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Multiple Myeloma with Unusual Hypopharyngeal Involvement: A Case Report

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Abstract

Multiple myeloma is a blood cancer of monoclonal plasma cells that accumulate in the bone marrow and produce monoclonal immunoglobulin. Extramedullary involvement is rare at the time of initial multiple myeloma diagnosis (about 3,3% of all cases) and is generally associated with multiple relapses and poor prognosis. We present an extremely rare case of multiple myeloma with unusual hypopharyngeal involvement in an 83-year-old patient, who had a previous localization of plasmacytoma at the level of the cranial vault and was referred to our attention for a clinical picture of dysphonia persisting for approximately two years.

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Abstract

Multiple myeloma is a blood cancer of monoclonal plasma cells that accumulate in the bone marrow and produce monoclonal immunoglobulin. Extramedullary involvement is rare at the time of initial multiple myeloma diagnosis (about 3,3% of all cases) and is generally associated with multiple relapses and poor prognosis. We present an extremely rare case of multiple myeloma with unusual hypopharyngeal involvement in an 83-year-old patient, who had a previous localization of plasmacytoma at the level of the cranial vault and was referred to our attention for a clinical picture of dysphonia persisting for approximately two years.

Keywords: *Multiple Myeloma, Hypopharynx, Extramedullary Disease, Dysphonia, Plasmacytoma, Otolaryngology, Hematologic Malignancy*

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1. Introduction

Multiple myeloma is the second most common haematological malignancy in high-income countries, and typically starts as asymptomatic precursor conditions—either monoclonal gammopathy of undetermined significance or smouldering multiple myeloma.

Multiple myeloma is a mature B-cell neoplasm defined by >10% of clonal plasma cells within bone marrow or biopsy-proven bony or EMP and it's complicated by organ dysfunction: hypercalcaemia, renal insufficiency, anaemia, and bone destruction (traditional CRAB features).

Multiple myeloma accounts for approximately 1% of all neoplastic diseases, with an incidence of 4.5–6 cases per 100,000 individuals and a median age at diagnosis of around 70 years.

A higher incidence has been reported in Western Europe, North America, and Australasia than in Asia and sub-Saharan Africa, which may be attributable to differences in diagnostic criteria and practices.

Risk factors for multiple myeloma include obesity, chronic inflammation, and exposure to pesticides, organic solvents, or radiation.

Inherited genetic variants also contribute to the development of multiple myeloma.

Advances in treatment, particularly the use of novel agents such as proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies targeting cell surface antigens, as well as high-dose therapy followed by autologous stem cell transplantation (ASCT) in younger patients, have markedly improved survival and overall outcomes in multiple myeloma.

2. Case presentation

We report the case of an 83-year-old patient who presented to the ENT clinic at Chivasso Hospital, in the province of Turin, for a two-year history of dysphonia. His medical history was notable for ascending aortic ectasia, hiatal hernia, and episodes of transient global amnesia. Previous surgical history included multiple endoscopic procedures for nasal polyposis, a prior transurethral resection of the prostate (TURP) for prostatic adenoma, and hospitalization in 2017 for lumbar spondylodiscitis in the context of MSSA sepsis.

In autumn 2024, the patient developed a swelling of the cranial vault in the right parietal region and underwent a bone biopsy, which was consistent with a plasmacytic myeloma lesion exhibiting kappa light chain clonality.

A bone marrow biopsy confirmed myeloma infiltration of 30%, with IgG kappa plasma cells.

The patient underwent 10 sessions of radiotherapy targeting the cranial lesion.

During the ENT examination, oropharyngoscopy was unremarkable.

Flexible fiberoptic endoscopy revealed a neoplasm on the medial wall of the left piriform sinus, adjacent to the aryepiglottic fold, with apparently intact mucosa and no abnormal pattern on narrow-band imaging (NBI). Partial adduction of the left hemilarynx was observed, without macroscopic alterations in vocal cord mobility.

Contrast-enhanced neck CT confirmed the presence of a solid tissue mass measuring approximately 30 × 12 mm, obliterating the left piriform sinus and involving the ipsilateral thyroid cartilage, resulting in a lytic erosion. These findings were initially interpreted as consistent with a localization of the underlying disease.

Therefore, after a thorough informed discussion, the patient was scheduled for direct microlaryngoscopy with multiple biopsies of the hypopharyngeal lesion.

Approximately one month after the endoscopic evaluation, the patient underwent biopsy of the lesion under general anesthesia. Following placement of a rigid laryngoscope in suspension and under microscopic guidance, the previously noted exophytic, non-ulcerated, violaceous mass in the left piriform sinus was visualized, and multiple biopsy samples were obtained.

Microscopic analysis revealed hypopharyngeal mucosa associated with a fragment composed of numerous cells with abundant cytoplasm and round-to-oval nuclei exhibiting some irregularities. Immunohistochemical staining demonstrated a phenotype positive for CD79a and partially positive for CD38, while CD20 and CD30 were negative. Light chain restriction was observed, with an unbalanced expression of kappa light chains. The morphological and immunohistochemical findings were consistent with a localization of multiple myeloma.

The patient was referred back to the hematology team, and following interdisciplinary evaluation, initiation of hematologic therapy with a Velcade–Melphalan–Prednisone regimen was indicated.

3. Discussion

Multiple myeloma is a hematologic neoplasm characterized by the clonal proliferation of abnormal plasma cells within the bone marrow, leading to uncontrolled growth and potentially resulting in osteolytic bone lesions, renal impairment, anemia, and hypercalcemia. The median age at diagnosis is approximately 70 years, with nearly 63% of affected individuals being older than 65 years. In the vast majority of cases, multiple myeloma develops from pre-existing conditions known as monoclonal gammopathy of undetermined significance (MGUS) or smoldering multiple myeloma (SMM).

These precursors are characterised by the absence of signs or symptoms related to multiple myeloma or other lymphoproliferative diseases.

MGUS carries a risk of progression to symptomatic multiple myeloma of about 1–2% per year, with an estimated cumulative 20-year progression risk of approximately 18%.

Smoldering multiple myeloma (SMM) represents a more advanced premalignant plasma cell disorder, with an annual progression rate to overt multiple myeloma of roughly 10%.

The most common clinical manifestations of multiple myeloma include anemia (defined as hemoglobin <12 g/dL) in 73% of patients, osteolytic lesions on conventional radiographs in 79%, and elevated serum creatinine levels in 19%. Additional findings include hypercalcemia (13%), lymphadenopathy (1%), leukopenia (20%), and thrombocytopenia (5%).

At the time of multiple myeloma diagnosis, a thorough medical history, physical examination, and laboratory assessment should be performed. Evaluation of myeloma-related bone disease requires cross-sectional imaging.

Low-dose whole-body CT is recommended due to its rapid acquisition and greater sensitivity compared with conventional radiography. Current imaging guidelines also support the use of functional modalities, such as ^{18}F-fluorodeoxyglucose (FDG) PET/CT or diffusion-weighted MRI, for treatment response assessment.

Bone marrow evaluation is necessary to quantify plasma cell infiltration, which can be assessed through histopathology of the biopsy specimen or by morphological and flow cytometric analysis of the aspirate.

Clinical outcomes in multiple myeloma are influenced by multiple factors, including intrinsic tumor cell characteristics (such as cytogenetic abnormalities, gene expression profiles, extramedullary involvement, and lactate dehydrogenase levels), tumor burden indicators (including β2-microglobulin levels and thrombocytopenia), and patient-related factors, such as age, comorbidities, and overall frailty.

Proteasome inhibitors and immunomodulatory agents constitute the current cornerstone of multiple myeloma therapy and typically serve as the standard backbone in clinical trials to which novel agents are added.

Corticosteroids, commonly dexamethasone or prednisolone, are consistently incorporated into treatment regimens. A fourth class of therapeutics, CD38-targeting monoclonal antibodies, has emerged as a critical component of both first-line and relapse-directed therapies.

Median overall survival among patients eligible for autologous stem cell transplantation is approximately 10 years, compared with 4–5 years in those who are not transplant candidates.

Extramedullary involvement is uncommon at the time of initial multiple myeloma diagnosis (about 3,3% of all cases) but occurs more frequently in patients with multiple relapses and is associated with a poor prognosis.

Extramedullary disease arises from hematogenous dissemination of malignant plasma cells and is characterized by the presence of soft tissue masses at extraosseous sites, such as the skin, lymph nodes, or brain, as well as pleural effusions or leptomeningeal involvement

Extramedullary disease (EMD) may be detected either at initial diagnosis or during the course of the disease, particularly at relapse. Its occurrence is often associated with high-risk cytogenetic abnormalities and elevated serum lactate dehydrogenase (LDH) levels.

These factors contribute to a more refractory disease course, which is characterized by an increased risk of multiple relapses and diminished responsiveness to treatment.

Extramedullary disease is associated with a more aggressive clinical course, both at diagnosis and in the relapsed setting.

The management of extramedullary disease in multiple myeloma necessitates a personalized approach, with therapeutic strategies tailored according to the anatomical site, extent of disease dissemination, and underlying biological characteristics. Treatment varies depending on the location and burden of extramedullary involvement. In localized lesions, radiotherapy alone may be adequate, whereas in other cases, a combined approach incorporating both radiotherapy and surgical excision may be required.

When extramedullary involvement arises in the setting of systemic multiple myeloma, such as in the specific case we report, management generally involves systemic therapy using various combinations of anti-myeloma agents.

4. Conclusions

In the hypopharynx, squamous cell carcinoma remains the most frequent histological subtype, with approximately 84,000 new cases per year (2020 data).

Laryngeal involvement by multiple myeloma represents an extremely rare manifestation occurring within the context of systemic disease. Although cases of laryngeal plasmacytomas or laryngeal multiple myeloma have been described in the literature, hypopharyngeal localization appears to be a unique event. Based on the patient's clinical history and computed tomography findings, as well as the recent medical history—including the diagnosis of multiple myeloma involving the cranial vault in the preceding months—it could be hypothesized that the aerodigestive tract might represent a site of disease involvement. However, given the peculiarity of the case, the lesion was ultimately an incidental endoscopic finding.

The diagnosis was established by our pathology colleagues, and subsequent management was undertaken by the hematology team, who initiated a specific pharmacological treatment in light of the systemic nature of the disease. We therefore emphasize the crucial importance of interdisciplinary collaboration for the accurate

diagnostic assessment and appropriate therapeutic management of such complex cases.