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Management of intracranial plasmacytoma

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The authors report on a study of eight cases of intracranial plasmacytoma to identify the risk of progression to multiple myeloma and suggest the treatment required for cure of solitary lesions. The diagnosis of multiple myeloma or myelomatous changes was made in the immediate postoperative period in four patients (50%), two of whom had skull base lesions. Of the four remaining patients, three were treated with complete surgical resection and radiation therapy and had no recurrence of plasmacytoma or progression to multiple myeloma during mean follow up of 12 years (range 2–25 years); one patient underwent subtotal surgical resection and had recurrence of the tumor despite radiation therapy.

It is concluded that multiple myeloma is unlikely to develop during the long term in patients with intracranial plasmacytoma who do not develop multiple myeloma or myelomatous changes in the early postoperative period. However, lesions that infiltrate the skull base are not likely to be solitary, and patients who harbor these neoplasms should undergo complete evaluation and close follow-up review to exclude multiple myeloma. A recurrence of solitary intracranial plasmacytoma is possible with subtotal surgical resection despite radiation therapy. Definitive treatment should consist of complete surgical resection with adjuvant radiation therapy.

KEY WORDS • plasmacytoma • multiple myeloma • brain neoplasm • surgery • radiation therapy • chemotherapy

INTRACRANIAL plasmacytoma is a solitary myeloma plasma-cell tumor that affects the skull, meninges, and brain. It is well known that plasmacytoma, a benign lesion, may progress to multiple myeloma, a malignant and often fatal neoplasm. Only a few case reports of intracranial plasmacytoma have been described in the literature.[8] From these reports, it is not clear which patients with intracranial plasmacytoma are likely to develop multiple myeloma and which patients can expect to be cured. We report our experience in eight patients with intracranial plasmacytoma, discussing treatment options, surgical techniques, and outcomes.

Clinical Material and Methods

We conducted a retrospective review of the charts of eight patients with intracranial plasmacytoma diagnosed and treated between 1969 and 1994 at two institutions, the University of Cincinnati Mayfield Neurological Institute (four patients) and The University of Texas M. D. Anderson Cancer Center (four patients). The patients' histories, treatments, and outcomes are summarized in Table 1. We use the term "plasmacytoma" to refer to a solitary myeloma and the term "myelomatous changes" to refer to an abnormal plasmacytosis on bone marrow evaluation that does not meet the criteria for multiple myeloma, but suggests the disease is not localized.

Results

Presentation and Diagnosis

The median age of the patients at diagnosis was 51 years. The presenting signs and symptoms included headaches, mental status changes, and cranial nerve palsies. None of the patients had a history of myeloma except the patient in Case 6, who had a right scapular mass diagnosed as myeloma 8 months prior to neurosurgical evaluation and was treated with chemotherapy (dexamethasone, vincristine, doxorubicin, and cyclophosphamide) and 5000-cGy radiation therapy. She had complete remission until she later presented with a right parietal mass as a solitary lesion.

Seven patients were evaluated for an intracranial mass by computerized tomography (CT) or magnetic resonance (MR) imaging. One patient (Case 5) was treated in the

TABLE 1

*Clinical data for eight patients presenting with intracranial plasmacytoma**

Case No.	Age (yrs), Sex	Presenting Symptoms	Location	Surgery	Bone Flap Involved	XRT (cGy)	Follow Up	Follow-Up Interval	Repeat Treatment
1	51, F	diplopia	pituitary, sphenoid	craniotomy, subtotal	no	5000	symptomatic at 7 & again at 8 yrs	8 yrs	craniotomy, transsphenoidal
2	51, F	mental status change	lt parietal	craniotomy	yes, removed	5000	no recurrence	2 yrs	NA
3	43, F	headache	falx	craniotomy	no	3700	no recurrence	8 yrs	NA
4	30, M	headache, 6th nerve palsy	clivus–dural	La Forte maxillotomy	yes, clivus	4500	bone survey consistent with MM	3 mos	NA
5	47, M	headache	rt parietal	craniotomy	yes, returned	5000	disease-free 25 years	25 yrs	NA
6	65, M	hemiparesis, history of myeloma treated	rt parietal	craniotomy	no	none	died 1 mo postop of stroke	1 mo, death	NA
7	75, M	vertigo, hoarseness, swallowing difficulty	lt posterior	suboccipital craniectomy	yes, petrous mastoid	4500	bone marrow with myelomatous changes	4 yrs, death from MM	chemotherapy
8	82, F	mental status change	lt parietal	craniotomy	yes, removed	none	bone scan consistent with MM	6 mos, death	NA

* MM = multiple myeloma, XRT = radiation therapy, NA = not applicable.

pre–CT era and underwent angiography. All of the tumors involved the dura. The location of the tumor was parietal in four (50%) of the patients.

Pathological evaluation in all cases confirmed a monoclonal plasma-cell tumor, thereby excluding plasma-cell granuloma and meningioma with conspicuous plasma cell–lymphocytic component. Systemic evaluation of all cases included bone marrow evaluation, serum protein electrophoresis for evaluation of monoclonal gammopathy (M component), quantitative immunoglobulin analysis, urine protein electrophoresis for cases of urinary excretion of immunoglobulin elements, skeletal survey, and bone scan. One patient (Case 6) had preoperative lumbar puncture, which was negative for gammopathy.

Treatment and Outcome

Seven patients underwent complete surgical resection. One patient (Case 1) had a pituitary lesion subtotally resected at an outside institution and diagnosed as chromophobe pituitary adenoma. Despite treatment with 5000 cGy radiation therapy, the tumor had continued to grow and had to be subtotally resected 7 years later. The patient presented to our institution 1 year following the second resection with continued growth of the mass across the sphenoid wing and progressive neurological compromise. A transsphenoidal decompression (subtotal excision) of the tumor was performed. Pathological evaluation of the tissue revealed plasmacytoma. A retrospective review of the tumor samples obtained at the prior resection confirmed that the tumor was a recurrent plasmacytoma, rather than a chromophobe pituitary adenoma. She subsequently received stereotactic radiation therapy and chemotherapy and experienced tumor control as documented by volumetric analysis.

In five cases, the bone immediately adjacent to the tumor was infiltrated. In two of these cases, the bone flap was removed and a cranioplasty was performed; in one case, the bone flap was returned at the time of initial surgery, and the patient had no recurrent plasmacytoma or progression to multiple myeloma at 25-year follow-up examination. In two of these cases, the skull base was infiltrated (the clivus in one and the petrous and mastoid bones in the other) and the tumor-infiltrated bone could not be resected; both patients had progression to multiple myeloma.

Radiation therapy was administered to six patients after initial surgery. Of the two patients who did not receive radiation therapy, one patient died prior to treatment with radiation therapy, and the other refused further treatment. Two patients received chemotherapy postoperatively.

For three patients (Cases 4, 7, and 8), postoperative evaluation revealed more generalized disease, changing the diagnosis from solitary plasmacytoma to multiple myeloma. The patient in Case 7 had myelomatous changes noted on postoperative bone marrow evaluation, namely 6% plasmacytosis. Within 6 months, multiple lesions developed that were consistent with multiple myeloma. Of the three patients diagnosed with multiple myeloma postoperatively, two died and one patient was lost to follow up 3 months after treatment. One patient, who had a history of myeloma in remission, died 1 month following surgery.

Of the four patients with solitary intracranial plasmacytoma, none had progression to multiple myeloma during a mean follow up of 12 years (range 2–25 years).

Discussion

Intracranial plasmacytoma is a rare condition and descriptions in the literature consist of case reports only.[2,8] Our series of eight patients is the largest reported to date.

Evaluation and Diagnosis

The diagnosis of solitary intracranial plasmacytoma is made pathologically with systemic evaluation to exclude multiple myeloma. Evaluation of an intracranial mass

begins with CT or MR imaging. Usually, the lesion enhances homogeneously with administration of intravenous contrast material. There may be bone inclusions within the tumor mass, which on preoperative imaging is often confused with meningioma. However, the skull will often have lytic lesions, thus differing from usual cases of meningioma.[2–4,8,10,11,16]

Systemic evaluation includes bone marrow evaluation, skeletal survey, and bone scan to exclude multiple myeloma. Serum protein electrophoresis demonstrates a monoclonal gammopathy (M component) in 99% of cases of multiple myeloma and occasionally in cases of plasmacytoma; however, a generalized gammopathy is seen with plasmacytic granuloma. Quantitative immunoglobulin analysis and urine protein electrophoresis are performed for cases of urinary excretion of immunoglobulin elements when an M component is not seen on serum protein electrophoresis. A drop in the level of immunoglobulin in serum or cerebrospinal fluid is expected with cure of treated solitary plasmacytoma and can be followed as a tumor marker for recurrence.[12,14]

Treatment and Outcome

Intracranial plasmacytoma is very radiosensitive; some authors have reported its cure using biopsy and subtotal resection and radiation therapy.[12,14,16] Cure is also possible with complete surgical resection and no radiation therapy. Arienta, *et al.*,[2] presented two cases that were treated only with surgical resection and had no evidence of recurrent disease on follow-up examination at 5 years. However, the only previously reported case of recurrence of intracranial plasmacytoma occurred in a patient treated with subtotal surgical resection and 5000 cGy radiation therapy.[15] In our series, one patient had continued tumor growth after subtotal resection despite treatment with 5000 cGy radiation therapy. From this experience, we conclude that the only definitive treatment for intracranial plasmacytoma is complete surgical resection plus radiation therapy. Although the tumors are radiosensitive, a potential exists for treatment failure with radiation therapy and incomplete resection. Nevertheless, we continue to recommend radiation therapy as an adjunct to complete surgical resection.

Multiple myeloma was diagnosed in four patients in this series. The diagnosis of multiple myeloma occurred before (one case) or shortly after (three cases) resection of the intracranial mass. Our review of the literature failed to find a single proven case of intracranial plasmacytoma without myelomatous changes that presented as multiple myeloma months to years later.[1,5,6,8,9,17–20] With complete systemic evaluation, we believe the finding of myelomatous changes or multiple myeloma should be evident in the immediate postoperative period.

In our report, the two patients with skull base infiltrating lesions were later diagnosed as having multiple myeloma. A review of the literature on skull base–infiltrating plasmacytoma suggests the same finding. After excluding cases of possible plasmacytic granuloma, case reports with inadequate follow up, and inadequate postoperative evaluation, all remaining cases with disease infiltrating the petroclival bones were associated with multiple myeloma or myelomatous changes.[1,5,6,9,17–19] From our experience, we believe that plasmacytoma of the skull base is similar to plasmacytoma of the spine and carries a high risk of progression to multiple myeloma over long-term follow up.[7,13]

Of interest is treatment of an infiltrated bone flap. In two cases, the bone flap was removed, and in one case the bone flap was returned at initial surgery. This last patient was treated with radiation therapy and at 25-year follow-up examination had no recurrence of plasmacytoma or signs of multiple myeloma. As plasmacytoma is radiosensitive, this outcome is not unexpected and suggests that the infiltrated bone flap need not be removed. However, should the surgeon return the infiltrated bone flap, we would recommend radiation therapy and a cautious follow up to exclude recurrence of tumor.

Conclusions

We conclude that multiple myeloma is unlikely to develop during long-term follow-up review in patients with intracranial plasmacytoma without multiple myeloma or myelomatous changes in the early postoperative period. Lesions infiltrating the skull base are not likely to be solitary, and these patients should undergo complete evaluation and close follow up to exclude multiple myeloma. A recurrence of solitary intracranial plasmacytoma is possible with subtotal surgical resection despite radiation therapy. The definitive treatment is complete surgical resection with adjuvant radiation therapy.

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