Clinical Diagnosis

DYSPHAGIA SECONDARY TO A SOLITARY PLASMACYTOMA

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Introduction

Solitary plasmacytomas are tumors of plasma cell origin that constitute less than 10% of all plasma cell neoplasms. These tumors are categorized as extramedullary plasmacytomas (non-osseous) or solitary plasmacytomas of bone (osseous). Extramedullary plasmacytomas frequently remain localized and usually can be treated effectively with radiation therapy, whereas solitary plasmacytomas of bone frequently convert to multiple myeloma.

We report an unusual presentation of solitary plasmacytoma involving the cervical vertebrae and left petrous bone in a patient with dysphagia. Following radiation therapy and adjuvant chemotherapy, the patient improved clinically and his monoclonal spike disappeared. Sixteen months later, however, he progressed to multiple myeloma and presented with lytic lesions in his right hip and femur.

Case Report

A 68-year-old man with a medical history significant for coronary artery disease, hypertension, and cigar smoking sought medical assistance in November 1996 for neck pain that he attributed to arthritis in his neck. Radiological examination showed considerable degenerative disease at the level of C5-6 and C6-7 vertebrae, and he was placed on a physical therapy program. The neck pain continued into the spring, and at the same time, he gradually developed progressive difficulty with swallowing over a duration of four weeks. Evaluation for dysphagia was in progress when he developed complete inability to swallow and was brought to the emergency room.

Review of systems revealed a weight loss of 27 lbs in four weeks, slurred speech for the previous two weeks, but no other systemic complaints. Personal history was negative for alcoholic abuse.

Pertinent findings on physical examination included mild tenderness on the posterior aspect of the neck and limited range of movement of the cervical spine. The pharynx had pooled secretions, but no obvious lesion or bulging of nasopharyngeal or oropharyngeal walls was seen. The thyroid was not enlarged. Neurological examination demonstrated an absent gag reflex, paralysis of the vocal cords, protrusion of the tongue to the left, and slurred speech. The remainder of the cranial nerves were intact. Motor and sensory examination of the limbs was unremarkable, deep tendon reflexes were +2, and gait was normal.

Laboratory studies revealed mild anemia (hemoglobin level, 13 g/dL), normal white blood cell and platelet counts, serum creatinine of 1.9 mg/dL, elevated serum calcium of 11.5 mg/dL, total serum protein of 7.9 g/dL, and lactate dehydrogenase of 482 IU/L. Serum immunoelectrophoresis showed a monoclonal IgG spike (Table 1). Agarose electrophoresis and immunofixation studies of the patient’s urine revealed the presence of free kappa (Bence-Jones) protein migrating in the gamma region with an estimated concentration of 124 mg/dL.

Table 1. Results of Serum Immunoelectrophoresis

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<tr>
<th>Immunoglobulin</th>
<th>Results</th>
<th>Normal Values</th>
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<tr>
<td>IgG</td>
<td>1946</td>
<td>800-1700 mg/dL</td>
</tr>
<tr>
<td>IgA</td>
<td>35</td>
<td>100-490 mg/dL</td>
</tr>
<tr>
<td>IgM</td>
<td>&lt;29</td>
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A modified swallowing study showed an abnormal oral phase and weakening of the pharyngeal constrictors. These resulted in a buildup of thickened liquid in the pyriform sinuses that could not be propelled into the esophagus. Radiographs of the soft tissue of the neck showed no evidence of a soft-tissue mass.

Magnetic resonance imaging (MRI) revealed a large mass involving the base of the skull on the left extending into the left petrous bone and clivus (Figs 1A-B). The mass appeared to extend to the cervical spine at the level of C1-2 with narrowing of the ventral aspect and slight posterior displacement of the lower brainstem and proximal cervical cord. The majority of the mass appeared to be extracranial. It was thought to be most likely a metastatic lesion, but a primary malignancy could not be excluded. Computed tomography scan of the neck showed the same mass identified on the MRI. This mass was primarily situated in the left parapharyngeal space with involvement of the posterior triangle on the left. Bone windows demonstrated destruction of the left petrous bone, lateral aspect of the body of C1, and the pedicle of C2. There appeared to be involvement of the left posterolateral nasopharyngeal and upper oropharyngeal walls, with no obvious adenopathy.
Long bone survey showed merely normal variations in bone density. Laryngoscopy revealed a normal-appearing larynx with immobile vocal cords. Esophagoscopy was normal except for some brown material refluxing from the stomach. Bronchoscopy was unremarkable, and a biopsy of the underlying soft tissue at the level of the uvula showed sheets of plasma cells consistent with a diagnosis of a plasmacytoma.

Bone marrow contained 4% plasma cells and no evidence of metastatic tumor or granuloma. The patient appeared to have a solitary plasmacytoma of bone (left petrous bone and the clivus extending to the cervical spine at the level of C-1-2) at the time of initial staging, which resulted in lateral medullary syndrome.

The patient was given a course of radiation therapy to the upper parapharyngeal tissues and the base of skull to a total dose of 48.6 Gy. Although there were no lytic lesions on skeletal imaging studies, he also subsequently received chemotherapy (melphalan and prednisone) to achieve the highest likelihood of long-term control. The treatment resulted in markedly improved swallowing, better voice quality, and a reduction of the IgG peak to 1335 mg/dL. A follow-up MRI showed a significant reduction of abnormalities at six months. Follow-up studies after one year revealed stability of myeloma protein level and an unchanged MRI.

In March 1998, the patient returned with a pathological fracture of the right femur, back pain localized to the upper lumbar and lower thoracic spine, and fatigue. Swallowing and vocalization were normal. Laboratory findings included anemia (hemoglobin, 9.1 g/dL), hypercalcemia (10.2 mg/dL), elevated serum creatinine (8.7 mg/dL), serum total protein of 6.5 g/dL; platelet count of 109,000/mm³, white blood cell count of 4,200/mm³, and lactate dehydrogenase of 714 IU/L.

Serum immunoelectrophoresis showed a monoclonal peak of 2161 mg/dL of IgG (IgA = 33 mg/dL, IgM = 41 mg/dL). Radiographic skeletal survey showed mild demineralization of the skeleton and a large lytic defect in the lesser trochanter and subtrochanteric portion of the right femur. Bone marrow showed 60% plasma cells (Fig 2). Internal fixation was performed, and palliative radiation therapy (4 Gy x 5 fractions) was given to the lesion in the proximal right femur.

Discussion

The incidence of multiple myeloma is approximately 3.5 per 100,000 people per annum, with a median age at diagnosis of 69 years. Solitary plasmacytomas constitute less than 10% of all plasma cell neoplasms with a slightly lower median age of approximately 63 years. Most patients with solitary plasmacytomas are men, with a reported man-to-woman ratio of 3:1. Approximately half of these patients have a monoclonal gammopathy detected on serum or urine electrophoresis.

Plasmacytoma is further classified into two groups: osseous and non-osseous (extramedullary) primary lesions. Osseous lesions constitute approximately 70% of all plasmacytomas. They involve primarily marrow-containing bones, with a predilection for the vertebrae, femurs, and pelvis. Of the extramedullary lesions, approximately 80% occur in the head and neck region and frequently involve the upper respiratory tract.

In patients with solitary plasmacytomas, progression to multiple myeloma is common, and approximately 5% of all patients with multiple myeloma have an initial diagnosis of solitary plasmacytoma. Moreover, studies have shown a higher tendency for multiple myeloma to develop in patients with osseous tumors compared to those with extra-medullary tumors. The prognosis after progression to multiple myeloma is also poorer for osseous plasmacytoma than for extra-medullary plasmacytoma as evidenced by multiple retrospective studies. These differences suggest a difference in the biological behavior of the two types of tumor, which is further augmented by immunohistochemical staining and flow cytometry analysis. The biological differences found in such studies include higher population of aneuploid cells, proliferating cell-nuclear antigen index, and S-phase fraction. Prognostic factors that are harbingers for ultimate conversion into multiple myeloma include lesion size (a large-sized lesion correlates with a more ominous prognosis), total serum protein levels, and the presence of a monoclonal spike on serum electrophoresis. The persistence of myeloma protein after radiation can serve to identify patients who are at high risk of early progression. MRI studies can detect patients with occult myeloma.

Due to the difficulty in predicting survival, patients with an apparently solitary plasmacytoma of bone deserve aggressive radiotherapeutic and appropriate orthopedic management. Radiation therapy is the primary modality of treatment. The recommended dose of radiation is 50 to 60 Gy in five to seven weeks. Surgical intervention may include fixation of pathologic fractures, prophylactic fixation to prevent fracture, and decompression and stabilization of spine lesions.
development of myeloma. Adjuvant chemotherapy may be beneficial in patients with either persistent myeloma protein or nonsecretory disease who are at a high risk for developing multiple myeloma. Many prognostic factors have been suggested, but none has clearly predicted the ultimate conversion to multiple myeloma. Immunohistochemical markers and flow cytometry analysis may enable the use of cytotoxic therapy on a more selective basis. Any advantage incurred by a delay in progression to multiple myeloma must be compared with the side effects of chemotherapy involving an alkylating agent that can be leukemogenic.  

Interferon alpha has shown promise in the clinical activity in newly diagnosed disease and may prolong remission time. The role of interferon alpha in selected patients who are most likely to progress to multiple myeloma after radiotherapy for osseous solitary plasmacytoma requires further investigation.

The involvement of the nervous system is a common complication of plasma cell neoplasms. Cranial myelomas (osseous, such as skull bones) and intracranial myelomas (other than bones, ie, extramedullary, such as hypothalamus) can be broadly classified into three clinical groups as shown in Table 2.

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This patient falls into clinical group I suggesting cranial myeloma that involved the left petrous bone and cervical vertebrae. This caused dysphagia secondary to lateral medullary syndrome and resulted in paralysis of the 10th and 12th cranial nerves. Lateral medullary syndrome is one of the brainstem vascular syndromes that occur due to the occlusion of posterior inferior cerebellar artery or one vertebral artery, which may lead to dysphagia, vertigo, vomiting, ipsilateral paralysis of soft palate, ipsilateral Horner’s syndrome, ipsilateral hypotonia and ataxia, and dissociated sensory loss. The body of the sphenoid and the apex of the petrous bone are the most common sites of involvement. The tumors may be either small or discrete, or they may grow to large dimensions. These lesions have a greater tendency to expand locally rather than to disseminate, a property that may be controlled by specific cytokines. The bone is probably the site of origin; however, they may arise from mucosa contained within the sphenoid and petrous bones, since non-osseous myelomas are common.

The cranial nerves can be affected either by local distortion or by direct destruction, such as that which occurs with invasion of the cavernous sinus or jugular foramen region, or the effect could be secondary to a “toxin” and therefore similar to the polyneuritis that occurs in approximately 5% of patients with myelomatous diseases. POEMS is an acronym applied to the constellation of clinical findings in addition to polynondiopathic in which M designates the presence of the monoclonal protein: P = polynoepathy, O = organomegaly (hepatomegaly and adrenopathy), E = endocrinopathy (decreased testosterone level, hypercalcemia, impotence, hyperprolactinemia, hyperglycemia), M = monoclonal protein, and S = skin lesion (hyperpigmentation, white nails, and hypertrichosis). The neuropathy is chronic and slowly progressive and appears to be an axonopathy with secondary demyelination. High titers of anti-MAG (myelin-associated glycoproteins) are seen in patients with neuropathy. Effective radiotherapy of solitary plasmacytomas may be accompanied by the reversal of neuropathy in addition to the nonneurological manifestations of the disease. Similar but less dramatic effects also have been achieved in patients with disseminated disease treated with chemotherapy. Involvement of the 5th, 6th, and 8th cranial nerves is most common.

The differential diagnosis for our patient’s presentation includes nasopharyngeal carcinoma, extra-sellar extension of a chordoma, primary malignant neoplasm of sphenoid or petrous bone, metastatic carcinoma, or eosinophilic granuloma as well as a plasmacytoma. In patients with solitary plasmacytoma, the 10-year survival is approximately 70%. Approximately 20% develop recurrence by 2 years, and 85% develop multiple myeloma by 10 years. Those who do not progress to myeloma tend to be younger and have disease in the spine.

Conclusions

Our case is unique in its presentation in which a 68-year-old man presented with dysphagia secondary to a plasmacytoma. In addition to radiotherapy, he also underwent adjuvant chemotherapy, but even then, he progressed to multiple myeloma in 16 months. This further underlines the higher tendency for multiple myeloma to develop in patients with osteos solitary plasmacytoma, thereby suggesting a difference in the biological behavior compared to extramedullary plasmacytoma and the failure of chemotherapy to delay the time to progression.

We suggest that when cranial nerve symptoms similar to those we observed are associated with lesions in cervical vertebral bodies or the petrous bone, a solitary plasmacytoma should be considered in the differential diagnosis. Further clinical, biochemical, and radiological follow-up of such patients is necessary since the presence of an osseous solitary plasmacytoma is a harbinger of ultimate development of multiple myeloma. A definitive analysis of prognostic factors including immunohistochemical markers, flow cytometry analysis, and therapeutic modalities, particularly chemotherapy, needs to be conducted on a multi-institutional basis.

**References**


**Table 2. Involvement of Nervous System in Plasma Cell Neoplasm**

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