***Case report***

**Subglottic Plasmacytoma as an Extramedullary Relapse of Multiple Myeloma: a case report**

Abstract : Extramedullary plasmacytoma (EMP) is a rare plasma cell neoplasm arising outside the bone marrow and represents a minority of plasma cell disorders. EMP predominantly occurs in the head and neck region, with laryngeal involvement being exceedingly rare. Subglottic plasmacytoma is an uncommon manifestation and poses diagnostic and therapeutic challenges due to its potential for airway obstruction and frequent association with systemic plasma cell disorders such as multiple myeloma (MM).

This case study details the rare occurrence of a subglottic plasmacytoma in a 62-year-old male with a history of MM in remission. The patient was presented with progressive dyspnea, stridor, and hoarseness. Imaging revealed a subglottic mass causing airway narrowing, while biopsy confirmed the diagnosis of plasmacytoma with systemic dissemination of MM. The multidisciplinary management included tracheotomy, chemotherapy, and systemic monitoring.

Timely recognition and multidisciplinary intervention are essential for managing EMP, given its potential progression to MM. This report underscores the significance of imaging, histopathology, and systemic evaluation in EMP diagnosis and treatment. While radiotherapy remains the cornerstone for localized EMP, systemic therapies are crucial for cases associated with MM. Sharing rare presentations, such as subglottic plasmacytoma, contributes to improved understanding and management of this rare pathology

**Keyword: case report, Extramedullary plasmocytoma, subglottic, multiple myeloma.**

**Introduction**Extramedullary plasmacytoma (EMP) is a rare plasma cell neoplasm that arises outside the bone marrow and accounts for a small fraction of all plasma cell disorders. The majority of EMP cases occur in the head and neck region, particularly in the upper aerodigestive tract, involving sites such as the nasal cavity, paranasal sinuses, oropharynx, and larynx. Among these, laryngeal involvement is exceedingly rare, comprising only 0.04% to 0.45% of all malignant tumors of the larynx (1,2).

Subglottic plasmacytoma is an especially uncommon presentation, with few cases reported in the literature. This rarity poses significant diagnostic and therapeutic challenges, particularly due to its potential to obstruct the airway and its frequent association with systemic plasma cell dyscrasias, such as multiple myeloma (MM). Given the clinical and therapeutic implications of EMP, timely recognition and multidisciplinary management are essential.

This case report describes a rare presentation of subglottic plasmacytoma in a patient with a history of MM in remission. The report emphasizes the diagnostic process, imaging findings, histopathological confirmation, and therapeutic strategy, along with a review of the relevant literature to enhance understanding this unusual pathology of an extramedullary recurrence of a multiple myeloma involving exclusively the larynx.

**Case Report**

A 62-year-old male, a former smoker with a history of multiple myeloma treated successfully with autologous bone marrow transplant, he had been in complete remission for three years. He complained of a gradually progressive dyspnea, stridor and hoarseness of voice for one month duration. The patient had an oxygen saturation of 96%, was placed on oxygen, and given corticosteroid therapy. Indirect laryngoscopy revealed reduced mobility of the right vocal cord but no visible lesions in the glottic or supraglottic region (Figure.1 ). Bronchoscopy identified subglottic stenosis with regular edges and normal mucosa (Figure.2). A CT scan of the neck demonstrated a hemicircumferential soft tissue process in the glottic and subglottic regions, narrowing the airway. There was evidence of cartilage lysis involving the cricoid and arytenoid cartilages (Figures 3).

The patient underwent tracheostomy and a laryngotracheoscopy with targeted biopsies. Histopathological examination showed undifferentiated tumor proliferation with diffuse CD138 positivity and were conclusive for plasmacytoma. Other markers, including AE1/AE3, CD3, and CD56, were negative. PET-CT and biological evaluations revealed systemic dissemination of MM(F4). The patient’s history was discussed in the multidisciplinary head and neck oncology meeting, and he was additionally treated with chemotherapy associated bortezomib, thalidomide and dexamethasone. The patient died six months after diagnosis due to *disease-related complications.* The patient developed progressive cytopenia complications his clinical course. He subsequently deteriorated due to sepsis and within months of treatment.

**Discussion**

According to the International Myeloma Working Group, among the major criteria for diagnosing multiple myeloma is the discovery of an extramedullary plasmacytoma is biopsy-proven bony or extramedullary plasmacytoma (Table 1)(3). EMP can affect various sites of the larynx (in decreasing order of frequency): the epiglottis, vocal cords, ventricular bands, the arytenoids, and finally the subglottic region (4).The median age at diagnosis is 60 years, with a male predilection of 2:1 (5,6).Clinical symptoms are related to the location of the tumor and the degree of impairment of the laryngeal structure (7). The main symptom is hoarseness, often accompanied by dyspnea, dysphagia, and other symptoms (5). The laryngoscopy findings (of the three segments of the larynx) are nonspecific and may present various morphologic forms, ranging from a single, smooth polypoid mass to diffuse swelling of the tissue. In our case, it was a subglottic stenosis. Imaging examinations such as CT and MRI of the neck are used to identify the location of the tumor and cervical lymphadenopathy, evaluate the involvement of adjacent structures, and assess the curative effect. Computed tomography (CT) usually reveals a homogeneous laryngeal mass with well-defined margins, appearing with mild-to-moderate contrast enhancement [2]. calciﬁcation and areas with low densities in the thyroid cartilage and inﬁltrative growth pattern also can be fined [8,9].

The diagnosis of an EMP is histological, based on the presence of plasma cells. Immunohistochemistry and immunophenotyping demonstrate monoclonality, pointing to its neoplastic nature. Most cells may test positive for CD138, CD38, CD79a, and negative for CD20, CD3 (7).

Differentiation between Solitary EMP and MM is important for the prognosis.so After defining the locoregional extent of the disease, additional hematological, biochemical, and radiological tests are performed to identify or exclude the presence of other plasmacytomas or systemic dissemination to multiple myeloma, like our case who describe an EMP as recurrence of MM (2,3). Therefore, histological diagnosis should be supported by hematological and radiological examination. The blood count in MM patients may reveal anemia and/or leukopenia and/or thrombocytopenia. In 95% of the MM cases, electrophoresis and immunofixation indicate the presence of an M component. A urine test is only useful for detecting light chains (Bence Jones protein). Bone marrow biopsy shows an excess of plasma cells (>10% of the total nucleated cell population), which may extend to total replacement of the normal myeloid parenchyma. Immunohistochemistry is crucial for determining positivity of B lymphocytes and plasma cells for the CD138 marker in the bone marrow as well as in extramedullary sites (10,11). For prognostic purposes, the determination of the serum concentration of b2-microglobulin is relevant (12). For initial workup, whole-body low-dose CT scan or whole-body fludeoxyglucose F 18 PET with CT is recommended to evaluate for lytic bone lesions (13), they have Superior detection rate for lytic bone lesions compared with conventional radiography/skeletal survey (13-16). The whole-body MRI scan may be useful if results from low-dose CT or PET-CT scans are negative because it can detect focal bone marrow lesions suggestive of myeloma even in the case of intact mineralized bone (17)

The differential diagnosis includes plasma cell granuloma, pseudo lymphoma, undifferentiated carcinoma and metastases. The PEM has been differentiated from the benign form of plasma cell granuloma by immunophenotyping, in which this disease presents polyclonal chains and other inflammatory cells (18)

Treatment is complex and directed by a medical oncologist, along with specialists, to manage various aspects of the disease and its complications. Several treatment strategies may be adopted, including surgery, radiotherapy, and chemotherapy: Radiotherapy is the treatment of choice for solitary EMP, as it is highly radiosensitive. However, patients receiving radiotherapy for head and neck EMP have a higher risk of conversion to MM (19). Surgery should be avoided in head and neck EMP but may be combined with adjuvant radiotherapy for patients with involved surgical margins, as this approach can offer better survival outcomes compared to radiotherapy alone (20). Chemotherapy is indicated for patients with refractory disease or both therapies as in MM. Systemic therapy typically consists of a 2 to 4 drug combination, which may include the following: Proteasome inhibitors(Bortezomib, Carfilzomib, Ixazomib), Anti-CD38 monoclonal antibody(Daratumumab, Isatuximab). Immunomodulating agent(Thalidomide, Pomalidomide), Corticosteroid(Dexamethasone, Prednisone) and DNA-alkylating agents( Cyclophosphamide,Melphalan) . As there is to date no cure of MM, a life-long oncologic follow-up is essential [21]

The conversion of the PEM to MM ranges from 10 to 30%. Kapadia et al (1982) and HOLLAND et al (1992) observed the progression to MM in their patients over a period of two years, suggesting this period as high risk. Most authors recommend a “follow-up” long since found cases of conversion to MM 15 years after diagnosis of localized disease [22].

The prognosis is related to the location of the tumor, cartilage and bone destruction, and regional lymph node involvement. Survival is higher in patients with localized disease than in those with MM, with a five-year survival of 18% in patients with MM and approximately 66% among those with PEM [23]. Patients who developed MM after the diagnosis of PEM have a longer survival than those who have MM as the initial diagnosis [24].

**Conclusion**

This case highlights the importance of considering EMP in patients with laryngeal symptoms and a history of MM. Prompt diagnosis using imaging and histopathology is crucial for effective management. While EMPs have favorable outcomes with localized treatment, systemic surveillance remains essential due to the risk of progression to MM. Sharing such cases enriches the collective understanding and guides optimized management strategies for this rare pathology.

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*Figure 1 indirect laryngoscopy showing normal mucosa in glottic and supraglottic regions*



Figure 2 Bronchoscopy showing a stenosis of subglottic region, with regular edges and a normal mucosa



Figure 3 Computed tomography of the neck reveal a glottic and subglottic tissular process, hemicircumferentiel ,reduicing the lumen of the larynx



Figure 4 Pet scan showing metastatic localization in the skeleton

Table 1: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smouldering multiple myeloma

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| Definition of multiple myeloma Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary plasmacytoma\* and any one or more of the following myeloma defining events: • Myeloma defining events: • Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically: • Hypercalcaemia: serum calcium >0·25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2·75 mmol/L (>11 mg/dL) • Renal insufficiency: creatinine clearance 177 μmol/L (>2 mg/dL) • Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value 1 focal lesions on MRI studies¶ |
| Definition of smouldering multiple myeloma Both criteria must be met: • Serum monoclonal protein (IgG or IgA) ≥30 g/L or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60% • Absence of myeloma defining events or amyloidosis |

PET-CT=¹⁸F-fl uorodeoxyglucose PET with CT. \*Clonality should be established by showing κ/λ-light-chain restriction on fl ow cytometry, immunohistochemistry, or immunofl uorescence. Bone marrow plasma cell percentage should preferably be estimated from a core biopsy specimen; in case of a disparity between the aspirate and core biopsy, the highest value should be used. †Measured or estimated by validated equations. ‡If bone marrow has less than 10% clonal plasma cells, more than one bone lesion is required to distinguish from solitary plasmacytoma with minimal marrow involvement. §These values are based on the serum Freelite assay (The Binding Site Group, Birmingham, UK). The involved free light chain must be ≥100 mg/L. ¶Each focal lesion must be 5 mm or more in size.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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