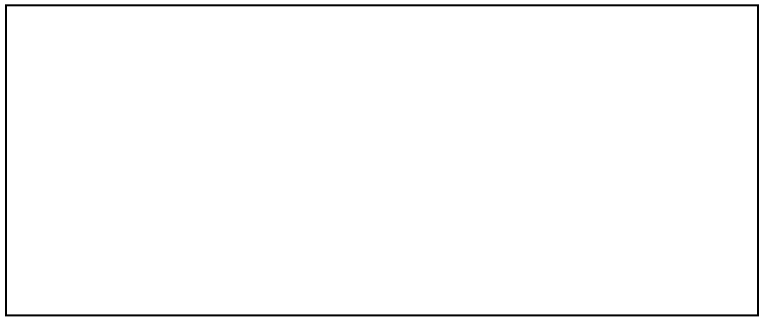

Figure 2. Brain CT scan with contrast shows homogenously enhanced large left fronto temporal convexity meningioma with midline shift

DISCUSSION

Cushing and Eisenhardt were the first to describe the relationship between pregnancy and the rapid increase of neurologic symptoms in women with meningiomas[7].

The expression and potential role of estrogen, progesterone, and androgen receptors in meningioma have been investigated thoroughly. The phenotypic profile of hormone receptor status in meningiomas had been classified into: a high percentage of tumours displaying high level of progesterone receptor (PR), a smaller subgroup containing moderate concentrations of androgen receptor (AR), while the level of oestrogen receptor (ER) has always been equivocal, ranging from low to virtually undetectable by immunohistochemistry[8]. In vivo measurement of the receptor density and occupancy can now be done by the use of Positron emission tomography (PET)[9].

Two of our patients were positive for progesterone and negative for estrogen receptor. The patient with the recurrent meningioma was negative for both progesterone and estrogen receptors.

In a vitro study on meningioma, it was seen that the falling level of human chorionic gonadotrophin (Hcg); the absence of Luteinising hormone (LH), and Follicle-stimulating hormone (FSH) in the second and third trimesters of pregnancy may play a role in the acceleration of meningioma growth in these stages of pregnancy[10].

The incidence and pattern of expression of androgen receptors are similar to those observed for progesterone receptors. Several studies have shown positive correlation between the binding activity of both androgen and progesterone suggestive of androgen rather than estrogen regulating the progesterone receptor[11]. These results imply functional relationship for androgen and progesterone receptors in meningioma, as has been described for benign prostatic hyperplasia, prostatic carcinoma, and breast tumor[12]. The presence of positive progesterone receptors correlate with worsening symptoms of meningiomas[13]. Under the influence of progesterone, the tumor enlarges by fluid retention and enhanced vascularity, similar to that of a fibroid. After delivery, the fall in the progesterone level leads to the shrinkage of the neoplasm[14].

The symptoms of headache, nausea and vomiting are often encountered in pregnancy. These will add to the confusion in the evaluating the central nervous system in pregnant patients. Symptoms of increased intracranial pressure, as well as seizures and visual disturbances in preeclampsia may have the same picture as intracranial meningioma, which tends to grow rapidly and become symptomatic as pregnancy progress[4].

Therefore, in women presenting with worsening neurological symptoms in late pregnancy with or without the presence of focal signs, intracranial pathology should be considered.

The management of intracranial tumors in pregnancy must be individualized depending on the patient's physical condition, tumor location, gestational age, and other concomitant factors in relation to pregnancy. Surgical intervention during pregnancy should be avoided if possible, due to increased risk to both mother and fetus. Postpartum surgical intervention poses less risk due to decreased tumor size and vascularity. Some authors recommend immediate abortion once signs of increased intracranial pressure have manifested, whereas others advise non-operative management to decrease the intracranial pressure until fetal lung maturity is ensured[13].

Roelvink et al, in his report showed that 60% of intracranial meningiomas in pregnant women were basal meningioma, which require a planned surgical approach[14].

Four patients in this study had basal meningiomas. The operated patient with tentorial meningioma with total resection and radiotherapy had a large basal recurrence after further pregnancy. The recurrent tumor was proved to be an aggressive type rhabdoid meningioma with bad prognosis[6]. Surgical excision is a primary management of meningioma. Complete resection is determined to some extent by the tumor site[15]. Mirimanoff et al, associated the total excision to the accessibility of the tumor (96% for convexity and 28% for sphenoid wing meningioma)[15].

The diagnosis of atypical or anaplastic meningioma carries a high risk of recurrence[16]. The prognostic factors for recurrence have been studied intensively. May et al, suggested that a proliferative index greater than or equal to 20%, irrespective of the histopathological appearance, is a strong indicator of recurrence[17].

Recently, the calculation of the bromodeoxyuridine (BudRL1) or the number of argyrophilic nucleolar organizer regions (AgNoRs) has been used to identify intracranial meningioma with higher propensity to recur. Perry et al, emphasized the great clinical importance of the implication that complex karyotypes, dicentric or ring chromosomes, and abnormalities of chromosome 1, 3, and 6 might serve as predictors of aggressive biologic behaviour in otherwise histologically benign meningiomas[20].

The Southwest Oncology group treated 19 patients with unresectable or refractory meningioma with tamoxifen, 53% demonstrated progression, and 32% remained stable for a mean duration of 31+ months and 22% reported subjective improvement[21]. The tumor receptors identification was not available at that time, so our patient with tumor recurrence was treated with a standard dose of Tamoxifen, but a repeat CT scan a month later showed progression of the tumor. Therefore, this method of treatment was terminated.

Mefipristone, a potent antagonist of progesterone and glucocorticoid, is used in the treatment of unresectable, or recurrent meningiomas. Objective improvements are noted in 25% of patients receiving this medication[22].

CONCLUSION

Pregnant woman with presenting symptoms of repeated vomiting, nausea, and headache may not always be related to gestational changes or toxaemea of pregnancy. Patients should be examined carefully and when suspicion high, should be subjected to neuroradioliogical investigation preferably by MRI. Those women who had a history of meningioma during previous pregnancies should be counseled for effective birth control to prevent tumor recurrence.

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