Regression of a presumed meningioma with the antiestrogen agent mepitiostane

Case report

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MENINGIOMAS are benign tumors that arise from cranial and spinal arachnoid cells. For most of these lesions, surgery provides effective and sufficient clinical results. However, some meningiomas recur or are resected subtotally because of anatomical problems such as their location at the skull base. To date, the only effective treatment for such recurrent and/or subtotally resected meningiomas has been limited to radiotherapy.4,16

Meningiomas occur predominantly in women, and often contain steroid receptors such as estrogen and progesterone receptors.2,19 Additionally, in many in vitro studies2,10,18,19 it has been suggested that hormone therapy is a promising option for treatment of meningioma, but no hormonal agents except tamoxifen6,14 and mifepristone7 have been shown clinically to contribute to the regression of a meningioma. In this report, we describe a case of presumed meningioma that regressed as a result of treatment with the antiestrogen agent mepitiostane.9

Case Report

This 68-year-old woman underwent a distal gastrectomy for gastric cancer in August 1994. A presumed meningioma of the falx was found incidentally on a staging examination of the gastric cancer, but the meningioma was not treated with surgery. Instead, after gastrectomy the patient received tegafur as adjuvant chemotherapy until February 1996, when she was readmitted to the hospital because of loss of appetite and emaciation but with no recurrence of the gastric cancer. A computerized tomography scan obtained during this second admission showed no change in the meningioma. To improve her general condition, tegafur was discontinued and she was started on a course of the antiestrogen agent mepitiostane. Administration of mepitiostane for approximately 2 years resulted in a marked regression (73%) of the meningioma. This is the first reported case of a presumed meningioma that regressed as a result of use of the antiestrogen agent mepitiostane.

KEY WORDS • antiestrogen • hormone therapy • meningioma • mepitiostane

Abbreviations used in this paper: CT = computerized tomography; MPA = medroxyprogesterone acetate.
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Fig. 1. Axial CT scans obtained before gastrectomy. Left: Plain CT scan revealing an oval and slightly high-density tumor just around the falx in the left occipital lobe. Right: Contrast-enhanced CT demonstrating homogeneous enhancement of the tumor, which is 5.4 × 4.3 cm in diameter.

Fig. 2. Axial plain CT scan obtained after administration of mepitiostane for 6 months, demonstrating no change in the tumor.

with intravenous hyperalimentation, and was discharged on July 31, 1998. She continued to receive mepitiostane and had no evidence of regrowth of the meningioma as of February 1999.

Discussion

Radiotherapy provides the only effective alternative to surgery in the treatment of meningiomas. The other alternatives to surgery such as chemotherapy and immunotherapy have not yet become standard for the treatment of meningiomas.

Many authors have suggested that antiestrogen or antiprogesterone therapy may be effective for meningiomas, based on the fact that these tumors often contain estrogen and progesterone receptors. However, in clinical trials only two objective responses to tamoxifen (that is, >50% reduction in tumor size) have been reported, and no objective response to other hormonal agents such as MPA and mifepristone has been reported.

In this case, we had not intended to treat the presumed meningioma with the antiestrogen agent mepitiostane; it was administered to improve the general condition of the patient. The use of mepitiostane for approximately 2 years failed to achieve this goal, but incidentally resulted in a marked regression of the meningioma. When we noticed the tumor regression, we initially thought that the marked decrease in serum estrogen levels caused by weight loss might have contributed (that is, spontaneous regression). However, on further investigation we came to believe that the meningioma should not have regressed with the decrease in serum estrogen levels because the patient’s serum levels of estradiol, the main estrogen, were high for her age.

Bernstein, et al., reported an incidental regression of meningioma with administration of 5-fluorouracil, folic acid, and levamisole for the treatment of rectal cancer.

Our patient received tegafur as adjuvant chemotherapy for gastric cancer, which might also have contributed to the regression of the meningioma. However, after she had been treated with tegafur for approximately 2 years, a plain CT scan of the brain showed no regression of the meningioma. Thereafter, the patient received no other chemotherapeutic and/or hormonal agents except mepitiostane. Thus, it is reasonable to assume that the meningioma regressed as a result of the antiestrogen mepitiostane.

Of the many antiestrogen agents now available, tamoxifen is the most commonly used in patients with breast cancer because of its high antitumor activity and few adverse effects. On the other hand, tamoxifen is known to have not only antiestrogenic properties, but also weak es-
trogenic activity. Jay, et al. reported that tamoxifen accelerated the progression of meningioma cells in vitro. However, it is still unclear whether meningiomas are clinically affected by the weak estrogenic activity of tamoxifen.

Of the two steroid receptors for estrogen and progesterone, meningiomas often contain more progesterone than estrogen receptors. Markwalder and colleagues reported that MPA is an attractive therapy for meningioma because administration of this agent downregulates progesterone receptor contents and inhibits the growth of meningioma as measured by Ki-67. However, they and Jaakskelainen, et al. reported that no meningioma actually responded to MPA. Grunberg, et al. reported that an objective response was found in five of 14 patients with unresectable meningioma after treatment with the antiprogestosterone agent mifepristone. All five responders, however, had only minor decreases in tumor size.

In our case, a 2-year maintenance on mepitiostane resulted in a marked regression of the meningioma. On the other hand, administration of mepitiostane for approximately 6 months initially caused no marked change in the meningioma. These findings indicate that mepitiostane should be administered for a longer period for the treatment of meningioma. We think that long-term administration of this agent is preferable for the following reasons. First, the onset of tumor regression with hormone therapy is generally slower than that with chemotherapy in breast cancer, and perhaps also in meningioma. Second, estrogen receptor levels in meningioma are much lower than those in breast cancer. Third, a disruption of hormone therapy may accelerate the regrowth of meningioma. Finally, the adverse effects of mepitiostane are very mild.

Conclusions
This is the first reported case of a presumed meningioma that regressed markedly after administration of the antiestrogen agent mepitiostane. Because it has already been proven that the efficacy of tamoxifen and mifepristone against meningioma is limited, a prospective study in which mepitiostane is used against recurrent and/or unresectable meningioma should be undertaken.

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