CASE REPORT

Plasma Cell Tumors of the Skull Base: Four Case Reports and Literature Review

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ABSTRACT

Four patients (mean age, 46 years; range, 28 to 60) with skull base plasmacytomas are presented along with a review of the literature examining the progression of anterior and central skull base plasma cell tumors to multiple myeloma. The primary sites were the nasopharynx, orbital roof, sphenoid, and clivus. Three patients presented with extensive local spread of tumor. Two patients were diagnosed with multiple myeloma and treated with chemotherapy. Patients with an isolated plasmacytoma were treated with external beam radiation. A partial or complete response to therapy was seen in all four cases. Skull base plasma cell tumors are uncommon with only a limited number of published reports. Previous literature demonstrates that nasopharyngeal extramedullary plasmacytomas have a lower rate of progression to multiple myeloma than other sites. Patients with clivus, sphenoid, and petrous apex-based plasma cell tumors appear to have a higher risk of developing multiple myeloma than patients with plasma cell tumors involving the nasopharynx.

KEYWORDS: Solitary plasmacytoma of bone, extramedullary plasmacytoma, multiple myeloma

Tumors of plasma cell origin are categorized as localized or diffuse. Extramedullary plasmacytomas (EMPs) and solitary plasmacytomas of bone (SPBs) are isolated neoplasms that represent less than 10% of all plasma cell tumors. Multiple myeloma, a malignant diffuse plasmacytosis, is thought

to represent an endpoint in disease progression for patients with an isolated EMP and SPB.

EMPs are vascular, soft-tissue masses of submucosal origin without marrow extension. SPBs, also known as medullary plasmacytomas, occur as isolated lytic lesions in the absence of generalized

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marrow plasmacytosis. Both entities represent isolated monoclonal proliferations of plasma cells. A significant difference between the two diagnoses exists in their likelihood of progressing to multiple myeloma; multiple myeloma is two to three times more common with SPB than EMP. The presence of a plasmacytoma in patients with the concurrent diagnosis of multiple myeloma is not a rare finding. An evaluation for multiple myeloma is needed to establish the diagnosis of an isolated EMP or SPB.^{1,2,3}

A plasmacytoma involving the skull base is unusual, and a limited number have been reported. We present the clinical history and radiographic findings of four patients with a plasma cell tumor of the skull base and review the rates of progression of skull base primary sites to multiple myeloma.

METHODS

From 1997 to 2000, four patients (two males, two females; mean age, 46 years; Table 1) with skull base plasmacytoma were treated at the University of Rochester Medical Center. The mean interval to diagnosis from onset of symptoms was 10 months. Three patients presented with eye-related complaints ranging from ptosis and diplopia to decreased visual acuity. Three patients had nasal symptoms, including anosmia, obstruction, and recurrent epistaxis. Three patients had aggressive local extension of their tumor as seen by osteolytic changes on computed tomography (CT), magnetic resonance

imaging (MRI), or both. Operative findings, treatment response, and follow-up were evaluated for each patient.

All histologic specimens were evaluated and graded using criteria established by Bartl et al.⁴ for multiple myeloma (Table 1). Lesions were classified as low, intermediate, or high grade. Low-grade lesions display an appearance similar to normal plasma cells and possess the characteristic "clock-face" nuclei and perinuclear halos. Intermediate-grade lesions demonstrate enlarged nuclei and prominent nucleoli. Histologic variants representative of intermediate-grade lesions are cleaved, polymorphous, and asynchronous types. High-grade lesions, also known as plasmablastic, demonstrate large nuclei with very prominent nucleoli with little cytoplasm.

A literature review was performed using the MEDLINE database and reference lists from pertinent publications. Fifteen studies, totaling 32 patients, were identified with the diagnosis of skull base plasma cell tumor. Patients with nasopharyngeal, sphenoidal, clival, and petrous apex plasmacytoma were compared for rate of progression to multiple myeloma.

ILLUSTRATIVE CASES

Case 1

A 60-year-old female had a 6-month history of left frontal headaches and new onset epiphora with chemosis. At examination, left orbital proptosis was

Table 1 Clinical Summary of Four Patients with Plasma Cell Tumors

Case No.	Age (yr)/ Sex	Primary Site	CT/MRI Findings	Histologic Grade	Multiple Myeloma	Treatment
1	60/F	Orbital roof	Invasive	Intermediate	Yes	Chemotherapy
2	48/M	Sphenoclival	Invasive	High	Yes	Chemotherapy
3	48/M	Nasopharyngeal	Isolated	Intermediate	No	XRT/SRS
4	28/M	Sphenoclival	Invasive	Low	No	XRT

XRT, external beam radiation; SRS, stereotactic radiosurgery

Figure 1 (A) Coronal and (B) axial CT scans of Case 1 show a soft-tissue mass with associated bony destruction involving the superior orbit and left frontal and ethmoid sinuses.

evident. CT scan revealed an erosive left supra-orbital mass, measuring 4×3 cm involving the frontal and ethmoid sinuses (Fig. 1). Biopsy of the mass demonstrated sheets of plasma cells consistent with a plasmacytoma. Immunohistochemical studies showed lambda light chain restriction. A skeletal survey demonstrated multiple lytic lesions in the upper and lower extremities. Bone marrow biopsy revealed extensive infiltration with myelomatous cells ($>30\%$) confirming the diagnosis of multiple myeloma. The patient began a chemotherapy regimen of vincristine, adriamycin, and dexamethasone and has shown a partial response after two cycles of treatment.

Case 2

A 48-year-old male, positive for human immunodeficiency virus, recovering from esophagectomy for an atypical plasma cell tumor 1 month earlier, sought treatment for a right periorbital headache, perioral

paresthesias, and recurrent epistaxis. MRI revealed a mass, $7 \times 4 \times 4.6$ cm, destroying the clivus and involving multiple skull base foramina and both cavernous sinuses (Fig. 2). Endoscopic biopsy was positive for a plasma cell neoplasm with kappa light chain expression. A bone marrow biopsy and skeletal survey were negative. Within 1 month the patient experienced a pathologic fracture of the femur. Another evaluation of the marrow showed progression to multiple myeloma. Chemotherapy was initiated and the femur was treated with external beam radiation. An early initial clinical response has been noted.

Case 3

A 48-year-old male had a 12-month history of nasal congestion, anosmia, and recent recurrent epistaxis. On physical examination, he had a left abducens nerve palsy. CT revealed a nondestructive nasopharyngeal mass. Biopsy of the mass demonstrated plasmacytoma with kappa light chain predominance (Fig. 3). The patient underwent radiation treatment

Figure 2 (A) Sagittal T1-weighted MRI and (B) axial CT scan of Case 2 show a soft-tissue mass involving the clivus, sphenoid sinus, posterior ethmoid air cells, and nasal cavity.

to a total dose of 5,040 cGy. Six months after completion of radiation, MRI and a clinical examination revealed a smaller yet persistent mass, again without local invasion. A biopsy confirmed persistent plasmacytoma. Clinically, the patient was asymptomatic and initially refused further treatment. Evaluations

for multiple myeloma remain negative, and serial MRI has demonstrated no further growth of the tumor. Recently, the patient underwent stereotactic radiosurgery to address the remnant tumor. Assessment 2 months after radiosurgery showed no change in the 2-cm mass (Fig. 4).

Figure 3 (A) Coronal and (B) axial CT scans of Case 3 show a large homogeneous, soft-tissue, nasopharyngeal mass with mild contrast enhancement.

Figure 4 (A) Sagittal and (B) axial T1-weighted MRI of Case 3 2 years after radiation therapy show a 2-cm nasopharyngeal mass with heterogeneous gadolinium-based contrast enhancement.

Case 4

A 28-year-old female had a 1-year history of nasal obstruction, intermittent epistaxis, and frequent bifrontal headaches. She sought treatment after experiencing decreasing visual acuity and horizontal diplopia for 4 days. MRI revealed a $6 \times 7 \times 5.5$ -cm growth, eroding intracranially through the cavernous sinus and extending laterally to the infratemporal fossa (Fig. 5). Ophthalmologic evaluation revealed atrophy of the optic nerve related to mass effect, and dexamethasone was started. A biopsy of the mass showed a plasma cell tumor with kappa light chain expression. No evidence of multiple myeloma was noted at evaluation and radiation therapy was planned. The patient received a total dose of 5,400 cGy to both primary site and neck bilaterally. Follow-up MRI showed a decrease in the size of the tumor and her vision returned to baseline. During an evaluation for pelvic discomfort, the patient was diagnosed with bilateral avascular necrosis of the hips. The necrosis was considered related to the patient's prolonged treatment (3.5 months) with systemic steroids. The pa-

tient required curettage with bone grafting of both femoral heads.

RESULTS

No patient experienced significant central nervous system-related complications. Two patients had complications related to treatment of their tumor (avascular necrosis of the hips related to steroid use in Case 4 and hypothalamic insufficiency related to external beam radiation in Case 3). Two patients were diagnosed with multiple myeloma (Cases 1 and 2) at presentation or during a limited follow-up. All patients experienced at least a partial response to treatment. Only one patient (Case 3) underwent salvage treatment for persistent disease.

There were one low-grade lesion, two intermediate-grade lesions, and one high-grade lesion (Table 1). A comparison of the literature on plasmacytomas of the skull base (Tables 2 and 3) showed that the rate of progression to multiple myeloma for

Figure 5 (A) T1 axial and (B) fat-suppressed short TR/TE coronal MRIs of Case 4 show a large gadolinium-enhancing lesion involving the clivus, sphenoid sinus, and ethmoid air cells bilaterally. TR, repetition time; TE, echo delay.

each group (petrous apex, clivus, and sphenoid) ranged from 9.5 to 63.6%.

DISCUSSION

EMPs manifest in the head and neck in more than 80% of all cases. Most of these tumors are located in the nasal cavity and paranasal sinuses.^{1,2,3} Reports of solitary plasmacytomas of bone are focused on extremity, vertebral, and calvarial presentations. Establishing the diagnosis of an isolated plasmacytoma before multiple myeloma is diagnosed can profoundly affect prognosis. Such patients have a higher response rate to chemotherapy and a prolonged overall survival compared with those with the sole diagnosis of multiple myeloma.¹

Diagnostic evaluation for an isolated plasmacytoma requires pathologic evidence of a monoclonal plasma cell infiltrate in soft tissue or a lytic bone lesion and a lack of systemic involvement. Evaluation requires skeletal survey, bone marrow

biopsy, and serum and urine evaluations. Serum assays evaluate for the presence of an abnormal quantity of monoclonal protein and assess the preservation of uninvolved immunoglobulins.¹

Several studies have examined the prognostic significance of metastatic adenopathy and amyloid in patients with isolated plasmacytomas. Reports are divided concerning the impact of associated adenopathy and amyloid accumulation on disease progression or response to treatment.^{1,5} In addition, reports have failed to show an association between specific immunoglobulin type or light chain predominance and progression to multiple myeloma.⁵

Skull base presentations of plasmacytomas are reported in limited numbers. The features that lead to diagnosis are usually related to a functional disturbance created by the growth of the mass. As in our patients, nasal obstruction with anosmia, recurrent epistaxis, headaches, and orbital symptoms were common findings. Clarke⁶ noted that the presentation of myeloma at the skull base was associated with specific cranial nerve palsies. He found abducens palsy to be the most common cranial

Table 2 Summary of 21 Patients with Nasopharyngeal EMP Reported in the Literature

Reference	Age	Primary Site
Nikolidakis et al. ¹¹	62	NP
Hotz et al. ¹²	77	NP/tongue
	59	NP
	44	NP
	45	NP/larynx
	63	NP**
	63	Larynx/nasal fossa/NP
Sulzner et al. ¹³	56	NP
Corsetti et al. ¹⁴	51	NP
Wax et al. ²	65	NP
Miller et al. ³	76	NP
	64	NP
	49	NP
	20	NP
	47	NP
	63	NP
Susnerwala et al. ⁵	48	NP**
	72	NP
	42	NP
	73	NP
	74	NP

NP, nasopharynx.

**Indicates progression to multiple myeloma.

nerve neuropathy followed by vestibulocochlear and trigeminal.⁶ Dural involvement or extension into the brain by skull base plasma cell tumors is rarely reported.⁷

Both CT and MRI can provide valuable information for the diagnosis of these lesions. The primary radiographic differential diagnosis for EMP is that of lymphoma. On both T1- and T2-weighted MRIs, plasmacytomas are associated with a homogeneous, high-signal intensity. However, unlike the findings associated with other skull base pathologies, plasmacytomas exhibit a higher signal intensity on T1-weighted images than on T2-weighted images. This finding reflects the densely packed cells within the tumor that cause the relative total water content to be low. For SPBs, chondrosarcomas and chordomas are more relevant diagnoses to exclude

Table 3 Summary of 11 Patients with Sphenoid, Petrous Apex, and Clival Plasma Cell Tumors Reported in the Literature

Reference	Age	Primary Site
Alegre et al. ⁷	40	Petroclival/sphenoid**
Nofsinger et al. ¹⁰	70	Clivus**
	79	Clivus**
Toland and Phelps ¹⁵	19	Petrous apex
Miller et al. ³	47	Sphenoid
Alexiou et al. ⁸	56	Sphenoid
Marais et al. ¹⁶	64	Sphenoid
Sully et al. ¹⁷	65	Sphenoid**
Bindal et al. ⁹	51	Sphenoid**
	30	Clivus**
Vijaya-Sekaran et al. ¹⁸	62	Petrous apex**

**Indicates progression to multiple myeloma.

because of their site of origin within the skull base. In contrast to SPBs, chondrosarcomas and chordomas are typically heterogeneous on imaging with areas of calcification. Other considerations within the differential diagnosis for these lesions are dural-based meningiomas (which may appear indistinguishable from a calvarial plasmacytoma), metastatic lesions from distant primaries, and glomus tumors.

To examine the behavior of skull base plasmacytomas, a number of anatomic locations require review. The nasopharynx is the skull base site most frequently involved, representing 18% of all head and neck cases. Sphenoid, clivus, and petrosal apex presentations are far less common.⁸ Bindal et al. noted that petroclival infiltration was often associated with the development of multiple myeloma.⁹ However, most reports of skull base plasmacytomas have been individual cases or small series, making observation of similar trends difficult to substantiate.

The smoldering course of our patient with nasopharyngeal EMP (Case 3) prompted investigation of whether prognosis varies according to skull base sites. For EMPs and SPBs, the most significant factor in predicting the prognosis of disease is the likelihood of progression to multiple myeloma.¹⁰ The distinction between EMPs and SPBs for specific skull base sites has not been addressed.

An EMP originates from a submucosal plane and may be associated with bone destruction from an advancing margin, yet by definition is extramedullary. Nasopharyngeal plasmacytomas are considered extramedullary lesions.

Conversely, SPBs arise within the medullary space, and bone destruction is expected with their focal presentation. The clivus and petrous apex are regions rich in marrow and consequently are candidate sites for SPBs.¹⁰ The likelihood of progression from isolated EMP to multiple myeloma is less than 30%, with a 10-year survival rate of 70%. For SPBs, the rate of progression is greater than 50%, with a 10-year survival rate of only 16%.¹

In the literature, 32 plasmacytomas were identified from 15 studies with a primary site that was either the nasopharynx, clivus, sphenoid, or the petrous apex.^{2,3,5,7-18} The overall rate of associated multiple myeloma for all sites was 28% (9/32). We divided these lesions into anterior (nasopharyngeal) and central (sphenoid, clivus, petrous apex) groups (Tables 2 and 3). The striking finding was the different rate of progression to multiple myeloma in the two groups. In the nasopharyngeal group that rate was 9.5% (2/21), a rate consistent with that reported for EMPs. In the petroclival and sphenoid group, however, the rate of multiple myeloma was much higher—63.6% (7/11). This rate of progression to multiple myeloma is consistent with that of SPBs. This finding suggests that central skull base plasmacytomas can be viewed as more analogous to extremity and vertebral lesions rather than to other soft-tissue sites of the head and neck.

Establishing the diagnosis of plasmacytoma requires a biopsy. Histopathologic examination must distinguish between several closely related pathologies, including plasma cell granulomas, plasmacytoid lymphomas, and large cell lymphomas (immunoblastic type).¹⁹ Given the potential need to perform immunophenotypic studies to differentiate plasmacytomas from these pathologies, biopsy with frozen-section examination appears to be imprecise unless used to evaluate margins in an established case of plasmacytoma.

The treatment of skull base plasmacytomas, which is applicable to both groups, relies on the radiosensitivity of the tumor. When complete removal is possible, surgical intervention is an excellent primary treatment option. Additional reported treatment options include stereotactic radiosurgery and cryoablation.¹⁴ For patients with the diagnosis of multiple myeloma and a skull base plasma cell tumor, chemotherapy for the systemic disease often takes precedence. As in our series, the response of the skull base lesion to chemotherapy may be notable.

In patients with recurrent or persistent tumor despite primary chemotherapy or radiation, surgical salvage remains an option. Various well-described anterior skull base approaches may be considered to attain the complete resection of nasopharyngeal EMPs in either a primary therapeutic or salvage modality. Although many of these same operative approaches could be considered for sphenoidal and petroclival lesions, the associated morbidity rate would likely be greater. Thus primary surgical management is less favorable for SPBs than EMPs.

As in Case 2, if primary therapy were to fail, surgical salvage of a patient with bilateral cavernous sinus involvement would appear to be technically demanding. The findings from the literature review strongly suggest that patients with an isolated skull base SPB have an unusually high likelihood of being diagnosed with multiple myeloma, which, by definition, requires a more systemic modality of treatment. The specific role of surgical management in the treatment of skull base plasmacytomas, beyond biopsy, includes patients with a recurrence after chemoradiation and the primary treatment of isolated lesions when the morbidity and mortality rates associated with the procedure are comparable to those of radiation and chemotherapy.

Orbital plasma cell tumors, as in Case 1, demand further consideration. In a review of 50 orbital lesions, Mewis-Levin et al.²⁰ noted that the orbit was more often involved with plasmacytoma

associated with multiple myeloma than an isolated SPB or EMP. In selected cases salvage surgery with exenteration was possible.²¹

Susnerwala et al.⁵ reviewed which lesions best respond to chemotherapy, in addition to primary radiation therapy. Using criteria originally intended for the grading of multiple myelomas,⁴ tumors were classified as low, intermediate, and high grade. EMPs with a low-grade histology were controlled by primary external beam radiation in 83% of cases. Lesions considered to be intermediate to high grade had only a 17% control rate with primary external beam radiation. There was a significant difference in local control but not overall survival. These authors recommended the use of adjuvant chemotherapy in patients diagnosed with intermediate- and high-grade EMP.⁵ Others advocate a similar philosophy in using adjuvant chemotherapy for poorly differentiated or bulky tumors.²² The two cases associated with multiple myeloma in our series had intermediate- and high-grade histologies (Table 1).

CONCLUSION

Plasmacytoma of the skull base can manifest with a variety of symptoms depending on the site of origin. Nasopharyngeal plasmacytomas, which are extramedullary plasmacytomas, have a favorable prognosis with several treatment options. Sphenoidal, clival, and petrous apex-based lesions behave in a fashion more consistent with solitary plasmacytomas of bone. Consequently, these lesions have an increased propensity for being associated with multiple myeloma and require close follow-up.

REFERENCES

1. Dimopoulos MA, Kiamouris C, Mouloupoulos LA. Solitary plasmacytoma of bone and extramedullary plasmacytoma. *Hematol Oncol Clin North Am* 1999;13:1249-1257
2. Wax MK, Yun KJ, Omar RA. Extramedullary plasmacytomas of the head and neck. *Otolaryngol Head Neck Surg* 1993;109:877-885
3. Miller FR, Lavertu P, Wanamaker JR, et al. Plasmacytomas of the head and neck. *Otolaryngol Head Neck Surg* 1998;119:614-618
4. Bartl R, Frisch B, Fateh-Moghadam A, et al. Histologic classification and staging of multiple myeloma: a retrospective and prospective study of 674 cases. *Am J Clin Path* 1987;87:342-355
5. Susnerwala SS, Shanks JH, Scarffe JH, et al. Extramedullary plasmacytoma of the head and neck region: clinicopathological correlation in 25 cases. *Br J Cancer* 1997;75:921-927
6. Clarke E. Cranial and intracranial myelomas. *Brain* 1954;77:61-72
7. Alegre A, Tomas JF, Pinilla I, et al. Multiple myeloma presenting as plasmacytoma of the base of the skull [letter]. *Am J Hematol* 1996;52:60-61
8. Alexiou C, Kau RJ, Dietzfelbinger H, et al. Extramedullary plasmacytoma: tumor occurrence and therapeutic concepts. *Cancer* 1999;85:2305-2314
9. Bindal AK, Bindal RK, van Loveren H, Sawaya R. Management of intracranial plasmacytoma. *J Neurosurg* 1995;83:218-221
10. Nofsinger YC, Mirza N, Rowan PT, et al. Head and neck manifestations of plasma cell neoplasms. *Laryngoscope* 1997;107:741-746
11. Nikolidakis AA, Skoulakis CE, Papadakis CE, et al. Solitary extramedullary plasmacytoma of the nasopharynx. *J Otolaryngol* 2000;29:254-257
12. Hotz MA, Schwaab G, Bosq J, Munck JN. Extramedullary solitary plasmacytoma of the head and neck: a clinicopathological study. *Ann Otol Rhinol Laryngol* 1999;108:495-500
13. Sulzner SE, Amdur RJ, Weider DJ. Extramedullary plasmacytoma of the head and neck. *Am J Otolaryngol* 1998;19:203-208
14. Corsetti RL, Ready NE, Wanebo HJ. Cryotherapy for a plasmacytoma of the nasopharynx: a newer approach to a difficult surgical access site. *Surg Rounds* 2000;December:707-712
15. Toland J, Phelps PD. Plasmacytoma of the skull base. *Clin Radiol* 1971;22:93-96
16. Marais J, Brookes GB, Lee CC. Solitary plasmacytoma of the skull base. *Ann Otol Laryngol* 1992;101:665-668
17. Sully RE, Mark EJ, McNeely WF, McNeely BU. Case records of the Massachusetts General Hospital: weekly clinicopathological exercises. Case 21-1992. *New Engl J Med* 1992;326:1417-1724
18. Vijaya-Sekaran S, Delap T, Abramovich S. Solitary plasmacytoma of the skull base presenting with unilateral sensorineural hearing loss. *J Laryngol Otol* 1999;113:164-166
19. Rosai J. *Ackerman's Surgical Pathology*. 8th ed. St. Louis: Mosby-Year Book, Inc; 1996:1880
20. Mewis-Levin L, Garcia C, Olson S. Plasma cell myeloma of the orbit. *Ann Ophthalmol* 1981;17:477-481

21. Erza E, Mannor G, Wright JE, Rose GE. Inadequately irradiated solitary extramedullary plasmacytoma of the orbit requiring exenteration. *Am J Ophthalmol* 1995;120:803-805
22. Kapadia SB, Desai U, Cheng VS. Extramedullary plasmacytoma of the head and neck. *Medicine* 1982;61:317-329

Commentary

The authors present their experience with four cases of plasmacytomas involving the skull base and nasopharyngeal soft tissues and review the literature. Plasmacytomas in this region are divided into two groups according to whether the tumor has arisen primarily from soft tissues or bony structures. The prognosis for long-term survival depends on whether the patient progresses to

multiple myeloma and on the histological grade of the tumor. The progression to multiple myeloma is substantially higher in patients with primary bone disease compared to those with soft tissue disease.

Skull base involvement by plasmacytoma is an uncommon disease. If a patient is found to have such a lesion, the histological grade should be established and an evaluation for multiple myeloma should be performed. Both provide important prognostic information and help guide therapy. Surgical resection is advocated for a solitary lesion, if possible. Radiation should follow. The authors recommend chemotherapy for multiple myeloma. Close follow-up of a patient with solitary plasmacytoma is needed to detect when myeloma develops.

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