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# CLINICAL PATHOLOGIC REVIEWS

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# Characteristics of Orbital Multiple Myeloma: A Case Report and Literature Review

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**Abstract.** Multiple myeloma is a plasma cell malignancy that destroys skeletal, renal, and neurological function. Orbital involvement is rare, but has been considered an initial presentation for the malignancy. Furthermore, an association between the subtype of multiple myeloma and the likelihood of orbital infiltration has been suggested. We present a case of an orbital mass that was a recurrence of multiple myeloma. A literature search was performed to evaluate the presentation characteristics of orbital multiple myeloma, plasmacytoma and primary (or solitary) extramedullary plasmacytoma. Past reports were analyzed for age, sex, symptoms at presentation, time from symptom onset to presentation, prior diagnosis before presentation for orbital symptoms, radiological characteristics, immunoglobulin subtype, and survival times. Less than half of published cases had orbital multiple myeloma as the primary presentation. Proptosis is the major presenting sign of orbital multiple myeloma, and radiological evaluation shows that the majority of masses originate in the superotemporal quadrant. The dominant immunoglobulin subtype was IgG. (**Surv Ophthalmol** 54:697–704, 2009. 

**Key words.** eye • multiple myeloma • orbit • plasmacytoma • primary/solitary extramedullary plasmacytoma

Multiple myeloma (MM) is a malignant proliferation of plasma cells that is destructive to bone marrow. The median age for presentation is greater than 70 years, with African Americans more frequently affected than white patients.[32] Although ophthalmic signs tend to occur later in the disease, they may sometimes be the first signs of MM.

## Multiple Myeloma

Multiple myeloma is the second most common blood cancer (10%), after non-Hodgkin lymphoma. Up to 30% of patients are diagnosed incidentally while being evaluated for unrelated problems.[39] Bone pain, typically in the axial skeleton, is the most common clinical presentation. In addition, patients also present with other systemic symptoms such as fatigue, weight loss, and frequent infections.

Multiple myeloma accounts for 10% of all hematologic malignancies in white patients and 20% in African American patients. It is more common in Native Pacific Islanders and less common in Asians. There is also a slightly increased incidence in men, with a male-to-female ratio of 1.4:1.[39] The majority of patients are older than 65,





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with only 1% of patients younger than 40.[17] The disease is uncommon in children.

The diagnostic laboratory finding in MM is monoclonal hypergammaglobulinemia. The MM cell produces excess monoclonal and free light chain proteins. Monoclonal immunoglobulins may be identified on serum or urine protein electrophoresis. Both heavy chain (IgA, IgD, IgG, IgE, or IgM) and light chain (kappa or lambda) components (Bence-Jones protein) of the immunoglobulin complex may be present, but in 15% of cases immunoglobulinemia is absent.[4] IgG myeloma is the most common, followed by IgA myeloma. As a result of bone destruction, hypercalcemia is a common manifestation and can be difficult to manage. Other laboratory abnormalities include anemia, elevated alkaline phosphatase levels, hyperuricemia (as a result of elevated cell turnover), and elevated erythrocyte sedimentation rate. Electrophoretic analysis shows increased levels of immunoglobulins in the serum, as well as free light chains (Bence-Jones protein) in the urine.

Almost 90% of patients with myeloma have osseous involvement. Radiologically, MM is characterized by multiple discrete destructive lesions of the pelvis, vertebral column, ribs, femur, and skull, or severe diffuse demineralization. Occasionally, a single lytic lesion is discovered and is referred to as a plasmacytoma (solitary myeloma). Because bone loss occurs mostly in the axial skeleton, patients with MM are at risk for compression fractures of the spine and other major weight-bearing bones.

In the United States, the incidence of MM per year is 4.4 cases per 100,000 persons. Multiple myeloma is responsible for 10–20% of hematologic malignancies.[39] In the United States, approximately 10,000 people die of MM per year. The International Staging System[17] can help to predict survival, with a median survival of 62 months for stage 1 disease, 45 months for stage 2 disease, and 29 months for stage 3 disease.

Renal complications are frequent manifestations of MM. The proteinemia in MM often exceeds the resorptive ability of the kidney tubules, resulting in proteinuria (i.e., Bence-Jones protein found on urine electrophoresis). In addition, amyloidosis is a frequently associated with MM (8–15%) and further contributes to kidney parenchymal dysfunction. Elevated uric acid and calcium levels form renal calculi, which can also contribute to renal failure and death.

Skeletal survey by conventional radiography and bone scans have limited usefulness in diagnosis, because at least 30% cortical bone loss is required to visualize a destructive process, such as MM, with radiographs. In addition, as this is a disease of older patients, MM can present with diffuse demineralization, indistinguishable from osteoporosis. Magnetic resonance imaging (MRI) is a more sensitive imaging modality for patients with MM, although specificity is limited. Some reports have suggested that an MRI of the spine may be of value in staging patients as radiographically occult lesions may be found that can affect therapeutic intervention. The finding of more than one lytic lesion on imaging indicates stage III disease.[17]

## Orbital Multiple Myeloma

Orbital MM may present as three distinct entities, each lacking certain findings that are typically present in MM with systemic involvement. First, plasmacytoma is an isolated tumor of monoclonal plasma cells in the absence of other skeletal lesions. These tumors respond well to localized radiation and have better clinical outcomes than MM. Despite the better prognosis of plasmacytoma, systemic MM will develop in 50% of cases following treatment.[11]

Primary/solitary extramedullary plasmacytoma (PEP) is a plasma cell malignancy that develops in soft tissue rather than bone. These tumors are commonly located in the upper respiratory tract and may invade the orbit from the surrounding sinuses.[15] Similar to plasmacytoma, PEP has a much better prognosis than multiple myeloma. PEP carries a life expectancy of eight years, whereas a patient with newly diagnosed multiple myeloma has an average life expectancy of just 24 months.[11]

Necrobiotic xanthogranuloma (NXG) is a rare histiocytic disease clinically characterized by indurated dermal and subcutaneous nodules that infiltrate the eyelids and periorbital structures. Approximately 10% of patients with NXG are found to have multiple myeloma.[36]

The eye is frequently affected in MM.[22,27,34,35,46,52] Common ocular manifestations include exudative macular detachment, crystal or copper deposition in the cornea, ciliary body cysts, and retinal hemorrhages or cotton-wool spots. Fung classified eye findings as ocular, orbital or neuro-ophthalmic.[13] These changes were attributed to two pathophysiological processes: tissue infiltration by plasma cells and hematological abnormalities from increased blood viscosity.

Orbital involvement in MM is considered rare. Since the study by Rodman et al in 1972, more than 40 publications (written in English) have described orbital MM or involvement by other related entities (plasmacytoma, PEP, and NXG) in a total of 52 patients.[40] Orbital presentation is frequently considered to be the first manifestation of MM[13,40,48]