Female Patients With Meningioma of the Sphenoid Ridge and Additional Primary Neoplasms of the Breast and Genital Tract

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Of 283 meningioma patients seen at the University of Kansas from 1948 to 1984, eight women acquired two primary extraneural cancers in addition to their meningiomas. Of these eight patients, six (75%) had sphenoid ridge meningiomas compared with 15% of meningioma patients overall ($P < 0.001$). Seven (87.5%) had at least one breast or genital cancer ($P < 0.001$). Of the six with sphenoid ridge meningiomas, five (83.3%) had both of their additional tumors in these two organ systems, and the sixth had one such tumor. It is proposed that this grouping of sphenoid ridge meningioma, breast cancer, and genital cancer represents a unique constellation of neoplasms in women.

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MENINGIOMA and breast cancer have been associated in several studies.[1-5] Like breast cancers, meningiomas often contain progesterone receptor protein and may also contain estrogen receptor protein.[6-9] Because meningioma has long been known to be more common in women than men, it is appropriate to study the associations between meningiomas and other neoplasms in women. In this study we analyzed the synchronous and metachronous occurrence of cancers in meningioma patients, focusing particularly on breast and female genital cancers and the distribution of meningiomas among various subsites.

Methods

The records of 283 intracranial meningioma patients were reviewed. These cases include 177 women and 106 men diagnosed with meningiomas at the University of Kansas Medical Center from 1948 to 1984. The diagnoses were confirmed from the hospital records and the pathology reports contained therein, the Kansas University Medical Center Tumor Registry, and the Cancer Data Service (the regional cancer registry). Data on the occurrence of second or third tumors in these meningioma patients were obtained from existing records. Both metachronous and synchronous second and third neoplasms were identified. In order to test the possibility of chance occurrence of sphenoid ridge meningiomas with multiple malignancies involving the breast or female genital tract, chi-square tests were performed.

Results

Of the 283 patients with meningiomas, 42 had 50 additional malignant tumors (Table 1). These included 12 breast cancers, five uterine corpus cancers, three uterine cervix cancers, and one vaginal cancer. Forty-three patients (15%) had meningiomas on the sphenoid ridge; this group included 29 women and 14 men. Forty-nine individuals had meningiomas on the convexity, 35 in the parasagittal area, 18 in multiple sites, 17 in the parasellar region, 16 in the falx, and the remainder in other sites (Table 2).

Eight women (19% of those with additional tumors) had two cancers in addition to their meningiomas (Table 3). Breast cancers were reported in five of these eight patients, uterine corpus cancers in three, and uterine cervix cancers in two. Altogether, seven of these eight women had at least one lesion in the breast or genital organs and five had lesions in both sites. No patient had more than three tumors.

In six of the eight women with two additional cancers (75%) the meningiomas were found on the sphenoid ridge. A seventh patient had a parasellar meningioma, and the eighth had an olfactory groove meningioma. Of these six sphenoid ridge meningiomas, five occurred on the medial or middle third, and one occurred on the lateral third, the pterion. Compared with all meningioma patients, those with two additional tumors were more likely to have sphenoid ridge meningiomas than meningiomas at other sites ($P < 0.001$; they were also more likely to be women ($P < 0.05$). Compared with patients with meningioma and one additional tumor, those with two additional tumors were more likely to

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TABLE 1. Sites of 50 Malignant Primary Tumors Occurring Synchronously or Metachronously in Association With Meningioma

Breast	12
Female genital	10
Gastrointestinal	10
Brain	6
Thyroid	3
Lung	3
Hematopoietic	2
Melanoma	2
Prostate	1
Unknown	1
Total	50

TABLE 2. Sites of Occurrence of 283 Intracranial Meningiomas, University of Kansas Medical Center, 1948–1984

Site	Total	Women	Men
Convexity	49	27	22
Sphenoid ridge	43	29	14
Parasagittal	35	23	12
Multiple sites	18	13	5
Parasellar	17	12	5
Falx cerebri	16	13	3
Olfactory groove	11	9	2
Other	94	51	43
Total	283	177	106

have an associated breast or genital cancer than cancer with a different primary focus ($P < 0.001$).

Of the eight patients with two additional cancers, the subgroup of six with sphenoid ridge meningiomas included the five patients whose additional tumors were breast cancer(s) ($P < 0.05$) and the three whose lesions were uterine corpus cancer (not significant). This subgroup of six with sphenoid ridge meningiomas also included the five patients who developed both of their additional extraneural neoplasms in the breast and genital tract ($P < 0.05$). Table 3 lists the neoplasms and ages at diagnosis in these eight patients.

The eight meningioma patients were categorized by the histologic subtype of the meningioma if available. Three meningiomas were classified as meningothelial, two as fibroblastic, and one as transitional. The remaining two meningiomas were not classified. Five of the eight patients had family histories of cancer. Two patients had four first-degree relatives with malignancies, two had three such relatives, and one had two affected relatives.

The eight patients developed a total of 16 tumors in addition to their meningiomas; nine of these neoplasms were diagnosed before the meningioma, three after, and four synchronously. The earliest neoplasm was discovered 29 years before the meningioma, and the latest one was found 20 years after the development of the meningioma.

Discussion

We have described a subset of female meningioma patients at high risk for acquiring additional neoplasms. Seven of 17 patients (41%) with meningioma and either breast or female genital cancer developed a third tumor compared with one of 25 with meningioma and a second lesion in a site other than the breast or genitals ($P < 0.001$). Moreover, sphenoid ridge meningiomas occurred more frequently in patients with three tumors ($P < 0.001$). Because the associated tumors can precede or follow the meningiomas by 20 or more years, affected women remain at risk throughout their adult lives.

Endocrine factors may be operative in the occurrence of this unusual pattern of three neoplasms. Three lines of evidence support the idea that the sphenoid ridge may be more susceptible to the effects of endogenous female sex steroids than other sites of occurrence of meningioma. First, intracranial meningiomas have a two-to-

TABLE 3. Female Patients With Multiple Primary Malignancies Plus Meningioma

Patient	Age at diagnosis	Site of tumors*	Comments
1	79	Sphenoid ridge (pterion)†	Brain tumor in daughter and brother; breast cancer in two sisters
	79	Breast	
	81	Corpus uteri	
2	71	Sphenoid ridge†	
	58	Breast	
	66	Corpus uteri	
3	79	Olfactory groove†	Cancer of unknown primary site in four siblings
	79	Gall bladder	
	79	Hodgkin's disease	
4	67	Sphenoid ridge†	Cervical cancer in mother and two sisters
	57	Uterine cervix	
	59	Breast	
5	30, 38	Sphenoid ridge†	Meningioma recurred at age 38; corpus uteri cancer in two sisters; breast cancer in mother
	43	Corpus uteri	
	50	Lung	
6	45	Parasellar†	
	34	Thyroid	
	32	Cervix	
7	68	Sphenoid ridge†	Cancer of unknown site in 2 brothers
	39	Breast	
	51	Breast	
8	58	Sphenoid ridge†	
	51	Breast	
	58	Cystadenoid basal cell carcinoma of breast (different locus) with metastasis to meningioma	

* Combinations including basal cell and squamous cell carcinoma of the skin are not included.

† Designates meningioma; sites with no dagger are where other malignancies occurred.

one predilection for women, but meningiomas *en plaque* of the sphenoid ridge occur almost exclusively in women.[10] Second, meningiomas have been reported to enlarge with pregnancy, regress subsequently, and recur with subsequent pregnancies. These meningiomas tend to occur on the medial aspect of the sphenoid wing[11-13] and in the parasellar area contiguous to the sphenoid ridge.[14-17] Third, investigators have correlated clinical findings from meningioma patients with studies of the intensity and incidence of progestin binding to receptors on the tumor.[7,8,17] They found an increase in the intensity of progestin binding in meningiomas of the sphenoid wing and olfactory groove as compared with meningiomas at other sites. The same is true for meningothelial meningiomas as compared with those of other histologic classifications.[18] However, incidence of positivity in progestin receptor assays could not be correlated with the site of meningioma despite the presence of positivity in a majority of sphenoid wing meningiomas.[7,8]

Genetic factors may also play a role in the occurrence of these tumors. The patients we described developed multiple neoplasms at various unrelated sites throughout their adult lives. The family histories showed that similar neoplasms occurred in at least two first-degree relatives in a majority of these patients. These features typify family cancer syndromes.[19-22] However, these family cancer syndromes have not been previously reported for meningiomas.

Because the numbers of tumors are small, the tumors are relatively common, and survival after diagnosis varies widely among patients affected by these several tumors, we cannot absolutely exclude the possibility that the association of meningiomas, breast, and genital cancers has occurred only by chance. The fact that six of the 29 women with sphenoid ridge meningiomas had two additional neoplasms—quite separate from the association with breast and genital tract tumors—makes the association by chance quite unlikely when only two of the 148 women with meningioma at sites other than the splenoid ridge had two additional neoplasms ($P < 0.001$). Further studies should be done with a much larger data base, preferably a population-based registry such as one of the SEER registries, comparing the actual incidence of second and third tumors in women with sphenoid ridge meningiomas and women with meningiomas of the other intracranial sites.

The clinical ramifications of these findings are twofold. First, women with a history of multiple tumors involving the breast, genital tract, and sphenoid meninges may benefit from serial screening for additional malignancies. Second, patients who have had breast or endometrial cancer and who present with lesions of the sphenoid ridge may have meningiomas that are operable, rather than metastases of their primary neoplasms that are probably not operable.

That breast and genital malignancies occur with sphenoid ridge meningiomas suggests the possibility that tumors are responsive to female sex steroids. However, the clinical importance of the presence of estrogen and progesterone receptor protein in meningiomas is at present moot. This, along with evidence that supports a genetic basis for the tumors, indicates the need for further investigation into the etiology of this combination of lesions.

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