Recurrence of isolated multiple myeloma in the skull base: A case report and review of the literature

Omar F. Husein, MD; Abraham Jacob, MD; Douglas D. Massick, MD; D. Bradley Welling, MD, PhD

Abstract

Extramedullary plasmacytoma involving the skull base is rare. We describe what we believe is the first reported case of recurrent multiple myeloma presenting as an isolated lesion in the central skull base in a patient with no evidence of systemic involvement. We discuss the patient’s presentation, clinical course, and treatment, and we review the relevant scientific literature.

Introduction

Plasma cell tumors represent 0.4% of all head and neck malignancies; they tend to occur in the sixth decade of life, and they are more common in men than in women. These neoplasms are subclassified into three types along a clinical spectrum: multiple myelomas, solitary plasmacytomas of bone, and extramedullary plasmacytomas.

Extramedullary plasmacytomas account for 3% of all plasma cell tumors. Approximately 85% of these tumors arise in the head and neck—primarily in the nasopharynx, nasal cavities, and paranasal sinuses. Even so, only 50 cases of plasmacytoma of the nasal cavities and sinuses have been reported to date. Even more rarely reported locations of head/neck extramedullary plasmacytomas include the salivary glands, lacrimal glands, orbit, glottis, trachea, and thyroid gland. Head/neck extramedullary plasmacytomas are believed to originate in the mucosal lining of the sinonasal tract.

Monoclonal proliferations of plasma cells without evidence of systemic disease are referred to as solitary extramedullary plasmacytomas. These osteolytic soft-tissue masses are very treatable, and they are associated with a 10-year survival rate of 70%. However, solitary extramedullary plasmacytomas have been reported to progress to multiple myeloma in as many as 30% of cases. Multiple myeloma is a systemic process with an incidence of 4 per 100,000 population. Unfortunately, when a solitary extramedullary plasmacytoma progresses to multiple myeloma, the prognosis is grave; a mean survival rate of only 2 to 3 years has been reported for such patients.

Plasmacytomas involving the skull base are also rare. Our review of individual case reports and a small series in the English-language literature found only 35 cases. Ten of these tumors involved the central skull base and were amenable to transnasal biopsy. In every case, however, the plasmacytoma was either an isolated lesion or later progressed to multiple myeloma.

In this article, we present what to the best of our knowledge is the first report in the English-language literature of a multiple myeloma recurrence presenting as a solitary central skull base plasmacytoma in the absence of other systemic manifestations. We do not know whether this lesion is biologically distinct from traditional extramedullary plasmacytomas.

Case report

A 58-year-old woman presented to her physician with a 6-month history of slowly progressive headaches, facial numbness, and facial fullness, all on the right side. Her history was significant for Durie-Salmon stage III multiple myeloma, which had been diagnosed and treated 4 years earlier. Bone marrow aspirates obtained at that time demonstrated 50% plasma cells. The patient had undergone chemotherapy with vincristine, doxorubicin, busulfan, and cyclophosphamide, and this had been followed by autologous peripheral stem cell transplantation. She had remained in remission for more than 3 years.

Following a physical examination, magnetic resonance imaging (MRI) was obtained. The MRI detected a 26 × 22 × 19-mm mass in the right anterior petrous apex and clivus (figure 1). The mass tracked along the middle fossa dura and extended into the right cavernous sinus and right sphenoid...
sinus. The scan also demonstrated two other distinct areas of abnormal marrow signal—one in the right frontal bone and one in the left parietal bone (12 mm each).

It was suspected that the skull base lesion might represent recurrent myeloma, but a tissue diagnosis was required for confirmation. The patient was referred to the otolaryngology service for a biopsy. Her ENT history was significant for long-standing bilateral tinnitus; she denied hearing loss, otorrhea, diplopia, vision loss, vertigo, and disequilibrium. A general head/neck examination and neurotologic investigation demonstrated sensory abnormalities along the right anterior cheek, right nasal sidewall, right upper lip, and along the right superior alveolar ridge. Findings on the remainder of these examinations were normal.

Computed tomography (CT) was obtained to evaluate the bony anatomy of the anterior and lateral skull base. CT showed that the posterolateral wall of the right sphenoid sinus was eroded and that the lytic lesion had invaded the sinus (figure 2).

A neurotologic approach to the anterior petrous apex/clivus was considered initially, but in view of the extension of the disease into the right sphenoid sinus, it was thought that a transnasal endoscopic approach would result in less morbidity. Endoscopy revealed that the mass was smooth and lobulated, and a sample was obtained from within the sinus (figure 3). Histologic analysis of the specimen identified a dense, atypical plasmacytic infiltrate with vesicular chromatin and occasional small nucleoli—find-

Figure 1. Pre- (A) and postcontrast (B) MRIs show the 26 × 22 × 19-mm mass (arrows) in the right anterior petrous apex and clivus. The mass tracks along the middle fossa dura and extends into the right cavernous sinus and right sphenoid sinus.

Figure 2. Axial (A) and coronal (B) CTs (bone windows) demonstrate the erosion of the lateral wall of the right sphenoid sinus (arrows) and the presence of the soft tissue within the sinus.
ings that are consistent with multiple myeloma (figure 4, A). Immunologic staining showed diffuse expression of monoclonal kappa light chains (figure 4, B).

After the patient recovered from surgery, a systematic search was conducted to identify evidence of systemic myeloma. Findings on serum and urine electrophoresis, electrolyte, and renal function studies were negative, and a skeletal survey did not identify any osteolytic lesions. A bone marrow biopsy did not reveal any abnormal plasma cells. Therefore, the patient was diagnosed with recurrent myeloma of the skull base presenting as a solitary extramedullary plasmacytoma.

The patient was offered positron-emission tomography, but she refused. She underwent external-beam radiotherapy to the skull base to a total of 45 Gy. After 3 months, her headaches and facial pressure had fully resolved, but the right midfacial numbness, although diminished, persisted. However, at the 6-month follow-up, the facial numbness had completely resolved and she was entirely asymptomatic, and she remained so at 18 months.

Discussion
The original case series of cranial and intracranial involvement in multiple myeloma was published by Clarke in 1954.23 He classified his series of 25 cases into one of three categories: syndromes of cranial nerve palsies, intracranial tumor syndromes, and intraorbital tumor syndromes. The first group included all multiple myelomas or plasmacytomas that had invaded the skull base. Some of the affected patients were asymptomatic, while others had cranial nerve deficits. The cranial nerve most commonly affected was the abducens nerve, followed by the vestibulocochlear nerve and the trigeminal nerve. Our patient had facial numbness in the cranial nerve V2 dermatomal distribution.

Plasmacytomas of the sinuses, nasopharynx, and skull base are generally large at the time of diagnosis.24 MRI is the imaging modality of choice for defining the soft-tissue extent of the tumor.10,25 Plasmacytomas exhibit a low to intermediate signal intensity on T1-weighted imaging and a moderate to high signal intensity on T2-weighted imaging.6 CT is also useful for assessing the bone of the skull base and for surgical planning.11,22,26 However, it is important to remember that the radiographic appearance of extramedullary plasmacytoma is not specific on either
MRI or CT. Therefore, a biopsy and histologic analysis are necessary to confirm the diagnosis.6

Plasmacytomas are made up of abnormal plasma cells that exhibit monoclonal intracellular immunoglobulins.7,15 Histologic analysis of the tumor in our patient demonstrated a dense infiltrate of plasma cells with vesicular chromatin and occasional small nucleoli. Immunologic staining showed diffuse expression of monoclonal kappa light chains. Traditionally, histopathologic examination cannot distinguish multiple myeloma from extramedullary plasmacytoma.11 Recently, however, Kremer and colleagues used molecular and immunohistochemical techniques to show that extramedullary plasmacytoma and multiple myeloma are phenotypically distinct.27 They found that cyclin D1 and the neural cell adhesion molecule CD56 are universally expressed in multiple myeloma and absent in nearly all extramedullary plasma cell infiltrates.16,27

Radiation therapy is the treatment of choice for plasmacytomas, as plasma cells are highly radiosensitive.14,28 A total of 30 to 50 Gy has been recommended in most series. A recent series of 16 patients with extramedullary plasmacytoma, Chao and coworkers reported that radiotherapy resulted in a 100% local control rate both radiographically and clinically.14 The median dose in that series was 45 Gy, and the median length of follow-up was 66 months. Long-term oncologic surveillance is required for these patients.

Some authors have recommended total or subtotal surgical resection in addition to radiotherapy.5,26,29 Other treatment options include adjuvant alkylating chemotherapy and surgical resection alone.17 There has also been 1 reported case of a cavernous sinus plasmacytoma that was successfully treated with gamma-knife radiosurgery.7 Unfortunately, postradiation scans were not available to us in this case because the patient declined to undergo further imaging.

The role of surgery in most cases is now limited to biopsy. In the past, tumors of the sphenoid sinus and clivus have required invasive open procedures for diagnosis and treatment.20,29 Traditional approaches to the clivus have included transphenoid, transtemporal, transfacial, transpharyngeal, and transcervical routes, but these open techniques are associated with a high level of morbidity.30 Less aggressive means of obtaining tissue are preferable with a disease process for which the treatment of choice is radiotherapy rather than further surgery.20

---

Circle 120 on Reader Service Card
CT-guided needle biopsy is being increasingly used in the evaluation of skull base lesions. Ljung et al were able to perform aspiration cytology on 11 skull base lesions with CT guidance while avoiding injury to vital structures. One of these tumors was a plasmacytoma that had arisen from the sphenoid sinus.

Transnasal endoscopic management has also become more popular in recent years for accessing lesions of the sphenoid sinus and clivus. Technologic advances and a better understanding of sinonasal anatomy have resulted in excellent access and visualization of the sphenoclival region. The addition of image guidance with computer-assisted navigation has increased surgical confidence in this complex area. In a series of 15 patients, Kingdom and DelGaudio used endoscopic techniques to successfully diagnose lesions of the sphenoid sinus, orbital apex, and clivus, and they observed no complications. Image-guided assistance was used in each case, and 2 of these lesions were plasmacytomas located in the clivus. In our case, transnasal endoscopy provided ready access to the sphenoid sinus and superb visualization of the smooth-surfaced soft-tissue mass that had entered the right sinus through the posterolateral wall.

Acknowledgment
The authors express our appreciation to Dr. Eric Lang for his assistance with the pathology micrographs.

References