The normal pituitary gland may enlarge by as much as 50 to 70% during pregnancy. It is well known that pregnancy may also spur further growth in pre-existing pituitary adenomas; however, presentation with nonendocrine pituitary neoplasms, especially craniopharyngiomas, is rare during pregnancy. In a review of the literature, we were able to find only six cases of craniopharyngioma that had been diagnosed during pregnancy. To our knowledge, our case is the first one in which enlargement and recurrence of the tumor were seen during the course of two consecutive pregnancies.

Case Report

History and Examination. In December 1988, this 19-year-old woman presented with a 1-year history of secondary amenorrhea and galactorrhea. Results of pituitary function tests were normal except for elevated prolactin (PRL) levels; basal levels ranged from 126 to 132 ng/dl. Radiographic studies of the sella turcica revealed enlargement of the sella. Computerized tomography (CT) scans demonstrated a 1-cm-diameter intrasellar mass with calcifications (Fig. 1 upper). This was interpreted as a prolactinoma. The patient refused surgical intervention, and bromocriptine was therefore administered to induce shrinkage of the tumor.

Second Evaluation and First Operation. Seven months later, when she was 20 weeks pregnant, the patient developed sudden visual dysfunction. Emergency transsphenoidal surgery was performed to restore visual function, and the tumor was found to be a craniopharyngioma. The patient had spontaneous labor and delivered a healthy infant at term. The tumor recurred 4 years later, during her second pregnancy, and was again entirely removed via a second transsphenoidal approach. She again had normal term delivery. During the 5-year follow-up period she has demonstrated no endocrinological or visual dysfunction. Control magnetic resonance images have revealed no recurrence of the tumor. The transsphenoidal approach seems to be the safest procedure to use during pregnancy to achieve an immediate optic nerve decompression and to preserve pituitary function.

Key Words • craniopharyngioma • hyperprolactinemia • intrasellar tumor • pregnancy • rapid growth
Second Operation. Four years later, during her second pregnancy, the patient developed headache and visual deterioration at 22 weeks of gestation. Her basal PRL level was 170 ng/dl. Magnetic resonance (MR) images demonstrated an intra-suprasellar mass with calcification (Fig. 2 upper). An immediate transsphenoidal surgery was performed again, and the tumor was totally removed.

Second Postoperative Course. Surgery restored the patient’s normal visual acuity and visual field. On the 3rd postoperative day she developed transient diabetes insipidus for which she was treated with 1-desamino-8-arginine vasopressin (DDA VP), and her condition improved in 3 weeks. Histopathological examination showed the tumor to be a craniopharyngioma. The patient again delivered a normal infant at term. Resumption of ovulatory cycles was noted at 6 months postpartum. During the 5-year follow-up period her endocrinological and neurological functions have remained normal, and control MR images have revealed no recurrence of the tumor (Fig. 2 lower).

Discussion

Craniopharyngiomas account for approximately 2.5 to 4% of all intracranial neoplasms. They are more common among children but may present at any age with visual and endocrinological symptoms. Oligo/amenorrhea and hyperprolactinemia have been reported in patients with craniopharyngiomas by many authors. Hyperprolactinemia in these patients may result from direct encroachment of the tumor on the hypothalamus and/or pituitary stalk, which leads to disruption of the transportation of PRL inhibitory factor(s) through the hypothalamopituitary portal vessels. This kind of hyperprolactinemia is usually mild to moderate, rarely exceeding 100 ng/dl, but in three cases reported by Kapcala, et al., the portal system was shown to be intact.

Estrogens stimulate the lactotrophic tissue during pregnancy and spur growth of lactotroph adenomas. Enlargement of pituitary adenomas during pregnancy, especially prolactinomas, has been well documented. The literature includes a total of six cases of craniopharyngioma occurring during pregnancy. The first case was reported by Fisher in 1935, as discussed in Johnson, et al. In this case, the pregnant woman presented with visual deterioration. Six weeks after an induced abortion, she underwent surgery but became blind. The second patient presented with visual disturbance. The third patient presented with visual disturbance. The tumor was removed at 29 weeks of gestation, and the pregnancy progressed normally to term, culminating with vaginal delivery. The third patient presented during her second trimester, underwent operation 4 months postpartum because of visual deterioration. The fourth patient developed diabetes insipidus at 27 weeks of gestation. She was treated with DDAVP and underwent surgery 3 days after the delivery when progressive loss of visual acuity was observed. The fifth patient, who presented during her second trimester, underwent operation because of visual deterioration. Visual and endocrinological functions, including fertility, were preserved postoperatively. In the sixth patient, the initial presentation, operation, rapid tu-
mor regrowth, and reoperation occurred during the course of a single pregnancy.

In our patient, the pathogenesis of hyperprolactinemia (PRL > 100 ng/dl), rapid tumor expansion during pregnancy, and recurrence during a second pregnancy 4 years after the total removal of the tumor is difficult to explain. The investigations of Szeifert and colleagues12,13 showed secretory activity in craniopharyngioma, and these authors reported immunohistochemical positivity for pituitary hormones in scattered tumor cell groups. In a few molecular studies the presence of progesterone receptor (PR) and estrogen receptor (ER) messenger RNA has been demonstrated in almost all craniopharyngiomas.5,14 However, in immunohistochemical studies ER and PR proteins were observed only focally in a few cases. In addition, in one study insulin-like growth factors I and II and heterogeneous insulin-like growth factor–binding proteins were demonstrated in the cystic fluid of patients with craniopharyngioma.18 It is possible that pregnancy induces tumor growth by upregulating the transcription and translation of ER and PR messenger RNA into receptor proteins. More interesting is the report describing the growth of an ameloblastoma during pregnancy.3 Ameloblastomas and craniopharyngiomas originate from stomodeum epithelium. It is likely that ameloblasts also express ERs and PRs, although this has not yet been established. It is also tempting to speculate that the gingival hypertrophy associated with pregnancy may be related to the presence of ERs and PRs in gingival epithelium and soft tissue. Our review of the literature showed no study of gingiva for the presence of ERs and PRs. This is highly unusual because most of the literature indicates that gestational hormones play a significant role in the pathogenesis of gingival hypertrophy.17 We decided to perform ER and PR protein immunohistochemical staining retrospectively to investigate this possibility but could not find the paraffin blocks of tumor specimens.

The goal in the treatment of these tumors is to achieve a total removal with low morbidity and mortality rates.9 The more favorable type of the surgical procedure, transsphenoidal or transcranial, remains controversial. For pregnant patients, the transsphenoidal approach seems to be the safest procedure, especially if the tumor is localized mostly in the intrasellar region with minimal to moderate suprasellar extension. A transcranial procedure may be reserved as a postpartum option if the tumor cannot be removed totally.

Conclusions

We describe a case of rapid enlargement and recurrence of an intrasellar craniopharyngioma in one woman during the course of two pregnancies. This case illustrates that an expeditious transsphenoidal removal of the tumor maintains visual function and preserves the pregnancy. Long-term follow up in this patient has shown normal neuroendocrinological function and no recurrence of the tumor.

Acknowledgment

The authors are grateful to Faruk Aydin, M.D., for his valuable contributions.

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